Innovation Ecosystems, Competencies and Leadership

Human Spare Parts and Venture Finance Ecosystems under Scrutiny

Markku Sotarauta, Tuomo Heinonen, Pasi Sorvisto & Jari Kolehmainen (eds.)

Tekes
Markku Sotarauta, Tuomo Heinonen, Pasi Sorvisto & Jari Kolehmainen (eds.)

Innovation Ecosystems, Competencies and Leadership

Human Spare Parts and Venture Finance Ecosystems under Scrutiny

Tekes Review 329/2016
Helsinki 2016
Tekes – the Finnish Funding Agency for Innovation
Tekes is the main public funding organisation for research, development and innovation in Finland. Tekes funds wide-ranging innovation activities in research communities, industry and service sectors and especially promotes cooperative and risk-intensive projects. Tekes’ current strategy puts strong emphasis on growth seeking SMEs.

Tekes programmes – Tekes’ choices for the greatest impact of R&D funding
Tekes uses programmes to allocate its financing, networking and expert services to areas that are important for business and society. Tekes programmes have been contributing to changes in the Finnish innovation environment over twenty years.
Foreword

One of the Finnish leading business sectors will be a health care in the future. The exports of the health technology have grown rapidly in recent years. Therefore it seems that the health sector is one of those leading ecosystems that which create the competitive advantages and success of Finnish companies on the global market.

Main motivation of this research report is to add to our knowledge of how the regenerative medicine innovations and related treatments can be diffused to support society and the Finnish economy. In other words, it broadens our understanding of the innovation ecosystem around regenerative medicine and the prospective human spare parts industry. This research project has investigated, firstly, the key determinants and drivers of change of two different types of ecosystem i.e. human spare parts and venture finance, and their connections and, secondly, the ways in which self-organizing ecosystems are led towards the next stages of development. The study focused on how the two cases function as ecosystems and how their effectiveness might be improved for economic renewal and business growth. This report offers broad insights to the topic and therefore it is worth reading.

Tekes wishes to thank the researchers for their thorough and systematic approach. Tekes expresses its gratitude to all others that have contributed to this research project.

Helsinki, May 2016

Tekes
# Content

**Foreword** ........................................................................................................................................................................... 5

**List of contributors** ................................................................................................................................................................. 8

1  *Ihmisten varaosateollisuuden ja riskirahoituksen nykytila ja kehityshaasteet* .............................................................................................................................................................................. 9  
*Markku Sotarauta, Tuomo Heinonen, Pasi Sorvisto & Jari Kolehmainen*

1.1 Lähtökohta ........................................................................................................................................................................... 9

1.2 Tutkimuskysymiset ja aineisto ........................................................................................................................................ 9

1.3 Keskeiset käsitteet ................................................................................................................................................................ 10
  1.3.1 Innovaatioekosysteemi .................................................................................................................................................. 10
  1.3.2 Johtajuus hajautuneissa järjestelmissä ..........................................................................................................................11
  1.3.3 Kompetenssi................................................................................................................................................................. 11
  1.3.4 Kompetenssisetti ja tiedeperustainen innovaatioekosysteemi .............................................................................. 12

1.4 Regeneratiivinen lääketiede ja ihmisten varaosateollisuus ......................................................................................... 14

1.5 Johtajuus ihmisten varaosaekosysteemin vahvistamisessa ............................................................................................ 19

1.6 Varhaisen vaiheen yritysten rahoitus ............................................................................................................................... 20

1.7 Ihmisten varaosateollisuus ja rahoitus ............................................................................................................................. 25

2  *Where is the Human Spare Parts Industry Today?* .................................................................................................................. 30  
*Markku Sotarauta, Tuomo Heinonen & Jari Kolehmainen*

2.1 Point of departure ............................................................................................................................................................... 30

2.2 Aims and research questions ............................................................................................................................................ 30

2.3 Methodology and data ......................................................................................................................................................... 31

2.4 Key concepts ....................................................................................................................................................................... 31
  2.4.1 Innovation ecosystem .................................................................................................................................................. 31
  2.4.2 Competence set ............................................................................................................................................................ 32
  2.4.3 Generative leadership .................................................................................................................................................. 34

2.5 Human spare parts industry and regenerative medicine ............................................................................................... 35

2.6 Generative leadership in the human spare parts ecosystem ........................................................................................... 43

3  *Regenerative Medicine Cell Therapy Financial Market: How to Finance Potential Innovations* ......................................... 47  
*Tuomo Heinonen*

3.1 Introduction .......................................................................................................................................................................... 47

3.2 Theoretical background ........................................................................................................................................................ 48

3.3 Methodology ......................................................................................................................................................................... 48

3.4 Findings ................................................................................................................................................................................. 49
  3.4.1 Global RM cell therapy financial market .................................................................................................................... 49
  3.4.2 Potential Finnish RM cell therapy financial market .................................................................................................. 50
  3.4.3 Local ecosystem in Tampere, Finland .......................................................................................................................... 51

3.5 Discussion ............................................................................................................................................................................. 52

3.6 Conclusion .............................................................................................................................................................................. 53
4 New Technology, Old Story? A Locational Analysis of Stem Cell Startups in the USA

Martin Kenney & Donald Patton

4.1 Introduction ........................................................................................................................................... 53
4.2 The Historical Context .......................................................................................................................... 56
4.3 The Stem Cell Value Chain .................................................................................................................. 57
4.4 Measuring the Economic Impact ......................................................................................................... 60
  4.4.1 Patenting ........................................................................................................................................... 60
  4.4.2 Small Business Innovation Research Grants (SBIRs) ..................................................................... 61
  4.4.3 Venture Capital-Financing ............................................................................................................... 62
4.5 Discussion .................................................................................................................................................. 64
4.6 Conclusion ................................................................................................................................................ 64

5 Venture Capital Ecosystem in Finland – Fragile and Thin

Pasi Sorvisto & Markku Sotarauta

5.1 Introduction ............................................................................................................................................... 68
5.2 Venture finance and innovation ecosystems ......................................................................................... 68
5.3 Methodology and data ............................................................................................................................ 69
5.4 The big picture: The performance of the venture capital ecosystem .................................................. 70
5.5 The main bottlenecks: Drip-feeding, piecemeal funding and competencies ...................................... 74
5.6 The key points of the past policy debate ............................................................................................... 75
5.7 Discussion: From traditional policy-making towards evolutionary targeting? ............................... 76
5.8 Conclusion in the form of selected policy recommendations ............................................................. 78

Appendices

1 The publications produced in the EcoLead-project .................................................................................. 81
2 Venture finances in the EU countries as a whole and in Finland in comparison .................................... 82
3 Glossary with definitions and abbreviations for stem cells and regenerative medicine .......................... 83

Tekes Reviews ............................................................................................................................................... 84
List of contributors

M.Sc. Tuomo Heinonen is a doctoral student in School of Management at the University of Tampere, Finland. In 2011–2013, he worked in the healthcare IT industry mainly focusing on quality management and regulation. Since 2014 he has worked as a researcher and doctoral student in the School of Management at the University of Tampere. His research interests include technology and innovation management, technology transfer, and innovation systems.

Professor Martin Kenney, University of California in Davis, is a professor in the Department of Human and Community Development and a senior project director at the Berkeley Roundtable on the International Economy. He is the author and/or editor of 5 books and 120 articles examining venture capital, high-technology and regional development, and university–industry relations. He has been a visiting researcher at the Copenhagen Business School and Cambridge, Hitotsubashi, Kobe, Stanford, Tokyo Universities and the Research Institute for the Finnish Economy (ETLA).

Research manager Jari Kolehmainen works at the University of Tampere, School of Management (Research Group for Urban and Regional Development Studies, Sente). Previously he was a researcher at the Work Research Centre (University of Tampere), as a visiting researcher at the University of Newcastle-upon-Tyne and as a project manager at the Laurea University of Applied Sciences. Kolehmainen’s research interests cover various fields, such as: firms’ innovation activities, regional and local innovation systems and environments and strategic regional development processes, especially economic development and innovation policies. He has been involved in or leading about 40 externally funded research and development projects since year 1999.

Mr. Pasi Sorvisto is an internationally acknowledged professional in high growth venturing, venture finance, and high-technology business. He has more than 20 years’ international experience in new business development, entrepreneurship and venture finance with the special focus on health technology and high-tech business. He has top tier business and VC collaboration networks especially in North America, Europe and Israel, and has been an initiator of two seed stage venture capital funds in Finland. In 2008, the Finnish Ministry of Trade and Industry (current MEE) appointed him as a national coordinator of business development of health and well-being cluster, and later a national growth venturing initiator for all (13) industrial clusters in the Center of Expertise Programme. He has participated in strategic governmental initiatives also in the UK and the U.S. He is preparing a doctoral dissertation on ‘Competent System for High Growth Venturing and Venture Finance’.

Professor Markku Sotarauta is a Chair of Regional Studies in School of Management at the University of Tampere, Finland. In 2011–2013, he served as the founding Dean of the School of Management and, in 2009–2010, as the last Dean of the Faculty of Economics and Administration. Professor Sotarauta specializes in leadership, innovation systems, and institutional entrepreneurship in city and regional development. He has published widely on these issues in international journals and edited books. His latest publications include ‘Leadership and the city: Power, strategy and networks in the making of knowledge cities’, published by Routledge in 2016. Professor Sotarauta has worked with the Finnish Parliament, many Finnish ministries as well as cities and regions both in Finland and beyond.
1.1 Lähtökohta

Tässä raportissa esitellään ”Innovation Ecosystems, Leadership and Innovation Policy: Prospective Human Spare Parts and Venture Finance Ecosystems under Scrutiny” (EcoLead) -tutkimusprojektin päätulokset. Tutkimus kohdistui ihmisten varaosateollisuuden ja varhaisen vaiheen yritysrahoituksen ekosysteemeihin sekä näiden väliseen vuorovaikutukseen.


1.2 Tutkimuskysymykset ja aineisto

Tutkimus kohdistui ihmisten varaosateollisuuden ja varhaisen vaiheen yritysrahoituksen ekosysteemeihin sekä näiden väliseen vuorovaikutukseen. Tutkimuksen taustalla oli kuitenkin laajempi kysymys siitä, miten Suomen kulttuurin muodon vaiheeseen suoraviivaisesti suomen kielenä. Raportin k lookedessa, mutta merkittävä osa tässä esitetystä huomioista perustuu muilla areenolla julkaistuihin analyysihin. Muut julkaisut on esitelty liitteessä 1 (Appendix 1).

Tutkimuksen tavoitteet olivat:
- Tunnistaa kahden erilaisen ekosysteemin muutosdynamian
- Tarjota päätöksentekijöille ja kehittäjille uudenlaisen
  tavan hahmottaa ekosysteemien dynamiikan
- Käsitteellisen viitekehyn

Tutkimustyössä työskentiin eksploratiivisesti. Siinä ei

EcoLead-projekti oli luonteeltaan eksploratiivinen. Siinä et

Tutkimuksessa analysoitiin ihmisten varaosateollisuuteen

Markku Sotarauta, Tuomo Heinonen, Pasi Sorvisto & Jari Kolehmainen

Ihmisten varaosateollisuuden ja riskirahoituksen nykytila ja kehityshaasteet

### 1.3 Keskeiset käsitteet

#### 1.3.1 Innovaatioekosysteemi


Innovaation käsitte hyväksyntää on suhteellisen yksinkertainen, vaikka sen taustalla olevat prosessit ovat monesti monimutkaisia ja vaikeasti hallittavia. Innovaation määritelmät nojaavat varsin pitkälle teknologisen muutoksen teorioihin. Perinteisesti teknologisen muutoksen on nähty koostuvan kolmesta eri vaiheesta, jotka ovat keksintö, innovaatio ja leviäminen. Keksintöä voidaan luonnehtia uuden perustietämyksen ja uusien ideoiden luomiseksi, innovaatiota luodun tietojen ensimmäiseksi soveltamiseksi ja levimistä (diffuusio) vaiheeksi, jossa uusi tiedo ja uudet ideat vedään käytännöön tai jolloin uudet tuotteet ja palvelut levävät markkinoille. Käytännöissä innovaatiot ovat usein seurausta pitkistä ja monimutkaisista prosesseista, joissa syntyy monenlaisia innovatioita, ja joissa tarvitaan useita erityyppisiä innovatioita samanaikaisesti (Fagerberg 2005, 4-6). Innovaatio voidaan yksinkertaistamaan määritellä jokin uudeksi asiaksi tai ideaksi, joka on sovellettu ja josta tulee lisäarvoa. Innovaatio on suoritettava, joka on arvokkain tai jota on kehittänyt, ja jossa se on yhteydessä muiden tekijöiden kanssa.

Innovaatioekosysteemin käsitteenen soveltamista taloudellisiin kehityskulkuihin on kritisoitu siitä, että sen tuoma analyyttinen lisäarvo on jäänyt vähäiseksi ja käsitettä on käytetty lähinnä kuvailevaksi tekijöiksi (Paapioannou et al., 2009). Myös Suomen innovaatiopolitiikassa keskustelussa innovaatioekosysteemin käsitettä on käytetty lähinnä kuvailevaksi metaforana (Papaisou et al., 2009). Myös Suomen innovaatiopolitiikassa keskustelussa innovaatioekosysteemin käsitettä on käytetty tarkoittamaan milloin mitäkin tiedon, osaamisen ja innovaatioiden ympärille muodostunutta kokonaisuutta. Suurin osa käsitteen ympärillä käydystä keskustelusta on semantisesti tuolloin ja innovaatioekosysteemi liitetään niin innovaatiojärjestelmiin, -käytäviin, -keskittymiin kuin -alueihin. Innovaatioekosysteemi eikä ole kuitenkaan olla lähtökohtaisesti sen paremmin innovaatioekosysteemiä kuin jokin järjestelmä, vaan se määritellään ennen kaikkea tavoitteen mukaan. Innovaatioekosysteemiä käsittelee toimintoja ja toimintojen koordinoinnista sen paremmin yhteisten vi-sioiden vuoksi tavoitteidenkaan pohjalta. Toki on selvä, että joissakin liiketoiminta- ja innovaatioekosysteemissä ekosysteemi voi organisoida kumppanuusverkostosta, josta on

| Case Haastattelu Muu aineisto |
|---|---|---|
| Varhaisen vaiheen yritysrahoitus | 55 (+9 esihaastattelu) | Kehittämäsiasiakirjat, sanomalehtiartikkelit, aiemmat tutkimukset, yms. kyseisen case-tapauksen kannalta relevantti sekundääriaineisto sekä Euroopan ja Suomen pääomasijoitusyhdistysten tilastot. |

Taulukko 1-1. EcoLead-projektin tapaukset ja empiirinen aineisto.
mahdollista tunnistaa johtava toimija ja toimintaa ohjaa va visio. Tällaisia ekosysteemejä ovat esimerkiksi Googlen (Android), Apple OS:n ja Microsoftin (Windows) ympärille rakentuneet liiketoimintaekosysteemit.

Ekosysteemin käsite on lainattu biologiasta ja ekologiasta, joissa ekosysteemi määritellään toiminnalliseksi kokonaisuudeksi, joka ”nuoostuu luonnollisuudessaan yhtenäisellä alueella elävää, toisiinsa vuorovaikutussuhteessa olevista elöistä ja niiden elottomasta ympäristöstä” (Tie-teen termypankki; Thompson, 1994). Ekosysteemin käsite muistuttaa ensinnäkin siitä, että kaikki on kytökissä kaikkeen, ja että palauta virtaa ekosysteemissä läpi takaisin siihen itseensä eikä johonkin systematicin ulkopuoliseen koordinoi-vaan taoon. Keskinäinen riippuvuus on ekosysteemin itseensä eikä johonkin ekosysteemin ulkopuoliseen eikä liioisistä ja niidien elottomasta ympäristöstä” (Ti-teen, joissa ekosysteemi määritellään toiminnalliseksi kokonaisuuteen.


1.3.2 Johtajuus hajautuneissa järjestelmissä

Innoikeosysteemin dynamiikan vahvistamisessa vaikein kysymys ei välttämättä ole mitä pitäisi tehdä, vaan miten kaikki tavoitteet saadaan toteutettua. Käytän-nössä tämä kääntyvä kysymykseksi miten on mahdollista mobilisoida kompetenssi ja resurssit samaan suuntaan, ja miten toisaan poikkeavien potentiaalien välillä on mahdollista löytää yhteistyön mahdollistavat yhteiset nimitäjät.


Ydinkompetenssien tunnistamisen taustalla on oletus, että ydinkompetenssit muuttuvat hitaammin kuin tuotteet ja markkinat. Näin ollen organisaatioiden identiteettiin ei tulisi perustaa esimerkiksi tuotteisiin vaan johonkin pysyvään, johonkin joka on organisaation ja menestymisen ”ytimessä” (Tuomi, 1999, 82-83). Ydinkompetenssiäjattelua on sovellettu pääosin yritysmaailmassa, mutta sen avulla on mahdollista jäsentää innovaatioekosysteemien toimintaa tunnistamalla niissä tarvittavat kompetenssit ja kehitettävä tietoisesti kompetensseja tukemaan toisiaan. Johtajuuden ja ydinkompetenssin tunnistamisen ja kehittämisen perustuva kehittäminen ja tutkimus perustuvat ajatuksen, että niin organisaatioiden kuin kokonaisten ekosysteemien suorituskyvynään on pitkälle kyse siitä, mitä resursseja on käytössä ja miten niet kyetään hyödyntämään sekä sitä, miten kyetään vahvistamaan resurssiperusterann. Lisäksi kyse on siitä, millaisia kompetensseja ekosysteemissä on erilaisten resursseihin yhdistämiseksi ja kokoonmukaisesti tuotteeksi ja palveluksi. Ydinkompetenssien avulla kyetään hyödyntämään erilaisia kykyjä ja resursseja siten, että syntyy kestävä ja jatkuvasti uudistuva kilpailuettu.

13.4 Kompetenssisetti ja tiedeperustainen innovaatioekosysteemi


Tässä raportissa ei tarkastella yksityiskohtaisesti niitä geneerisiä kompetensseja, jotka muodostavat kompetenssistä. Niitä on tarkasteltu tarkemmin muissa julkaisuissa (ks. Sotarauta 2014; Sotarauta & Heinonen, tulossa). Kompetenssiset yksittävät ydinkompetenssit on mahdollis-
ta tunnistaa seuraavien teemojen avulla: (1) uuden tiedon
luominen, jakaminen ja hyödyntäminen, (2) yrittäjyys, (3)
rahoitus, (4) legitimisaatio, (5) markkinoiden synty, (6) syste-
maattinen tuotanto ja (7) loppuhyödyt (kuva 1–1). Teemat ja
niiden taustalla olevat kompetensseihin liittyvät kysymyk-
set on tiivistetty taulukkoon 1-2. Käytännössä seitsemän


| Geneeristen kompe-
<table>
<thead>
<tr>
<th>tenssien lähteet</th>
<th>Määritelmä</th>
<th>Kysymykset (esimerkinomaisesti)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tiedon tuotanto ja diffuusio</strong></td>
<td>Tietämystäkohtojen laajuus ja syvyys sekä uuden tiedon luominen, jakelu ja hyödyntäminen</td>
<td>Miten uutta tietoa luodaan ja jaetaan; mitä kanavia tiedon jakamisessa käytetään?</td>
</tr>
<tr>
<td><strong>Riskirahoitus</strong></td>
<td>Monetaariset investoinnit sellaiseen uuteen toimintaan, johon yleensä liittyvät riskejä</td>
<td>Mitkä ovat tärkeimmät yksityiset ja julkiset rahoituslähteet ja millä logiikalla ne toimivat? Miten on mahdollista päästä käsiksi riskirahoitukseen?</td>
</tr>
<tr>
<td><strong>Yrittäjyys</strong></td>
<td>Kannattavia mahdollisuuksia tunnistaminen ja hyödyntäminen sekä valmius ottaa riskiä</td>
<td>Mitkä teki tehneet ja rajoittavat rahoitustoteutusten valmistelua? Miten yrittäjät voivat halua riskoittaa?</td>
</tr>
<tr>
<td><strong>Legitimisaatio</strong></td>
<td>Sosiaalinen hyväksyntä uusille innovaatioille. Keskeistä on odotusten muodostuminen ja tulevaisuuden visioiden synty sekä regulatioiden ja lainsäädännön vaikutus innovaatioihin</td>
<td>Mitkä ovat tärkeimmät uusien tuotteiden ja palvelujen hyväksyntä ja miten se vaikuttaa innovaatiisiin?</td>
</tr>
<tr>
<td><strong>Markkinoiden muotoutuminen</strong></td>
<td>Taloudellisen toiminnan ja ennen kaikkea tarjonnan ja kysynnän suhteen muotoutuminen sekä jakumayan kysynnän syntyminen uusille tuotteille ja palveluille</td>
<td>Miten markkinoiden ja markkinointitavoitteiden vaikutus innovaatiisiin? Miten on mahdollista päästä käsiksi markkinointitavoitteisiin?</td>
</tr>
<tr>
<td><strong>Systemaattinen tuotanto</strong></td>
<td>Innovaation juurtuminen osaksi taloutta ja laajemmin osaksi yhteiskuntaa organisoidusti ja systemaattisesti</td>
<td>Miten innovaatio institutionalistoituu? Miten markkinoiden ja markkinointitavoitteiden vaikutus innovaatiisiin?</td>
</tr>
<tr>
<td><strong>Hyödyt</strong></td>
<td>Innovaation toivottavuus ja arvot sen erilaisille käyttäjille ja/tai niille toimijoille, joihin se vaikuttaa välillisesti.</td>
<td>Käytännössä on mahdotonta tunnistaa vielä tuntemattomien palvelujen ja tuotteiden loppuhyödyt, mutta olennaista on käydä niistä avointa keskustelua.</td>
</tr>
</tbody>
</table>
1.4 Regeneratiivinen lääketiede ja ihmisten varaosateollisuus


Päähuomiot


KOKONAIKUVA

A.1 Tampereen näkökulmasta katsottuna ihmisten varaosateollisuus viittaa kantasolu- ja biomateriaalitutkimuksen varassa kehittymässä olevaan regeneratiiviseen lääketieteeseen, jota tarjoaa radikaalilla tavallisia kohdennelua sairaalahoitojen uudistamiseen ja uusien liiketoimintamahdollisuuksien synnyttämiseen. Regeneratiivinen lääketiede sekä siinä läheisesti yhteydessä olevien teknologioiden kehittäminen ovat vakiintuneet varsin nopeasti osaksi Tampereen tiedemaailmaa (Sotarauta & Mustikkamäki, 2015). Tampereelle kehittyvän ihmisten varaosateollisuuden ekosysteemin ytimessä olevan tutkimuksen tieteellinen taso on arvioitu korkeaksi. Ihmisten varaosateollisuuden synnyttämiseen on keskeinen rooli Tampereella vahva ydin.


TIETE JA INSTITUTIONALISOITUMINEN

A.3 Tampereen regeneratiivisen lääketieteen juuret ovat yliopistojen lääketieteellisissä, lääketieteellisen teknologian ja biomateriaalien tutkimuksessa. Regeneratiivisen lääketieteen kehittämisessä päähuomio Tampereella on kohdistettu alan vakiinnuttamiseen


**Markkinakehitys**


A.10 Ihmisten varaoasteollisuus on synny niin muovivaiheisesti yhtiöiden ja markkinoiden synnyttämisestä yhteistyöstä. Ihmisten varaoasteollisuus on synny niin muovivaiheisesti yhtiöiden ja markkinoiden synnyttämisestä yhteistyöstä. Ihmisten varaoasteollisuus on synny niin muovivaiheisesti yhtiöiden ja markkinoiden synnyttämisestä yhteistyöstä. Ihmisten varaoasteollisuus on synny niin muovivaiheisesti yhtiöiden ja markkinoiden synnyttämisestä yhteistyöstä.

**Tiedon, teknologian ja osaamisen siirto**

YRITYSTOOMINTA


A.14 Tampereella ei käydyä analyyyttistä julkista keskustelua regeneratiivisen lääketieteen ja mahdollisen ihmisten varasoteelollisuuden hyödyistä ja haittoista eikä eettisistä kysymyksistä. Suomessa kokeileviksi pitävää tieteen ja teknologian ja mahdollista uusinta tieteen ja teknologian edistelyyn sekä kaupalliseen potenssiaan liittyviä kysymyksiä on käsiteltävä rasvanemmän.

SYSTEMAATTINEN TUOTANTO


LEGITIMISAATIO JA KESKUSTELUT HYÖDYISTÄ


A.14 Tampereella ei käy käydä analyyttistä julkista keskustelua regeneratiivisen lääketieteen ja mahdollisen ihmisten varasoteelollisuuden hyödyistä ja haittoista eikä eettisistä kysymyksistä. Suomessa kokeileviksi pitävää tieteen ja teknologian ja mahdollista uusinta tieteen ja teknologian edistelyyn sekä kaupalliseen potenssiin liittyviä kysymyksiä on käsiteltävä rasvanemmän.

A.15 Ihmistä koskevista regeneratiiviseen suhteeseen odotuksissa painottuvat työllisyysvaikutukset ja taloudelliset hyödyt (rahoittajat, alue- ja paikalliskehittäjät), tieteen kehitys (tiedeyhteisö) ja tieteellinen menestys (yksityis- ja työpaikkoja) ovat Tampereella lihmittäneet. On erittäin epätodennäköistä, että Tampereelle kehitetyn typinglüähdysvaikeus saisi olla maailman pääpörsseihin (Bionx ja Inion) ja sen seurana saatavissa lisäresursseja. Suomessa on tarjolla niukasti sellaista vähemmän, eikä Suomessa ole tuotannon sitoumuksen vahvistettua. Tampereella on esimerkkejä siitä, miten on mahdollista listautua maailman pääpörsseihin (Bionx ja Inion) ja näin saada lisäresurssia.


2 Tampereella on esimerkkejä siitä, miten on mahdollista listautua maailman pääpörsseihin (Bionx ja Inion) ja näin saada lisäresurssia. Suomessa on tarjolla niukasti sellaista rahoitusta, joka mahdollistaa kasvun tähtäävän yritystoiminnan. Esimerkiksi USA:ssa yhdistysten, saattueiden ja muita laajalti työllistävien potilaiden vahvistamisessa on tärkeä rooli. Koska Suomessa on tarjolla niukasti sellaista rahoitusta, on tarjolla sen paremmin markkinaa arvioiden mahdollisuuksia, mutta vaikutteita mahdollisuuksiin saattaa mahdollista. Tämä on mahdollistaan regulatoirin kehityksen nopeuden takia. 

16
Kaisujen etsimisen ja löytämisen. Tämä on suhteellisen yleinen tilanne sellaisilla nousevilla teollisuudenaloilla, joissa innovaatiot, markkinakehitys ja uuden teollisuudenalan syntyminen tapahtuvat samanaikaisesti regulatiivisten muutosten kanssa (Metcalfe  et al., 2005).

**Toimenpidesuositukset**

Toimenpidesuositukset perustuvat haastatteluissa esille nostettuihin ajatuksiin, analysoituihin raportteihin, tutkimuskirjallisuuteen ja työseminaarien (policy briefing) keskusteluihin. Toimenpidesuositukset perustuvat haastatteluissa esille nostettuihin ajatuksiin, analysoituihin raportteihin, tutkimuskirjallisuuteen ja työseminaarien (policy briefing) keskusteluihin.

Kuva 1-2. Regeneratiiviseen lääketieteeseen kohdistuneiden artikkeleiden huomion kohteet Aamulehdessä ja Kauppalehdessä. Media-analyysissä käytettiin hakusanoja "kantasolu" ja "ihmisen varaosat" niiden eri taivutuksissa. (Heinonen, forth-b.)

A.17 **Kehittämisien kolme strategista polkua.** BioMediTechin osaamisen kaupallistamiselle ja laajemmalle hyödyntämiselle voidaan nähdä olevan kolme potentiaalisesti toisiaan tukevaa reittiä: (1) Yhteistyön tiivistäminen alan isojen yritysten kanssa (esim. lisensointi, yhteiskehittäminen, tutkimusyhteistyö), (2) osaamisen kaupallistaminen start-up-yritysten kautta ja (3) osaamisen kaupallinen hyödyntäminen sairaalakontekstissa räätäilojyjen hoitojen ja palveluiden muodossa. Lisäksi lienee mahdollista tuoteesta ti-laustutkimus- ja kehittämispalveluja. Kaupallistamisen ja osaamisen hyödyntämisen polut poikkeavat toisistaan sekä riskipitoisuudeltaan että odotettavissa olevien hyötyjen suhteen. Tässä yhteydessä esitelään päästrategiat pääpiirteissään idean tasolla, koska niiden strateginen kehittäminen edellyttää syvälistä lääketieteellistä, terveysteknologian ja hoitomuotojen tuntemusta. Lima suuren yleisön kanssa lienee lähtökohtaisesti matalimman riskin strategia, mutta samalla sen potentialiset tuotot ja kerrannaisvaikutukset aluetalouden näkökulmasta saattavat jääda kaikkein pienimmiksi ottaen huomioon eri osapuolten neuvotteluvoiman ja resurssit.

- **Start-up-pohjainen lähestymistapa** on tunnetusti riskipitoinen strategia, jos asiaa tarkastellaan puhtaasti taloudellisesta näkökulmasta. Usein start-up-yrityksiltä odotetaan kasvua, mutta ne voivat muodostaa myös eräänlaisen alueellisen ”näyteikkunan”, johon siirretään yliopistosta suurimman kaupallisen potentiaalin teknologia ja osaaminen (IPR-oikeudet). Tämä mahdollistaa sen, että teknologian ja osaamisen hyödyntämisestä kiinnostuneiden yhteistyökumppaneiden on helpompia nähdä suurimman kaupallisen potentiaalin teknologia ilman tarvetta analysoida kaikkea yliopistossa tehtyä tutkimusta. Näin start-up-yritykset voivat houkutella alueelle kotimaisia ja ulkomaisia investointeja erityisesti yrityskuuppojen muodossa. Start-up-strategiassa erityisen keskeiseksi nousee kysymys kompetenteista management-työläistä, jotka kykenevät toimimaan sekä teknologisesti että taloudellisesti erittäin haastavassa taloudellisessa toimintaympäristössä.

- **Osaamisen kaupallinen hyödyntäminen sairaalakontekstissa räätäilojyjen hoitojen ja palveluiden avulla edellyttää, että Tampereen yliopistollinen sairaala (tai joku muu vastaava) ottaa regeneratiivisen lääketieteen strategisesti kehittämiskohteeksi ja aloittaa

Kuva 1-2. Regeneratiiviseen lääketieteeseen kohdistuneiden artikkeleiden huomion kohteet Aamulehdessä ja Kauppalehdessä. Media-analyysissä käytettiin hakusanoja "kantasolu" ja "ihmisen varaosat" niiden eri taivutuksissa. (Heinonen, forth-b.)
Kaupallistamisen ja osaamisen hyödyntämisen strategia mikä hyvänsä, nousee BioMediTechin sisäseksi avainkompetenssiksi kyky tuottaa tutkimusutoksestoa ja kehittämistä. Kyse on eräänlaista esikaupallistamisprosessista, joka on useimmissa tapauksissa edellyttävä liitus yhteistyöön ja tutkimushallintojen yhteistyöolosuhteiden avulla. "Proof of concept"-osaamisen kehittämistä on jatkettava ja siihen tulisi integroida myös yrityksellistä ja kaukolämpää taloudellista yhteistyöllekin. "Proof of concept"-osaamisen yrityksellä, uusien yritysten synnylle, on useimmissa tapauksissa edellytys niin suorana resursseja ja erikoisosaamista vaativalla alalla eikä vain ainoastaan resursseja ja erikoisosaamista vaativalla alalla eikä vain ainoastaan resursseja ja erikoisosaamista vaativalla alalla.

A.18 **Kehitysalustat.** Sekä ihmisten varaosateollisuuden ekosysteemin vahvistamiseksi kokonaisuutena että kehittämispolkujen konkretisoimiseksi BioMedi-Technin olisi yhdessä yhteistyökumppaniensa kanssa rakennettava sellaisia strategisen yhteistyön alustoja, jotka tuovat keskeisimmät toimijat (tutkijat, opiskelijat, kehittäjäorganisaatiot ja yritysten edustajat) säännöllisesti yhteen keskustelemaan niin alan kehittämistarpeista Tampereella kuin toimijoiden mahdollisuuksista hyödyntää uusinta tietoa ja osaamista. Tässä ei tulisi rajausta vain sellaisiin helposti tunnistettavissa oleviin toimioihin, jotka tavallissakin toimivat ihmisten varaosateollisuuden keräntä, vaan kehitysalustat tulisi avata myös sellaisiin muiden alojen toimijoille, jotka jatkuvasti etsivät uusia mahdollisuuksia. Tällaisia ovat esimerkiksi materiaaliteknologia-ohjelmi ja ohjelmistokehitysyritykset.

### Kuva 1-3. Tieteestä ihmisten varaosateollisuudeksi – kolme strategista kehityspolkua ekosysteemin vahvistamiseksi.

![Kuva 1-3. Tieteestä ihmisten varaosateollisuudeksi – kolme strategista kehityspolkua ekosysteemin vahvistamiseksi.](image-url)

1.5 Johtajuus ihmisten varaosakestuminen:...


1.6 Varhaisen vaiheen yritysten rahoitus

Varhaisen vaiheen yrityksille suunnattu rahoitus koostuu useista eri instrumenteista, joita ovat julkinen hallinnon tarjoamat kehittämisavustukset ja lainat, pankkien tarjoamat lainarahoitukset, erilaiset luotot, bisnesenkelirahoitus ja pääomarahoitus (venture capital, VC) sekä uusimpana lainarahoitukseksi (venture finance ecosystem). Useat tutkimukset osoittavat, että talouskasvu on monelta osin riippuvainen rahoitusekosysteemin toimivuudesta. Rahoitusekosysteemiin liittyvien instrumenttien ja rahoittajien toimintaa ja sosiaali-innovatiivisia ja toiminnallisia edistysvaikutuksia rahoitusekosysteemien kehityksen ja kehittämisen osalta on olemassa useita tutkimuksia ja analyysseja. Yksi tärkein tekijä on niitä, että varhaisen vaiheen yritysten rahoituksesta on tärkeää, että niitä on olemassa useita, ja että niitä on olemassa useita, joiden avulla voidaan saada parempi ymmärrys rahoitusekosysteemien ja rahoitusten vaikutuksiin.

Varhaisen vaiheen yrityksille suunnattu rahoitus koostuu useista eri instrumenteista, joita ovat julkinen hallinnon tarjoamat kehittämisavustukset ja lainat, pankkien tarjoamat lainarahoitukset, erilaiset luotot, bisnesenkelirahoitus ja pääomarahoitus (venture capital, VC) sekä uusimpana lainarahoitukseksi (venture finance ecosystem). Useat tutkimukset osoittavat, että talouskasvu on monelta osin riippuvainen rahoitusekosysteemin toimivuudesta. Rahoitusekosysteemiin liittyvien instrumenttien ja rahoittajien toimintaa ja sosiaali-innovatiivisia ja toiminnallisia edistysvaikutuksia rahoitusekosysteemien kehityksen ja kehittämisen osalta on olemassa se. Yksi tärkein tekijä on niitä, että varhaisen vaiheen yritysten rahoituksesta on tärkeää, että niitä on olemassa useita, ja että niitä on olemassa useita, joiden avulla voidaan saada parempi ymmärrys rahoitusekosysteemien ja rahoitusten vaikutuksiin.
Päähuomiot

Tässä alaluvussa esitetään varhaisen vaiheen yritysrahoitusekosysteemin analyysin päähuomiot. Analyysi perustuu asiuntijajaahastatteluihin ja kirjallisen aineiston analyysiin sekä Euroopan ja Suomen pääomasijoitushyödystyksen tilastojen analyysiin. Tarkemmat tulokset on esitetty luvussa viisi.

KOKONAIKUVA


yritysten yhteydessä toimivien 'corporate venture capital' (CVC) -rahastojen vähäinen toiminta Suomessa ohintaa rahoitukseen ekosysteemää. USA:ssa niiden rooli on keskeinen, ja suomalaisten yritysten tulisi nykyistä aktiivisemmin etsiä rahoitusten itselleen sopivista kansainvälisistä CVC-rahastoista.

B.5 Varhaisen vaiheen yritysrahoutusekosysteemin kehittämistä koskeva keskustelu ja ratkaisujen etsintä on ollut aktiivista 1990-luvulta alkaen. Vuosina 1987–2014 Suomessa on laadittu 164 sellaista jonkin virallisen tahon tilamaa tutkimusta, selvitystä ja arviointia, joissa on tavalla tai toisella analysoitu varhaisen vai-


<table>
<thead>
<tr>
<th>Aktiivinen ryhmä</th>
<th>2007</th>
<th>2009</th>
<th>2011</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yliopistot ja korkeakoulut</td>
<td>0.10</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Pankit</td>
<td>13.50</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.20</td>
</tr>
<tr>
<td>Pääomamarkkinat</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Teolliset sijoittajat</td>
<td>42.21</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Säätiöt ja lahjoittajat</td>
<td>0.00</td>
<td>0.00</td>
<td>12.00</td>
<td>3.15</td>
<td>0.00</td>
</tr>
<tr>
<td>Perheyhtiöt</td>
<td>1.00</td>
<td>2.44</td>
<td>2.00</td>
<td>5.15</td>
<td>0.00</td>
</tr>
<tr>
<td>Rahastojen rahastot</td>
<td>10.33</td>
<td>10.00</td>
<td>20.50</td>
<td>15.50</td>
<td>0.50</td>
</tr>
<tr>
<td>Julkisyhteisöt/valtionhallinto</td>
<td>58.43</td>
<td>37.22</td>
<td>55.92</td>
<td>49.75</td>
<td>20.29</td>
</tr>
<tr>
<td>Vakuutusyhtiöt</td>
<td>32.00</td>
<td>0.00</td>
<td>3.00</td>
<td>0.60</td>
<td>0.00</td>
</tr>
<tr>
<td>Muut hallinnointyhtiöt</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>2.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Eläkerahastot</td>
<td>70.00</td>
<td>0.00</td>
<td>10.00</td>
<td>5.38</td>
<td>0.00</td>
</tr>
<tr>
<td>Yksityishenkilot</td>
<td>6.00</td>
<td>0.00</td>
<td>11.50</td>
<td>6.05</td>
<td>16.90</td>
</tr>
<tr>
<td>Valtioliset pääomarahastot</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Luokittelemanat</td>
<td>25.27</td>
<td>7.32</td>
<td>14.30</td>
<td>1.50</td>
<td>24.90</td>
</tr>
<tr>
<td>Yhteensä</td>
<td>258.84</td>
<td>56.98</td>
<td>129.22</td>
<td>89.08</td>
<td>62.79</td>
</tr>
</tbody>
</table>
heen yritysrahoitusmarkkinan tilaa ja kehitystarpeita. EcoLead-projektissa kohdistettiin erityinen houmio oppimiseen eli siihen onko raporttien johtopäätökset otettu vakavasti ja onko havaittuihin ongelmiin tartuttu (ks. tarkemmin luku 5).

B.6 Suurimmaksi ongelmaksi analyysiessä on nostettu seuraavat tekijät: (a) Suomen varhaisen vaiheen pääomaisjoitustoiminta ovat pienet, kotikuntoiset ja varsin konservatiiviset ja (b) julkisen hallinnon rooli on hallitseva. Tärkein toistuvasti esitetty suositus on ollut yksityille sijoittajille suunnattujen kannustimien kehittäminen, jotta Suomeen syntyi aidot pääomarahoituskasvun rakenne. Raportissa viitataan vakaviin puutteisiin liiketoiminnan rakentajien ja rahoittajien kompetensseissa.

B.7 Vaikka raporttien toimenpidesuosituksissa on toistuvasti korostettu yksityisen yritysrahoitusekoisyyden kehittämisen merkitystä ja yksityisille sijoittajille tarjottavien kannustimien vahvistamista, toimenpiteet ovat suosituksen vastaisesti kohdentuneet suurelta osin julkinen hallinnon toimenpiteiden ja rahoituksen kehittämiseen. Vaikka pääomaisjoitustoiminnan ongelmia Suomessa ovat luonteeltaan se, että ihmiset ovat olleet yksityisiä, erillisiä ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä aluetta, joka on vaihtanut tiedotuksen ja yksityistä alueen merkitystä. Useimmiten tämä tapahtuu yrityskaupan tai pörssiliitämistä seurauksena. Varhaisen vaiheen pääomaisjoitajat sijoittavat huomattavasti riskipitoisia yrityksiä ja paikoillaan rahoitustekniikkaa, joiden luonteesta johtuen sijoittaja voi olla valmis yrityksen kanssa aikaa uurimassa ja riskiin suhdetut korkeassa tuottavuudessa. Tämä onnistuu harvoin ilman yrityskauppana tai yrityksen listautumista pörssin. Raportissa korostetaan, että Suomessa tulisi pohtia uutisuuksia kannustimia pörssiliitämistä ja yrityskauppojen aktivoimiseksi.

PIRSTALEINEN JA TIPOTTAIN TARJOUTUVA RAHOITUS


Kuvat 1-5. Pirstaleisen ja pienissä erissä toteutuneen rahoituksen aiheuttama noidankehä. (soveltaen Hale, 2005)

KOMPEITENSIKUULIT JA KOHTAANTO-ONGELMAT


B.13 EcoLead-projektin haastattelualueisto osoittaa, että asiantuntijoiden mukaan ulkomaalaisilta korkeatasoisilta pääomasijoittajilta rahoituksesta on eroa. Euroopan pääomasijoitustoiminnan ja kasvuvaiheen yritystoiminnan tilavuus ja rahoittajien heikot historialliset tuotot tukevat näitä huomiointia. Suomalainen yritys on vaikeaa, useimmissa tapauksissa mahdotonta. Kan-sainvälistä sijoittajia sijoittavat Suomessa pääosin vain suuren potentiaalin liiketoimintaan, jos sijoitukseentohteeessa ei ole mukana suomalaisista ankkurisijoittajista. Ankkurisijoittajien puuttuminen voi olla se sitä, että 1) toimialalle kohdennettujen rahastojen puuttuminen, 2) rahastojen liian pieni palkka, 3) rahastomanajerin puutuminen markkinaymmärrys, 4) rahastomanajerin osaamisen puutteen ja (5) puuttuekset kansainvälisillä päämarkkinoilla ja sitä kautta heikko kyky tuottaa yrityksille lisäävää.

TOIMENPIDESUOSITUKSET

Toimenpidesuosituksent on perustuut haastattelualueisto on sille nostettuihin ajatuksiin, analysoituuihin raportteihin, tutkimuskirjallisuuteen ja työseminareihin (policy briefing), jotta on oikein monin ulkopuolisten sijoittajien koulutusorganisaatioihin, yrityksiin ja rahoitusorganisaatioihin.

B.14 Kehittämisen kaksi strategista kärkeä. Suomen varhaisen vaiheen pääomarahoitusoiminnan ja kasvuvaiheen yritystoiminnan tila osoittaa, että liiketoiminnan rakentaminen ja rahoittamisen osaamistason vahvistaminen on edellytys kansainvälisten yritystoiminnan ja elinvoimaisen pääomarahoitustoiminnan syntymiseksi. Huomio ollisi lisättyä kunnianhimoiseksi sekä varhaisen vaiheen yritysrahoitusekosysteemin että pääomarahoituskelpoisten yritysten kehittämiseen – rahaa tarvitsee tuottavan kohteen ja yritys kasvaa edellyttämä rahoitusta. Tämä edellyttää kilpailukykyistä ja oikein mittedutettujen pääomarahoitosten ja muiden rahoitusuudistusten rakentamista.

B.15 Kompetenssien yhdistelmät. Kansainvälistä ja kasvavan liiketoiminnan rakentaminen ja rahoittaminen edellyttävät uudenlaisten kompetenssiyhdistelmien syntymistä. Kompetenssien vahvistaminen edellyttää (1) yritysrahoituksen osaamistason vahvistamisen nostamista strategiseksi prioriteettiiksi, (2) keskeyttämättä normaalina varten varhaisen vaiheen pääomarahoitustarvetta, ja (3) korkean tason rahoitussuunnitteen kohtaan.

1.7 Ihmisten varaose tollisuus ja rahoitus

Tässä alaluuvussa nostetaan esille tutkimuksen päähuomiot ihmisten varaose tollisuuden rahoituksen osalta. Luku täy- dentää ja täsmentää luvuissa 1.5 ja 1.6 esitettyjä huomiota. Koska regeneratiivisessa lääketieteessä yritystoiminta on vähäistä, ja koska ihmisten varaose tollisuus on vasta synty- mässä, tässä luuvussa viitataan terveysteknologia- ja biotek- nologiateollisuuteen laajemmin, koska on oletettava, että ihmisten varaose tollisuus kohtaa samantyyppisiä ongelmia kuin ne teollisuudenalat, joiden yksi osa se osa.

C.1 Terveysteknologian vienti Suomesta on kasvanut viimeisen 20 vuoden ajan; keskimääräinen vuosikasvu on ollut 9 %. Vuonna 2014 viennin kokonaisvolyymi oli 1,8 miljardia euroa (Suomen Terveysteknologiayh- distys, 2015). Tullitilastojen ja Suomen Terveystekno- logiayhdistyksen (FiHTA) mukaan toimiala edustaa jo puolta Suomen korkean teknologian viennistä (FiHTA, 2015). Tämän perusteella on oletettavaa, että Suo- messa on pääomasijoitukseleipäisiä yrityksiä terveys- teknologia-alalla.

C.2 Suomessa on niukasti lifescience / terveysteknolo- gia-alalle kohdentuneita yksityisiä varhaisen vaiheen

Kuva 1-6. Kasvuyrityksiä rakentavan ekosysteemin keskeiset kompetenssit ja julkkisen rahan kohdentuminen.
(soveltaen Sorvisto, 2005; 2008)


LÄHTEET


Heinonen, T. (forth-b) Economic growth, employment and health in the field of regenerated body parts; Science fiction or a potential new industry? Manuscript of a Doctoral dissertation. University of Tampere, School of Management; Tampere.


Where is the Human Spare Parts Industry Today?

Markku Sotarauta, Tuomo Heinonen & Jari Kolehmainen

2.1 Point of departure

The EcoLead project sought to investigate (a) the key determinants and drivers of change of two different types of ecosystem (human spare parts and venture finance) and their connections and (b) the ways in which self-organizing ecosystems are led towards the next stages of development. The study focused on how the two cases function as ecosystems and how their effectiveness might be improved to achieve economic renewal and business growth.

At the moment, little is known about the innovation ecosystem around regenerative medicine and the prospective human spare parts industry. What is known more than well is that Finland needs new sources of growth and well-being. It is believed here that they can be found beyond such obvious suspects as ICT, forestry, pulp and paper, machinery and automation, and services. Consequently, the EcoLead project departed, first, from the assumption that regenerative medicine and the human spare parts industry stemming from it have the potential to be one of the new avenues (among others) of economic renewal. Second, as the scarcity of venture finance is one of the core issues in the future development of the human spare parts industry, the EcoLead project paid special attention to venture finance and private equity side by side with the human spare parts industry. In addition to scrutinizing how venture finance, or the lack of it, influences regenerative medicine, we also studied venture finance as an ecosystem in its own right. The observations from the study focusing on venture finance are reported in Chapter 5.

The EcoLead project drew upon three intertwined theoretical concepts. First, the concept of an innovation ecosystem serves the analysis as a guiding metaphor, providing the study with an overall understanding of the organic and continuously evolving nature of the relationships between main actors and between actors and their environment. Second, the view enabled by the concept of an innovation ecosystem is complemented and specified by the competence set model, which serves the study as a generic analytical tool that focuses the attention on the core elements of an innovation ecosystem and its interrelations. Third, contrary to the prevailing understanding of ecosystems as self-organizing entities, the EcoLead project acknowledged the self-organizing nature of ecosystems but complemented this view by assuming that there are actors who may take the lead and show the way to entire innovation ecosystems and/or some parts of them. All these are assumed to provide innovation policy with knowledge of how innovation ecosystems adapt to a rapidly changing environment.

As most of the results presented here are published more broadly and in a detailed manner in scientific outlets and in the other chapters of this report, this chapter focuses, in a very straightforward manner, on the main observations and policy recommendations relating to the human spare parts ecosystem (see Heinonen, 2015; Heinonen, forth; forth-b; Chapter 3 in this report; Heinonen & Ortega-Colomer, 2015; Sotarauta & Heinonen, forth; Sotarauta & Mustikkamäki, 2015). The other publications related to the EcoLead project are presented in Appendix 1.

2.2 Aims and research questions

In the broadest terms, the main research question that the EcoLead project addressed was ‘how are innovation ecosystems transformed from potential to actual sources of business growth?’

The main aims were:

- To identify the key competencies needed to develop two different types of innovation ecosystem.
- To provide decision and policy makers at all levels with insights into how to build, enhance and facilitate innovation ecosystems for economic renewal and business growth.
- To provide practitioners with insights to find their own way to lead the reciprocal and non-hierarchical sets of actors that constitute innovation ecosystems.
The research questions were as follows:

- What kind of competence set is needed in the case ecosystems?
- What is leadership like in the case ecosystems?

2.3 Methodology and data

The EcoLead project was an explorative and intensive empirical study searching for a better understanding of the dynamics of the transformation of two types of innovation ecosystems. The study followed a single case study design with two independent but interrelated cases. At the core of the study was the specific case-based qualitative fieldwork, which was supported by secondary data. The first phase of the empirical study focusing on the prospective human spare parts industry included the analysis of secondary data, consisting of relevant newspaper articles, journals, annual reports and policy documents. The main aim of the first phase was to identify the current state of the human spare parts industry.

In the second phase, 24 key actors, who are involved in the development of regenerative medicine in Tampere Finland in one way or another, were interviewed. Of these interviewees, 15 were from BioMediTech (a joint institute of the University of Tampere and the Tampere University of Technology) and the rest were from local and regional development agencies and the Tampere University Hospital, the Ministry of Employment and the Economy, the Finnish Funding Agency for Innovation (TEKES) and local firms. The interviews followed semi-structured interview guidelines, and the interview guide was designed using the main themes of the competence set model. The main aim in the interviews was to collect data on generic competencies from a system-level perspective. In the human spare parts case, the main emphasis was on such generic competencies that are needed in the commercialization of new scientific knowledge and, more broadly, in securing its place in the society at large. Therefore, competencies related to actual scientific work were not touched upon, but their importance was, of course, acknowledged throughout the project. They are the core of the emergence of any science-based industry.

<table>
<thead>
<tr>
<th>Case</th>
<th>Interviews</th>
<th>Other material</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human spare parts</td>
<td>24 (and an additional 28 from an earlier study)</td>
<td>Earlier studies, policy documents and relevant reports. General interest in the human spare parts industry was pointed out by newspaper articles from Kauppalehti and Aamulehti (1994–2015) (figure 2-3).</td>
</tr>
</tbody>
</table>

2.4 Key concepts

2.4.1 Innovation ecosystem

It is a well-known fact that most breakthrough innovations and new businesses are not created in isolation but through collaborative arrangements that enable organizations to combine their individual offerings into coherent solutions. Consequently, the number of studies focusing on different kinds of innovation systems has been mounting during the past 25 years.

In the EcoLead project, the concept of an innovation ecosystem instead of that of an innovation system was used, the aim being to complement the relatively established focus of (national, regional, sectoral) innovation system studies that primarily address organizations (actors as components of systems), rules of the game (institutions), interaction patterns (networks), innovation activities, knowledge flows and recently knowledge bases (see e.g. Asheim & Gertler, 2005; Asheim & Isaksen, 2002; Braczyk, Cooke & Heidenreich, 1998; Sternberg et al, 2010). The EcoLead project joined the literature that aims to shift the academic and policy debates from innovation systems towards innovation ecologies and/or ecosystems. The innovation ecosystem approach provides this study with a generic analytical tool that appreciates the organic nature of systems and sees them not as fixed and static but as entities that need continuously to adapt to changing situations. This study also aims to examine critically Moore’s (1993) view that ecosystems tend to align themselves with leading companies. The assumption here is that there may also be other forms of leadership, and other leading actors, and thus we approach leadership as an open empirical question. All this highlights the ways in which complex inter-linkages among a variety of actors shape adaptation. In these kinds of settings, conflict, competition and co-operation are all present as specific objectives, strategies and/or interests of individual organizations may be aligned or in conflict.

According to Miller (1975; cited by Papaioannou et al, 2009), “an ecosystem implies that everything is connected to everything; everything feeds back through the ecosystem on itself. The interconnectedness preserves the overall system”; therefore, the systemic interconnections that are generated by a wider ecology form the centre of the analysis. As observed by Papaioannou et al (2009), “ecosystems evolve through adaptation of living organisms to their environment”. They argue further that this means that there is no need for external intervention as ecosystems have an internal dynamic that reproduces the interrelations between different actors and their environment. Furthermore, innovation ecosystems are assumed here to be multi-localational in nature and thus, from the point of view of the Finnish
innovation policy, there is also a need to discuss the multi-localational networks defining an innovation ecosystem (Crevoisier & Jeannerat, 2009) and to seek ways to enhance the capacity to participate in multi-locational knowledge flows and anchor both knowledge and talent in Finland.

The EcoLead project complements the innovation ecosystem approach with the competence set model and seeks to support strategic adaptation by identifying the competencies that are needed in the many efforts to boost the adaptation of an entire ecosystem and/or some parts of it. Our earlier study (Sotarauta & Srinivas, 2006) shows that resilient economies show strategic adaptation rather than pure (more passive) adaptation. Strategic adaptation refers to the sensitivity to various changes and the capacity to adapt to them, but at the same time it stresses the ability to create more or less collective perceptions of each phase of evolution as well as its own 'story of development' and its support. Strategic adaptation calls for a well-established set of integrated competencies.

2.4.2 Competence set

The EcoLead project began by following Eliasson, who argues that, in innovation ecosystems, “competencies (in direct and/or indirect interaction) generate, stimulate and/or frame the overall functioning of a system and its transformation” (Eliasson, 2000). Therefore, instead of focusing only on science and technology, there is a need to be more concerned with the transformation processes and new business formation. Eliasson’s competence bloc theory focuses on the minimum set of actors with competencies needed for an effective innovation ecosystem and business growth. According to Eliasson (2000), the purpose of a competence bloc “is to guide the selection of successful innovations through its competence filter, induced by incentives and enforced by competition, and to move the innovations as fast as possible towards industrial scale production and distribution”. The quality of a competence bloc is to be measured by its outputs and not its inputs, that is, “through a bundle of functionally related products and services in the market but not in terms of technologies or physical inputs” (Eliasson, 2000). Consequently, a competence bloc is geared to select winning technical and economic solutions and not to measure the inputs required to achieve them. The emphasis on selection aims to minimize two errors: (a) allowing losers to survive for too long and (b) rejecting potential winners. Importantly, a well-functioning competence bloc also attracts competent investors and other actors who contribute positively to the dynamism of an ecosystem; conversely, those whose contribution is not as positive are selected out. To become self-propelled into a growing industry, an innovation ecosystem requires a competence bloc with an adequate mass of critical competencies and a variety of actors.

Thus, the competence set model constructed and used here is highly inspired by the competence bloc theory, but as the competence bloc theory was constructed mainly to understand better and explain business growth in biotechnology, it needs to be extended by additional competencies to provide an analytical tool for the analysis of other innovation ecosystem types and broader purposes as well. Additionally, instead of using ‘bloc’, the concept of a ‘set’ is adopted to highlight the collection of competencies that belong together or are otherwise found together. This is only to simplify the discussion, as ‘bloc’ is often understood to refer “to a group of countries or political parties with common interests who have formed an alliance” or “a combination of persons, groups, or nations forming a unit with a common interest or purpose” (Merriam-Webster Dictionary), while ‘set’ refers to “a group or collection of things that belong together or resemble one another or are usually found together” (Merriam-Webster Dictionary).

The competence set is an assembly of generic competencies that in conjunction generate new knowledge and secure its diffusion and valorization in the society and economy. Such a set of competencies is needed that not only enhances the emergence of new knowledge but also links it to business growth, economic renewal and/or societal change. Subsequently, there is a continuous need to upgrade individual competencies and refine the entire competence set to adapt to the changing environment. Additionally, it may be the case that an innovation ecosystem as a whole, or some of its competencies, is not at an adequate level. Missing and/or poor competencies may freeze an innovation ecosystem and lock it into its past trajectory for these purposes.

All innovation ecosystems contain resources, but by no means are all of the actors embedded in them capable of utilizing these resources efficiently without adequate competencies. In organization and management studies, the concept of core competence has been used to analyse why some organizations perform well and others do not, and it is believed here that the concept of competence, especially when seen as an integrated set of competencies, may be of use in the scrutiny of innovation ecosystems too. Competence refers to capabilities and expertise that are distributed over many operations either within an organization or across them (Pralahad & Hamel, 1990). A core competence, applying the theory of Prahalad and Hamel (1990), is predominantly a collective learning process across the innovation ecosystem and thus much more than simply what an individual organization is good at. The core competencies of an innovation ecosystem may potentially differentiate it from competing ecosystems. A competence set model is constructed to identify how the competencies
of many actors could be integrated with one another so that such a constructed set would serve both the entire ecosystem and the actors embedded into it (Sotarauta & Heinonen, forth). Following Prahalad and Hamel (1990), it is also argued that the competence set could serve as a policy tool in the search for and construction of shared interests and problems as well as joint opportunities and capabilities.

In all events, the policy problem deals with how such policy catalysts can be inserted to initiate a competence set and/or induce it to boost an innovation ecosystem to reach critical mass faster and/or whether such catalysts are to be found in the science and/or business community. Additionally, it is assumed, following Avnimelech and Teubal (2008), that our understanding of innovation ecosystems, universities’ roles in them and related innovation policies ought to be dynamic and systems-evolutionary by nature to trigger, reinforce and sustain market-led evolutionary processes of the economy effectively. For these reasons, the main rationale in constructing a competence set model is: (a) to specify which competencies various actors bring into play in an innovation ecosystem; and (b) to identify the competencies that keep an innovation ecosystem continuously adapting to changing economic landscapes and thus renewing economies. A sole focus on actors and the relationships between them, typical of innovation system studies, may even blur the view on how systems actually function and what drives them; hence, it is important to make a distinction between organizations and competencies. As many organizations are large and heterogeneous entities (most notably universities) and have multiple roles and consequently also multiple goals and expectations, they may have many competencies that contribute to an innovation ecosystem. All in all, by approaching actors indirectly through competencies, it might be possible to clarify and specify the roles that they play in translating new knowledge into viable products and services.

Next, drawing upon the literature focusing on various functions of innovation systems, the competence set model is constructed to cover seven themes for the identification of the generic competencies. These are: (1) knowledge creation, diffusion and valorization; (2) entrepreneurship; (3) finances; (4) legitimization; (5) market formation; (6) systematic production; and (7) the identification of potential end-values (for more detail see Sotarauta & Heinonen, forth; Figure 1). Quite naturally, each of these includes a variety of specific capabilities that construct a generic competence. In a system-level analysis, the interaction of identified competencies provides further empirical analysis with a point of departure in identifying the specific capabilities in the context of a specific transformation process of a specific innovation ecosystem.

**Figure 2-1. The seven themes of the competence set model.**
Generative leadership

The approach developed here aims to understand and analyse evolving processes and actors’ competencies in them, instead of only classifying the outcomes of processes. This is relevant in the context of an innovation ecosystem, in which adaptation is a never-ending interplay between individual and collective intentions on the one hand and intentions and surprises on the other. Generative leadership is approached as a force that directs evolving processes in the desired directions. The main thesis is that different actors with different strategies play leading roles in achieving the desired outcomes. Therefore, the question is not about the leader–follower relationship in the here and now but about how different actors influence each other’s activities without necessarily having the authority to do so (Sotarauta & Mustikkamäki, 2012). Generative leadership is added to this broth, as there is an increasing need to understand how actors mould ecosystems, that is, the conditions for innovation and renewal, and how they aim to change the course of events and generate innovation; hence, a question arises concerning the place of generative leadership in the setting sketched here.

Generative leadership focuses on those processes that are geared to giving birth to something new and constructing local conditions for knowledge creation, circulation and valorization. As Sotarauta (2016) maintains, the main motive in generative leadership is not to find the best fit between the existing resources and the current opportunities but to create a misfit between resources and ambitions to challenge the actors to join the development efforts. Generative leadership is needed for (a) the creation of conditions to nurture and stimulate innovation and business growth, (b) the facilitation of the adaptation of an entire ecosystem to a changing environment, (c) the construction of collective intentions and strategies to enhance the productivity of an innovation ecosystem and (d) the generation of new processes that improve and change competence sets or bring

<table>
<thead>
<tr>
<th>Generic themes for the identification of competencies</th>
<th>Definition</th>
<th>Competence building related questions (examples)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge development and diffusion</td>
<td>The breadth and depth of the formal and informal knowledge bases and the ways in which knowledge is generated, diffused and combined in the system</td>
<td>What are knowledge dynamics like? How is new knowledge diffused; which channels are used?</td>
</tr>
<tr>
<td>Venture finances</td>
<td>Monetary investment to support the start of something new or different that usually involves risk</td>
<td>What are the most important private and public funding bodies and how do they function? How is the funding provided? How is it possible to access venture finance sources?</td>
</tr>
<tr>
<td>Entrepreneurship</td>
<td>The discovery and exploitation of profitable opportunities</td>
<td>What factors support and constrain entrepreneurship? How do entrepreneurs build market understanding for the selection of the most prominent opportunities on the one hand and creating them on the other hand?</td>
</tr>
<tr>
<td>Legitimization</td>
<td>Acquiring social acceptance of innovation; central features include the formation of expectations and visions as well as regulative and legislative alignment to support the emergence of new sources of economic growth and renewal</td>
<td>What is the socio-political situation in a given field like, and in what ways could the emergence of innovation be supported through a consciously defined legitimation process?</td>
</tr>
<tr>
<td>Market formation</td>
<td>The ways in which economic activity, and especially the forces of supply and demand, interact and change over time to create a constant demand for new products and services</td>
<td>What is the size of the market, who are the leading players and where are the dominant locations in the field in question? How do new markets emerge and existing markets transform? How can we position ourselves in the emerging markets?</td>
</tr>
<tr>
<td>Systematic production</td>
<td>Innovation becomes part of the economy and society at large with organized regularity that forms a system</td>
<td>How are innovations institutionalized? What are the main ways to achieve this in a case under scrutiny?</td>
</tr>
<tr>
<td>End-value</td>
<td>The desirability and/or worth of an innovation for its users</td>
<td>What is the whole array of potential users and benefits of an innovation? Of course, it is by default impossible to know what end-values unknown products and processes will generate in the future, but it is important to discuss the ways in which different societal groups may be affected by new developments.</td>
</tr>
</tbody>
</table>

Table 2-2. The core definitions related to generic competencies (definitions based on Bergek et al., 2008; Hekkert & Negro, 2009; Hekkert et al., 2007; Johnson, 2001; Shane & Venkataraman, 2000) and a few illustrative and exemplary questions related to generic competencies.
new elements of them into existence (Sotarauta, 2016).

Generative leadership is constructed as a process of influencing and teaching others to understand why and how certain activities and goals need to be accomplished (Yukl, 2008); therefore, as argued by Sotarauta (2016), there is a need not to see leadership as a static relationship between leaders and followers but to conceptualize it from a temporal perspective. Generative leadership is scrutinized as a relay process over time. In a leadership relay, actors are engaged in a task or activity for a fixed period of time and are then replaced by other actors. A leadership relay for innovation ecosystems differs significantly from our understanding of a relay in sports. In a generative leadership relay, it is much harder to know the team, coalition or organization of which one is a member, and it may be equally hard to know the meaning of the race and to detect its beginning and end. A leadership relay is not a conscious, smooth and predesigned process but rather a phase-by-phase process, an evolving search for the next steps and visions.

Generative leadership sees ecosystems as co-operative advantages in which leadership is a process of influence reconciling competing and conflicting interests (cf. Trickett & Lee, 2010). According to our studies, generative leadership consists of strategic leadership (sense of direction, consistency and persistency over time, etc.), interpretive leadership (collective belief formation, penetration of social filters, framing, etc.), institutional leadership (decision making, directing funds, etc.) and network leadership (constructing an atmosphere of trust, arbitrating conflicts, etc.) (for more see Sotarauta, 2016). Generative leadership draws closely on transformational leadership, which is based on four dimensions, applied in the context of an ecosystem in the brackets: (a) idealized influence (based on respect and admiration for influential actors); (b) individualized consideration (the extent to which the leader cares for the entire ecosystem); (c) intellectual stimulation (the degree to which the leader provides other actors with interesting and challenging projects that aim to change an ecosystem); and (d) inspirational motivation (the communication of visions and emerging opportunities from the point of view of an entire innovation ecosystem instead of individual goals) (Bass & Bass, 2008).

2.5 Human spare parts industry and regenerative medicine

How does one grow an upper jaw within a stomach muscle? Ten years ago, this question would have read like an excerpt from a science fiction novel. Today, based on a new tissue-engineering technology created in Tampere, more than 20 patients with serious bone deficiencies have been treated in this way in Finnish hospitals (Bionext, 2010). However, the emerging regenerative medicine concentration in Tampere and the prospective Finnish human spare parts industry does not yet have a direct antecedent in the economy and thus entails the need to construct new competencies and/or to transform existing ones to support the birth and enlargement of an embryonic industry (Heinonen & Ortega-Colomer, 2015; Sotarauta & Heinonen, forth).

The concept of regenerative medicine is now generally used to describe such biomedical approaches, which are developed to cure the body by stimulating endogenous cells to repair damaged tissues or by the transplantation of cells and/or engineered tissues to replace diseased or injured tissues (Riazi, Kwon & Stanford, 2009). Stem cells are the basic units in regenerative medicine. In clinical treatments, the capacity of stem cells is based on their multipotent ability. Stem cells are able to regenerate tissues and organs and act as building blocks for all the tissues in the body (National Institutes of Health, 2009). It has been suggested that regenerative medicine (RM), alongside medicine and surgery, is about to constitute the third discipline in human health care (Polak et al, 2010). From a commercial perspective, cell therapy is often seen as the fourth strand in the health care industry alongside biopharmaceuticals, pharmaceuticals and medical devices (Mason & Manzotti, 2009). Stem cell (SC) research holds the promise of treating many serious and disabling diseases and disorders by replacing damaged, lost or diseased cells through regeneration. It can be considered part of a new field of activity that emerged in the early 1990s, developed rapidly over the last decade and is commonly referred to as either tissue engineering or regenerative medicine (for basic definitions see Appendix 3).

Regenerative medicine, as defined by Greenwood et al (2006), refers to “an emerging interdisciplinary field of research and clinical applications focused on the repair, replacement or regeneration of cells, tissues or organs to restore impaired function resulting from any cause, including congenital defects, disease, trauma and aging. It uses a combination of several technological approaches that moves it beyond traditional transplantation and replacement therapies. These approaches may include, but are not limited to, the use of soluble molecules, gene therapy, stem cell transplantation, tissue engineering and the reprogramming of cell and tissue types.” Regenerative medicine has grown rapidly in the past decade and the scientific achievements have brought forth expectations of new treatments for severe, incurable diseases, including for example Parkinson’s disease, diabetes, heart diseases and cancer. So far, regenerative medicine, as the most negative commentators state, has been full of empty promises and more hype than actual treatments (Brown, 2003; Nadig, 2009). Consequently, today, the question is not how one grows an upper jaw within a stomach muscle but what prevents regenerative
Key findings

Knowledge creation, diffusion and valorization

E.1 In Tampere, the knowledge infrastructure related to regenerative medicine and the potential human spare parts industry is in place and has been evolving favourably during the past 15 years. The scientific research is based on close collaboration between the University of Tampere and the Tampere University of Technology. The first discoveries were based on collaboration between biomaterial engineers, clinicians, cell biologists, technical experts and animal model experts (Sotarauta & Heinonen, forth; Sotarauta & Mustikkamäki, 2015).

E.2 In 2013, the University of Tampere and the Tampere University of Technology established a joint research institute, the Institute of Biosciences and Medical Technology (BioMediTech), employing approximately 250 scientists.

E.3 According to an extensive international evaluation of research at the University of Tampere in 2014, the competencies related to scientific knowledge production in biomedical research are at a high level. The international evaluation panel concluded that “research conducted at BioMediTech has an excellent standing nationally and internationally and the number of research projects and output from these projects is commensurate with the size of the Institute”. The conclusion was also that the research projects are innovative and have clear translational potential in all the thematic research areas of BioMediTech (Hakala & Roihuvuo, 2014).

E.4 During the last 10 years, BioMediTech has filed more than 100 patents. In addition, more than 25 successful clinical treatments have been carried out. The prospective human spare parts industry has a solid core in Tampere and thus the future is full of promise. However, not all the competencies that are required to take steps forward in the integration of new technology and treatments into the existing health care system as well as to take advantage of an emerging market are in place yet.

Systematic production

E.5 The emerging human spare parts industry draws on high-quality scientific research. Firms that have an interest in the field need to have, one way or another, access to cutting-edge research (Prescott, 2011), as it is the scientists who introduce new ideas and have the personal-level networks needed to raise the needed funds and establish start-ups (Murray, 2004; Prescott, 2011). Moreover, universities need to nurture innovations in clinical trials before aiming for commercialization further than is usually the case in medical innovation or is normally expected before founding a start-up and seeking venture finance (Sotarauta & Heinonen, forth).

E.6 In regenerative medicine, the scientific community also needs to be competent in shaping the technology market and generating the demand for innovations. In practice, its members may be the only actors who truly understand the potential embedded in the stem-cell-based regenerative medicine in the early stages of development. For these purposes, governments, in the US and the UK for example, are establishing translation centres and funding clinical trials in cell therapy to support the construction of competencies in the academy (Mason et al, 2011).

E.7 Our interviews clearly revealed that the issues related to systematic production, either commercially or non-commercially, have been on the agenda in Tampere since the early days of regenerative-medicine-related research (early 2000s) (see also Sotarauta & Mustikkamäki, 2015). They also showed that BioMediTech has not found solutions for moving forward beyond clinical experiments and that it has faced similar challenges to other actors in the field globally. The generic competencies needed to move forward are not as developed as those in actual science. However, the attitude of the core scientists and BioMediTech’s management towards finding solutions is very positive, and it has aimed to tap into complementary competencies with partners in the USA and Belgium. BioMediTech has also recruited additional staff with complementary capabilities in issues related to commercialization, patenting and licensing. Additionally, BioMediTech has utilized the so-called ‘Tutli’ funding programmes of TEKES. This is a specific policy instrument not only to support the commercialization of
The experiences of the institutional home of Tampere-centric regenerative medicine, the University of Tampere, in technology transfer and commercialization are almost non-existent and hence the related competencies are poorly developed. This is due to the fact that the UTA is the most specialized social science university in Finland and hence there has been only limited demand for these kinds of services in the past. BioMediTech has clearly pushed the university to develop its competencies on these fronts too.

The Tampere University Hospital has not carried out any major strategic efforts to establish regenerative medicine in its standard repertoire, nor has it proactively constructed the required competencies. As a joint municipal authority of 22 municipalities, its mission is not to serve as an ‘innovation platform’ for technological development but to provide approximately 1 million Finns with timely and equal access to specialized medical care. However, the hospital’s attitude towards regenerative medicine may be crucial not only in becoming a legitimized part of the Finnish health care system but also in moving towards large-scale systematic production (Sotarauta & Heinonen, forthcoming). However, according to our interviews, the university hospital is not likely to adopt a more strategic approach in the near future if there is no significant pressure either from the society at large (in practice the public health care policy) or from abundant individual medical doctors.

Market formation

The market formation of the human spare parts industry has barely started. It is clearly an embryonic industry without an established position yet. There are approximately 700 companies globally in the field (of which 247 companies are dedicated to cell therapies) (ARM, 2014). The Alliance for Regenerative Medicine distinguishes 4 sub-groups in the industry: therapeutics and devices (56%), tools (19%), tissue banks (13%) and services (12%). Grand View Research (2013) estimates that, in 2013, the size of the regenerative medicine market was $30.16 billion, of which the stem-cell-based technology market accounted for $12.8 billion. The estimations vary extensively depending on which specific categories are included in regenerative medicine.

In Tampere, and more broadly in Finland, it is vital to construct competencies to monitor and understand market formation and access the main markets, that is, to seize the emerging opportunities. In locations like Silicon Valley, with abundant influential actors from different areas of the market, it is possible to witness markets evolving, but in more geographically peripheral locations like Tampere, there is a need for active construction of competencies for entering emerging markets and strengthening the local ecosystem and its global connections. The need to reach international markets and funding sources is well understood at BioMediTech, but it seems to be clear that the strategic awareness about emerging global markets still is fairly poorly developed and shared generic competencies in the ecosystem to exploit emerging opportunities are not systematically constructed. The core actors are not familiar with the international markets and there is no systematic monitoring of them either (Sotarauta & Heinonen, forthcoming). In sum, the awareness of the market potential is vague but gradually improving, as BioMediTech has received public funding from national and local sources to fortify its capacity to operate in the global markets. The interviewees implied that there is still a limited understanding of the need to strengthen the competencies related to accessing global markets in the ecosystem as a whole. Relatedly, there is also a need to make the collaboration with the Finnish hospitals more programmatic to gain first-user references close to home and ensure that the benefits of the science in question are available in the country that has funded the research (Sotarauta & Heinonen, forthcoming).

During recent years, the academic core actors developing the human spare parts industry in Tampere have been fairly inward looking and have not consciously aimed to develop the ecosystem instead of their own organizations. In other words, they have not aimed to tap into the expertise of public and/or semi-public development agencies, or other actors close to home, that work outside academic spheres to support the commercialization of scientific discoveries. Contrarily, there are signs of a widening gap between BioMediTech, development agencies and local firms. This is due to the fact that the earlier fairly well-established sharing of joint and individual competencies, resources and powers in the local ecosystem (Sotarauta & Mustikkamäki, 2015) has been fading away as the individual universities have been struggling with the many internal issues related to founding a joint institute.

In conclusion, the universities have strengthened their competencies in scientific knowledge production and have been able to improve their position in an international scientific scene, but the generic competencies in the broader ecosystem have not yet been developed accordingly. Additionally, despite immense expectations and desires, the human spare
parts market is only starting to emerge globally. Consequently, the business opportunities still seem to be at a fairly low level, generally speaking (see Kenney’s chapter in this report).

**Entrepreneurship**

E.14 As indicated above, science- and technology-related competencies have developed positively in Tampere, but the establishment of new businesses on a large scale has been slow. Some 10 spin-off firms have developed from BioMediTech and its predecessors, but they have faced struggles in entering the markets. Moreover, there are several biomaterial firms in Tampere but, at least so far, no entrepreneurs who would be interested in exploiting the discoveries made in BioMediTech. Furthermore, there are no strategic platforms to support dialogue between incumbent Finnish and international firms and no significant strategic initiatives to construct a supportive local ecosystem for start-ups to emerge and grow. Indeed, the current commercialization strategy of BioMediTech focuses especially on detecting major international dedicated actors to collaborate with and experimenting with everything that seems to work. It is not aiming to create a local start-up ecosystem. BioMediTech would benefit from a local start-up community that would serve it as a showcase for major international players who are willing to do some ‘window shopping’ in Finland. At their best, start-ups would serve as home bases for selected IPR and thus remove the need for the incumbent firms and venture financiers to screen all the research and discoveries made at local universities. Therefore, the start-up community might attract foreign investments in the form of acquisitions.

E.15 In sum, the idea of commercialization has been warmly welcomed in both the policy and the science community and several explicit support measures have been launched. The commercialization capacity at BioMediTech has been improved by recruiting IPR expertise, scientists have been trained for commercialization, partners have been sought from the US and Belgium and technology has been licensed to an external party. However, to repeat the main observation of this study from an ecosystem perspective, the efforts are based on enhancing competencies in a single organization instead of an entire ecosystem, and thus the actions do not meet the vastness of the challenges related to the broader utilization of new technology.

**Venture finance**

E.16 BioMediTech has been able to utilize public funding extensively. The public funding agencies have, without any reluctance, supported the emergence of regenerative medicine, but private venture finance has not found its way to Tampere. The catalytic role of venture financiers is often crucial in the emergence of new industries (Burg & Kenney, 2000; Florida & Kenney, 1988; Kenney, this report). BioMediTech is a research institute with strong commercial ambitions, but so far, as already indicated above, no entrepreneurs or incumbent companies have been attached to it that would be involved in co-creation processes or commercialization efforts. Consequently, there is a need to find an accurate balance between public funding, finding dedicated big-pharma companies to collaborate with and boosting the establishment of venture-finance-backed start-ups both to utilize and to display the local scientific potential and, of course, to become established players in the system by themselves.

E.17 The emerging human spare parts industry in Tampere is not alone in its lack of entrepreneurial activity and its difficulties in acquiring funding for commercialization (see Hellman et al, 2011; Johnson et al, 2011; Martin et al, 2006). Pisano (2006) argues that it is typical of this line of industry. Stem-cell-based regenerative medicine is a reasonable representative of a science-based field that is in an embryonic phase and that depends largely on public funding. Private venture financiers become interested in the potential of its innovations only in the later phases of clinical trials (Parson, 2008).

E.18 There are no Finnish venture capitalists who would invest in regenerative medicine, and Finnish venture capital as a whole is a scarce resource. The competencies to fund the commercialization of regenerative medicine are poorly developed in Finland. For these reasons, BioMediTech needs to seek venture funding from abroad, but the competencies to identify and hook up with foreign venture capital are still under construction. There are no effective connections to potential venture capital sources. The main finance gap is from the proof-of-concept stage to scaling business (see Figure 2-2).

**Legitimization**

E.19 In unison with the great expectations rooted in regenerative medicine, the emerging human spare parts industry encounters complex legislative and ethical issues: hurdles that are typically faced by emerging industries. Therefore, the emergence of the human spare parts industry cannot be addressed entirely without scrutiny of the issues related to legitimation. The generic competencies connected to legitimation are highly significant, as the question concerns legitimating the human spare parts indus-
try not in one particular system but in several systems and thus widely in the society. In the case under scrutiny, the systems to which the human spare parts industry needs to attach itself are the health care, science and innovation systems, as well as, to some extent, the local/regional economic development system. Pushing a new field through several systems and related policies calls for such navigational competencies that are not usually readily available at the universities, and this again highlights the need to bring into focus the generic competencies embedded in the entire ecosystem instead of only one organization.

E.20 A lack of legitimacy is often one of the main hurdles for new ventures operating in emerging industries and/or markets, as the new products, services and processes need to overthrow the existing regime or supplement it significantly. This kind of transformation quite naturally causes uncertainty and social anxiety. Consequently, reducing social uncertainty and dealing with resistance to change are among the generic competencies needed in an innovation ecosystem. These competencies are here merged with the concept of legitimization. Legitimization refers to the socio-political process of legitimacy formation through actions undertaken by various organizations and individuals (Johnson, 2001; Sotarauta & Heinonen, forth).

E.21 The essential traits of legitimization are the formation of visions and expectations as well as regulative alignment (including market regulations, tax policies and directions of science and innovation policy) (Bergek et al, 2008). Legitimization is about attaining social acceptance of innovation; therefore, ultimately, it is about making an innovation comply with the predominant institutions (norms, values, habits and regulations) and/or addressing the need to transform institutions for something new to emerge (Johnson, 2001). Legitimization is one of the most central selection mechanisms in any innovation system.

E.22 So far, the human spare parts industry has not been well defined, and the yardsticks and/or products and services to be used in the judgement of whether the industry is proper or not are scarce. Conversely, ambiguous or non-existing standards and yardsticks open windows of opportunity for new ventures, as they may take a lead not only in exploiting the opportunities but also in constructing the new industry – imposing the standards for it and establishing a dominant design for an entire field – and in this way they may boost the legitimacy of the industry. In practice, single actors usually do not have the powers or capacities to push for legitimacy alone, and more often than not legitimization calls for actions from several public, private and academic actors. There are many ways to legitimate a new industry. At the organizational level, ventures must build trust with customers, firms in related industries and industry members. They also need to develop a knowledge base by clearly defining the issues at stake (e.g. the level of abstraction, use of existing knowledge, internal consistency, etc.) (Aldrich & Fiol, 1994).
E.23 Regulatory bodies often struggle with the novel scientific understanding and possibilities of technology emerging from biomedical fields. In situations like this, as observed by Metcalfe et al (2005), regulation co-evolves with the innovation process and the emerging market. In Tampere, the experimental treatments have been regulated under Hospital Exemption for Advanced Therapy Medicinal Products (ATMP). Even after several successful experimental treatments and with established expertise to cultivate bone tissue from stem cells, regulators do not fully know what the regulatory details for these kinds of new products and treatments should be. There is actually an ongoing dialogue between the regulators and the representatives of BioMediTech to find out what is actually required and how to carry it out; thus, the Tampere case confirms the earlier observations that regulation co-evolves with the innovation process and the market in emerging industries.

E.24 Generally speaking, statutes concerning clinical medical research cover much of the stem-cell-based research. Only some countries have adopted legislation dedicated to stem cell research as such. The ethical atmosphere and legislation in Finland have mostly been permissive (Stem cell research..., 2007). Regenerative medicine is well legitimized in the Finnish science system, including science and innovation funding, but it is not as well legitimized in the health care system, as the treatments are mainly case-by-case experiments rather than established parts of the standard repertoire of the hospitals and the entire system.

E.25 The general atmosphere concerning regenerative medicine and new discoveries in general is favourable according to our media analyses. From 1994 to 2015, the articles in Aamulehti (local newspaper) and Kauppalehti (a leading national business outlet) mainly focused on introducing new scientific discoveries and technologies as well as related treatments. Significantly fewer articles focused on ethical issues or issues related to regulation (see Figure 2-3).

E.26 Innovation ecosystems consist of heterogeneous sets of actors that all have their own desires and anxieties. The principal activities in an ecosystem, and the promises embedded in them, are not as crisp and transparent as is often assumed – an innovation ecosystem is a nexus of many desires, anxieties and purposes. Hence, the question of what the potential end results may be also emerges as central. We need to reach beyond focusing on the potential end-uses of a specific innovation and scrutinize the whole spectrum of expected end-values, hopes and expecta-

Figure 2-3. The number of articles focusing on regenerative medicine in Aamulehti and Kauppalehti from 1994 to 2015. In the media analysis, the concepts ‘stem cell’ and ‘human spare parts’ were used in Finnish. (Heinonen, forth-b)
tions of very different stakeholders. Here it is crucial to remember that a ‘firm’, ‘product’ or ‘service’ is not an end-value, as is often seen, but the value generated for the society, the economy and the well-being of the individuals at large. In the era of demand and/or user-led innovation, innovation in the field of human spare parts is pushed forward by new developments in science, and the ‘customer imagination’ is not developed enough to demand these kinds of services.

**E.27** As the field is characterized by high hopes and global hype, a variety of expectations exist. Public policy makers and funding bodies are looking forward to increased employment and globally leading positions in a new trending field; our interviews revealed that this is the case in Tampere too. Scientists, for their part, aim to push the scientific frontier forward but also seek citations and fame. In addition, of course, ultimately, there are diseases that are incurable or difficult to cure and thus plenty of patients who might benefit from scientific breakthroughs in regenerative medicine, providing them with new hope. In the early stages of regenerative-medicine-related products and services, it is fairly hard to see user- or demand-led innovation emerging on a larger scale.

**E.28** Discussions around issues related to end-values have been meagre in Tampere. There have been no proper public debates on the variety of potential end-values. It may be that the lack of public debates is among the reasons why legitimization is still uneven depending on the sub-system, why market offerings have been slow to emerge and why the Tampere University Hospital has not adopted a more strategic attitude towards regenerative medicine. Additionally, there have not been any real efforts to initiate a public discussion on the public and/or private end-values of the money invested in regenerative medicine. It seems clear that there is no widely shared awareness of the importance of public debates in the emergence of a new industry and thus no competencies to set these in motion. Perhaps the human spare parts industry has not begun to emerge in Finland because it is globally underdeveloped and funding is scarce but also because there is no public debate concerning the end-values or potential risks involved in regenerative medicine and the human spare parts industry.

**Policy recommendations**

**E.29** From science to the human spare parts industry – three pathways. It is possible to identify, drawing on the relevant literature and the interview data, three potentially interlinked strategic pathways towards broader utilization of the knowledge and technology developed at BioMediTech. The three strategic pathways are not mutually exclusive but mutually supportive. They are: (1) deepening strategic collaboration with the large public companies operating in the field or close to it (joint research, co-development, licensing IPR, etc.); (2) boosting the establishment of start-up companies; and (3) establishing a specialized unit with the university hospital to carry out tailor-made and highly specialized (and experimental) treatments. The three strategic pathways differ from each other in terms of risk and expected benefits. Here, the three pathways are roughly outlined, as they are fairly well covered in the literature and as more detailed planning for this specific purpose would require a deep understanding of medicine, health technology and medical treatments and not only system-level knowledge of competencies and commercialization.

* In principle, commercialization through large public companies represents a fairly traditional route for many universities. Especially in the US and increasingly also in the UK, intimate links with large pharmaceutical firms and publicly funded research centres are the key to spin-off businesses in biotechnology (Cooke, 2001). Strategic collaboration with incumbents may potentially incorporate the lowest risk levels but, simultaneously, depending on the negotiation powers and resources of participating actors, its impact on the regional economy may remain at a low level.

* During the last decade or two, many universities have become more active in forming start-up companies around university-developed technology or licensing to small private firms rather than through the incumbent companies, hence also becoming more engaged in riskier forms of commercialization and entrepreneurial activity. As Gombers and Lerner (2004) points out, starting new ventures based on university technology is not a joyride but hard work that requires specialized competencies. As he also reminds us, in spite of the conviction of many academic entrepreneurs and university administrators, the process of establishing an economically sustainable new company is a very challenging one, and more often than not, university spin-off firms do not generate large revenues for academic institutions. On the contrary, modest returns are the norm (see also Lester & Sotarauta, 2007). Start-ups are usually expected to generate revenue and employment, but they can also be used as showcases of and exhibits for the best technology developed at the university. Following this tactic, the purpose is not to develop a growth company but to attract venture capitalists and/or incumbent companies by showcasing the most valuable and selected IPR through start-up
companies instead of a wide spectrum of research and technology conducted in the university.

- The third strategic pathway connects to the emerging but scarce literature on entrepreneurial hospitals (French & Miller, 2012; Grazier, 2015). As maintained by French and Miller (2012), an entrepreneurial hospital possesses the capacity to use innovation generated elsewhere and/or by local universities. Thus, it may count individual patients and patient populations amongst its human capital. In this way, it would be possible to link research, development and treatment to find new ways for improved and more cost-effective health care as well as new avenues for the commercialization of scientific discoveries. Thus, by drawing together care and research in novel ways, the entrepreneurial hospital would be able to increase the capacity for biomedical innovation. The Tampere University Hospital might be well positioned to develop novel operational models in the spirit of an entrepreneurial hospital, as it has actively searched for new organizational forms through the Heart Hospital and the Coxa Hospital for Joint Replacement. Working in concert, a closely linked ‘entrepreneurial university’ and ‘entrepreneurial hospital’ would promise to boost not only science and innovation but also the health care system more broadly. On this pathway, the core issue is to position a hospital as a passage point for biomedical innovation. All this might fit well in the tradition of the Finnish university hospitals as centre-pieces in academic education and research.

E.30 *Strategic platforms*. In pursuing one of the above or a combination of two or more of the strategic pathways, BioMediTech, in collaboration with its partners, ought to launch such strategic platforms that would enable a systematic and continuous search for new opportunities. Strategic platforms are constructed for the co-creation of long-term values among scientists, firms, public sector actors and customers. The core is the search for multiple values from many different perspectives and the simultaneous exploitation of the shared knowledge bases as well as the exploration of new knowledge. Hence, a platform is an integrated, systematic and sharing constellation for research, innovation, commercialization and the search for new discoveries. The platforms should involve not only the actors operating in the biomedical field but also such actors who are continuously searching for novel opportunities for other, sometimes surprising, fields of activity. These would include, for example, material technology and software scientists and firms. Furthermore, the strategic platforms should not only be local and/or national but also construct attractions for selected main players in the US and Asia as well as elsewhere in Europe.

E.31 *Savvy management teams*. All three strategic pathways, individually or in combination, call for savvy management teams that would be able to integrate individual scientific, business, hospital, care, commercialization and other relevant competencies into mutually supportive sets of competencies.

E.32 *National translational centre for regenerative medicine/human spare parts*. As the resources are limited in Finland, and as there is always a danger of national rivalry between fairly small science, technology and innovation concentrations, Finland might benefit from a centre that would focus on the implementation of new discoveries and existing knowledge into a clinical setting and search for such commercialization models that serve Finnish developments in the best possible ways. In a way, a national translational centre would serve the entire country as a strategic platform or a home base for several more focused platforms. Among the well-known translational centres or programmes is the SPARK programme of the University.

Figure 2-4. From science to the human spare parts industry – three pathways.

![Diagram](image-url)
of Stanford (see About Spark, 2016). The SPARK programme organizes (a) educational programmes and coaching for students and scientists to enhance their capacity to work in industry or in their own ventures and (b) weekly sessions to bring together financiers, industrialists, students and scientists.

**E.33 Specialized training programmes.** There are no degree programmes at the universities in Tampere that are dedicated to educating business professionals with a profound understanding of the dynamics of life sciences or life scientists with adequate expertise in business formation and dynamics. Therefore, it is proposed here that the University of Tampere and the Tampere University of Technology in collaboration should launch an ‘Innovation and Entrepreneurship in Life Sciences’ master’s programme to fill the gap in expertise. Alternatively, the programme could be planned and implemented in collaboration with the strategic partner universities of Eastern Finland, Turku and/or Oulu, or the University of Helsinki. For example, MIT and the University of Harvard have a joint master’s programme in which students study health, biomedicine and business and/or information and communication technologies; many combinations are possible. In Finland, it would be advisable to link degree and other educational programmes to business practices by exposing students to international networks and the main markets, their key actors and the funding sources of Finnish life sciences. Hence, students would be exposed not only to relevant academic knowledge but also to the practices and cultures of those networks that are crucial in their future work.

### 2.6 Generative leadership in the human spare parts ecosystem

In this chapter, the main observations concerning generative leadership in the emergence and strengthening of the human spare parts industry in Tampere are briefly discussed. Leadership, as well as the case, are analysed in more detail in Sotarauta (2014a), Sotarauta (2016) and Sotarauta and Mustikkamäki (2015) (see also Heinonen, 2015; Sotarauta, 2014b; Sotarauta, 2016; Sotarauta & Beer, forth; Sotarauta & Mustikkamäki, 2015).

- **Seeds of change** (the end of the 1990s). The local biomaterial actors began to see the potential embedded in stem cells and tissue engineering in the late 1990s. Two professors from two different universities took the lead in introducing the idea and making new prospects visible. Even though the local science capacity in relation to emerging opportunities was fairly well established in Tampere, at first the local academic community was hesitant to explore new opportunities. It saw the non-explicated ideas relating to new opportunities in stem cell research and regenerative medicine as being too applied and fuzzy and, hence, outside their realm. The two professors did not have the institutional power required to take major steps forward by themselves or knowledge of the policies and processes involved, but they were able to advocate the new potential of the local medical and biomaterial research and hence they were able to launch the process and push it forward. These two professors expressed interpretive leadership but were not positioned to exercise institutional leadership to move forward quickly.

- **Collective belief formation** (early 2000s). The early days of the emergence of regenerative medicine in Tampere barely produced a fresh state of affairs for the first coming of a science-based innovation. By definition, innovation challenges the prevailing social filters and practices and is often born in a climate of ambiguity, uncertainty and a lack of a clear vision (Lester & Piore, 2004). In the case of Tampere, the first movers lacked the capacity to simplify their proposition and convince the institutional and resource power holders outside the scientific core of the future potential of the science in question. For these reasons, policy makers and university leaders did not see the actual innovation through the cloud of scientific argumentation, which was seasoned with the global business noise generated by hype and hope, speculation and fairly hollow rhetoric embedded more in wishful thinking than in factual evidence. Therefore, a shared vision did not begin to emerge, as it did not have social grounds locally into which to put its roots. The formal institutions (the funding system, universities) as well as the cognitive-cultural institutions were not immediately supportive, on the one hand, but there was a local economic development system in place that proved crucial to keeping the process in motion, on the other hand. A local support community external to the academic spheres emerged to support the search for a collective belief initiated by the two professors.

- The support community appeared to be a central force in enabling the motion of the leadership relay. A support community is a group of actors who have a feeling of fellowship with others as a result of sharing common attitudes, interests and objectives in terms of their willingness to assist the process by all possible means at their disposal (see Sotarauta & Mustikkamäki, 2015). In the case under scrutiny, the support community included local and regional economic development actors as well as interested experts from the universities and the Tampere University Hospital. At the same time, the tissue-engineering industry (regenerative medicine) beheld
the progressive global interest and growth in scientific activity and interest in commercial potential (Lysaght & Reyes, 2001). Enthusiasm began to grow in Tampere, and the belief in the local capacity strengthened; fairly quickly, the support community became convinced that it would be possible to aim for a global business. The previous experience of one of the leading professors that this could actually be achieved and his status as a local role model in translating science into practice provided a strong impetus to the process. In all events, the collective belief formation phase saw new actors taking the lead. The leadership relay moved beyond the academic sphere when the support community began constructing a collective belief and a financial base for exploiting the global potential and expanding local opportunities by strengthening the local capacity and resources as well as searching for possible next steps.

- The first two phases were based on the conviction that there actually was a rapidly growing global market to be exploited, but it soon became obvious that the technology was not mature enough and true business opportunities were still too far away and beyond the horizon. Consequently, there was no business and hence no venture capital either; the entire field appeared risky and the enthusiasm started to wane. Indeed, no demonstrable progress was made along a selected path. The support community realized that it was not possible to accomplish the business plan; there were no global business or local business competencies to push this rather unique field forward. Even though the idea was almost abandoned, the leadership relay was not broken, and it was able to carry the idea forward through the difficulties. The local potential was seen as too promising not to be developed further, the feeling of prospective progress prevailed and new paths were actively sought. The discussion moved onto emphasizing both the basic and interpretive and network leadership, which was needed to move, to strengthening the entire ecosystem as a whole and thus the enhancement of competencies. New kinds of interpretive and network leadership are called for to push the relay over the hurdles identified in this report. However, according to the interviews and other data, it seems to be clear that such leadership that would work for the entire ecosystem has not yet emerged, and the focus is still on the scientific core and a few selected measures and networks. In a way, following the institutionalization phase the leadership relay is in an institutional leadership mode, while the next stage calls for a new collective belief regarding

- **Launch of activity** (mid 2000s). The leadership relay was not broken as the key actors were able to learn and reinterpret their beliefs and find new solutions. In the third phase, the leadership relay moved to consist of the research and clinical community. This also meant that interpretive and network leadership, which was so dominant in the launching of the relay and the construction of a collective belief, started to diminish and institutional and resource leadership took the driver’s seat again. The leadership relay moved from the support community back to academia, especially into the hands of the leadership of the university and the director of the newly established research institute. What proved to be important was that the collective belief constructed earlier was enticing enough to attract a broader range of stakeholders. It was now substantially more painless for the resource holders and decision makers to identify the actual potential in the local science capacity. Thus, instead of aiming to establish a business venture, the launch of the activity included three main actions: (a) the establishment of a tissue bank, (b) the eventual establishment of the Regea Institute for Regenerative Medicine and (c) the recruitment of person(s) to lead Regea.

- **Institutionalization** (late 2000s and early 2010s). The actual institutionalization of regenerative medicine in Tampere witnessed breakthrough treatments, the establishment of an institute and further reorganizations of the institute, first within the University of Tampere and later between the two universities. The collective belief constructed earlier provided the actors with solid enough ground to operate on and the issue basically concerned making all the necessary decisions. The institutional leadership exercised by the leaders of the universities became central in this phase. Basically, this report focuses on the latter part of the institutionalization process. The Tampere-based regenerative medicine is successfully institutionalized in the local and national science system but not yet in the health care or the industrial system.

- **Strengthening the ecosystem** (late 2010s). The network and interpretation that were constructed during the first two phases enabled the launching of activity and the institutionalization of regenerative medicine in the science system. Next, the emphasis will move, or perhaps should move, to strengthening the entire ecosystem instead of its core, the universities. This implies the construction of platforms for more elaborate local partnerships and international collaboration. Indeed, as pointed out throughout the report, in this emerging phase of the leadership relay, there is a need to focus on the innovation ecosystem as a whole and thus the enhancement of competencies. New kinds of interpretive and network leadership are called for to push the relay over the hurdles identified in this report. However, according to the interviews and other data, it seems to be clear that such leadership that would work for the entire ecosystem has not yet emerged, and the focus is still on the scientific core and a few selected measures and networks. In a way, following the institutionalization phase the leadership relay is in an institutional leadership mode, while the next stage calls for a new collective belief regarding
how to proceed as well as novel networks for doing so, that is, interpretive and network leadership. For the ecosystem, there is a need to launch a new support community for the construction of a new dominant and collective belief and several cross-organizational, savvy management teams to lead the internationalization, planning for an entrepreneurial hospital and business development.

REFERENCES


3 Regenerative Medicine Cell Therapy Financial Market: How to Finance Potential Innovations

Tuomo Heinonen

3.1 Introduction

In human healthcare, there are four pillars: pharmaceutical, biotechnology, medical device and cell therapy industries (Mason & Manzotti, 2009; Mason et al., 2011). All of them are important, having distinctive core technologies and therapeutic products (Mason et al., 2011). While the others are more matured industries, cell therapy industry is an emerging one. Regenerative medicine (RM) that aims to restore or regenerate human cells, tissues or organs (Mason & Dunnill, 2008) draws from all the industries, but cell therapy industry is especially important. Hopes are great for RM, as it is a third discipline besides surgery and medicine, enabling not only treatment but also regeneration of body parts, hence, opening an avenue for many treatments that were not possible before (Polak et al., 2010). Cell therapy industry and RM depend on academic research and progress of science, and it is important for firms to have an access to high-quality research in academia (Prescott, 2011).

Product development in the RM sector is expensive and time consuming, because products have to go through clinical trials. Product development and firm creation became even more challenging as financing sources of firms changed somewhere in 2005, from venture capitalists, pharmaceutical companies, US stock market and NASA, to public finance, philanthropists and military (Mason, 2007). This change has led to problems with funding, as it is difficult to get venture capital (VC) financing until there is strong evidence from clinical trials (Parson, 2008). In the RM sector, the lack of funding is evidently a big challenge (Johnson et al., 2011). The change also means that universities have to develop potential products further. University-based start-ups and academic entrepreneurs have been studied a lot (Meyer, 2003; Hoye & Pries, 2009; Abramo et al., 2012), and in some studies, potential problems have been identified, e.g., good scientists may not be good managers of new venture (Bower, 2003; Lerner, 2005) and academia, in general, lacks market awareness (Bower, 2003; Johnson et al., 2011). Hence, a viable business environment is beneficial and essential for the successful commercialisation of these innovations.

Motivation for this study comes from challenges the RM sector faces in terms of funding for early clinical trials. It means that in many cases, academia has to manage the research and development (R&D) and subsequent early clinical trials by themselves. This study is based on a case study made in Tampere, Finland, aiming to scrutinise needed competencies and resources in this conquest. In particular, the aim of this study is to scrutinise the RM cell therapy financial market in the global and national level and its effects in the local level. The question is how the university is able to use its R&D efforts for advantage in the RM cell therapy field in order to commercialise developed technologies.

As most of the university-based technologies are transferred in the early phases of development, further development is needed (Jensen & Thursby, 2001). Especially for science-based technologies, a significant amount of R&D is essential in order to find their way to market someday. R&D of these technologies can be conducted in start-ups (Druilhe & Garnsey, 2004) or it can be continued in the form of proof of concept in academia (Gulbranson & Audretsch, 2008; Maia & Claro, 2013; Heinonen, 2015). However, in both of the cases, successful commercialisation of these technologies requires an extensive amount of funding, especially in the case of science-based technologies, like RM cell therapy products. Hence, financial markets and end-users’ acceptance is critical in determining the commercial success of new technologies (Bower, 2003). The RM cell therapy industry is similar to the biotechnology industry, where scientific research produces technological advances (Jensen et al., 2007) and thus, this study uses competence bloc theory (Eliasson & Eliasson, 1996) as a theoretical background, as it emerges from biotechnology viewpoint. Competence bloc provides a set of actors needed for commercial success. However, as this sector is a globally emerging one that lacks funding, product concept must be nurtured in academia.
3.2 Theoretical background

Eliasson and Eliasson (1996) developed competence bloc theory in the early 1990's for the purpose of explaining the development of biotechnology industry. Competence bloc theory consists of actors and their competencies that are needed for sustainable economic development. In the working competence bloc, allocation of resources is efficiently done by two rules: (1) losers must be terminated and (2) winners must be recognised as fast as possible. In this process, entrepreneurs are important actors in competence bloc, because:

- they are in a key position to select those innovations that can be exploited in a commercial way
- their businesses must be scalable so that money can be invested in them with the expectation of a good return of investment.

Other actors in the competence bloc are customers, innovators, venture capitalists and industrialists. In addition, Johansson (2010) introduced the inventor and skilled labourer to the theory. There must also be an environment where venture capitalists and entrepreneurs can expect better profit, i.e., an exit-market. Entrepreneurs, being able to attract venture capital, have to have a potential exit-market as an incentive for both themselves and venture capitalists. An exit for a venture capitalist in this context is through an initial public offering (IPO) or a trade sale. A viable stock market is important, as it allows companies to draw money from an IPO. In the case of a trade sale, the acquirer has the needed resources to continue development. In both cases, the role of industrialist is important, as it brings the product of the entrepreneur to full-scale production. The independent roles of the entrepreneur and the industrialist are important and, in some cases, small firms in the biotechnology sector are more efficient in carrying out discoveries than in-house R&D of large companies (Hopkins et al., 2007).

The role of venture capitalists is critical, as they recognise and fund those entrepreneurs who are capable and competent to make commercially viable products. Venture capitalists use VC, which can be defined as “independently managed dedicated pools of capital that focus on equity or equity-linked investments in privately held, high growth companies” (Gompers and Lerner, 1999: 349; cited in Avnimelech & Teubal, 2006). VC organisation (here, venture capitalists) is an organisation that invests in privately held, high-growth companies between one and five years old (narrow definition) or between one and ten years old (broad definition) (Avnimelech & Teubal, 2006). Then private equity (PE) companies focus on both high growth companies and mature companies, either privately or publicly traded (Avnimelech & Teubal, 2006). It is important for the purposes of a successful technology transfer to identify the appropriate market and create and verify a commercial concept, bridging the gap between invention and product development (Auerswald & Branscomb, 2003). Venture capitalists have an important role, not only in funding businesses, especially in the case of university-based technology. According to Reynolds et al. (2013), in some cases, a venture capitalist combined the IP from different universities and formed the initial team and firm because of seeing the potential for a new technology. However, Hall and Lerner (2010) point out that a VC model has its limits as a solution of funding gaps for regions where PE markets for venture-capitalist exits are not developed.

Regarding emergence of new industry, it is critical to create a needed mass of resources, skills and activities that make it possible to initiate a cumulative process with a strong momentum (Avnimelech & Teubal, 2008). Critical mass of competencies is needed in order to have a sustainable economic success. The customer needs to be active, competent and resourceful (Eliasson & Eliasson, 1996) and innovators find out how to put things together creating the technical aspects of innovation. Finally, a local ecosystem is important for start-ups, because it provides financing, labour and other resources needed. For start-ups, especially in the beginning of growth, quick access to diverse talent and possibility to hire fast is important (Reynolds et al., 2013). However, because of globalisation, it is possible for foreign firms to acquire local companies, and thus, it is a shorter period to leverage R&D in terms of production and associated national economic impact (Reynolds et al., 2013).

3.3 Methodology

Primary empirical data about local ecosystem in Tampere, Finland were gathered in 2014. The Finnish Funding Agency for Technology and Innovation (TEKES) has fostered development of this local ecosystem, as they have funded the Human Spare Parts research program in BioMediTech, which is a joint institute of the University of Tampere and Tampere University of Technology, and which combines biosciences and medical technology from both universities. In this study, a semi-structured theme interview was used as a method to conduct data. Altogether, there were 24 interviews: fifteen interviewees were from BioMediTech, three interviewees were from the University Hospital of Tampere,
and the rest were from local and regional development agencies, the Ministry of Employment and the Economy, TEKES, and a local firm. The focus of the interviews was to obtain an overall understanding about the current RM ecosystem in Tampere and to address the following themes: research environment, finance, entrepreneurship, market, legislation, hospital environment and end-value.

Secondary financial data about investments were gathered from Alliance for Regenerative Medicine (ARM) and Finnish Venture Capital Association (FVCA). There are no regional data available regarding RM, but ARM has moved forward with a global database, and most likely, they have found most of the major RM cell therapy and gene therapy companies in the field. At least it is possible to see the direction of the financial situation in RM cell therapies and gene therapies globally. Data about RM investments were gathered from ARM annual reports (years 2011-2014). As the industry is developing, reports were not yet standardised, and comparable numbers were possible to get only from years 2013 and 2014. However, for the purposes of this study, years 2011 and 2012 were estimated and calculated from known data to be as comparable as possible. Financial data of Finland were received from FVCA, including pharmaceuticals and drug delivery, and drug development technology sectors between 2007 and 2013. Biopharmaceutical sector was excluded here, because it is reported as part of biotechnology sector. Venture capitalists in these sectors are the closest ones who could invest in RM cell therapy firms in the future. Altogether, data included investments (in the case of Finnish investors, both domestic and foreign investments) from three private venture capitalists, three public VC organizations and some amount of non-disclosed foreign venture capitalists.

3.4 Findings

3.4.1 Global RM cell therapy financial market

Ford and Nelsen (2014) studied the change of the life science investor landscape. They link the start-up and seed phase funding to R&D, the next investment rounds to pre-clinical studies, and subsequent investment rounds to clinical studies. According to them, new investors have come to the investor landscape, and among these are family offices, foundations, patient groups and venture philanthropists who are active from the seed investments phase to the strategic partnership phase. Another significant change is that pharmaceutical and biotechnology companies have started to invest already in the R&D stage, and this change is also noticeable in the RM cell therapies, where milestone partnership payments have grown significantly. However, venture capitalists, even though they claim that they are active in early stages, are not often engaging in deals (Ford & Nelsen, 2014). If this is a situation regarding the life science sector, it is even more challenging in RM. However, as RM cell therapy industry develops further, it is advantageous for the companies that the existing investment landscape is more diverse than it used to be. Since venture capitalists are not willing to invest until in Phase II or Phase III, product development depends on other investors.

Nevertheless, the role of venture capitalists is important in the competence bloc. In the case of the emerging RM financial market, the amount of investments have started to grow recently (Figure 3-1), which is promising for the emerging RM cell therapy sector. What is remarkable is that from 2013 to 2014, partnership milestone payments grew from $2.4 billion to $8.9 billion (ARM, 2015). This means that...
pharmaceutical and biotechnology companies also support product development processes in the RM companies. This change is important for the future, because pharmaceutical and biotechnology companies have investment potential, but they are also possible acquirers, acting as industrialists.

Academia is important in the RM sector, not only due to the development of science but because current opinion in the RM cell therapy industry is that it is not reasonable to shift research to companies before there is clear evidence from Phase II clinical trials that the solution is working (Mason et al., 2011). This also means that a significant amount of R&D is conducted in the university environment instead of the firm. Around the year 2005, financial sources changed from VC to public financing, but now private investments seem to be growing again. Focus on commercially successful products (Mason, 2007) may have increased the number of potential products for investments, which is what may partially explain the growth in VC in recent years.

However, the lack of VC in the RM sector has led to a situation where universities should develop product concepts further, and in some cases, even conduct early clinical trials before the product opportunity is possible to transfer to firms and get venture finance for it. Even though the situation seems to be changing, this is still the common understanding among practitioners. Since there is a funding gap for early clinical trials in RM cell therapy, some countries have established RM translation centres to fill this gap and to fund cell therapy clinical trials (Mason et al., 2011). Some examples of translation centres are Catapult Cell Therapy in the UK, the Centre for Commercialisation of Regenerative Medicine (CCRM) in Canada, and the California Institute for Regenerative Medicine (CIRM) in the US. In Finland, the Finnish Funding Agency for Technology and Innovation has funded research translation projects with a dedicated pool of funding, but these projects are more general and do not focus only on RM.

According to Bonfiglio (2014), during the product development, the estimated need for grants is $5-10 million for academic research, and the need for venture investments is $10-15 million for Phase I, $20-25 million for Phase II and $50-75 million for Phase III. Then IPO or partnership deals should provide $75-100 million. IPO is important, because it helps companies to fund the long product development process (Reynolds et al., 2013) but also gives venture capitalists an opportunity to make an exit.

### 3.4.2 Potential Finnish RM cell therapy financial market

In Finland, there are only a few investors in the pharmaceutical and biopharmaceutical fields. Figure 3-2 presents the total amount of investments and the average investment size in the fields of pharmaceuticals, drug delivery and drug development technologies. These fields were chosen for this study, because they show the direction of the Finnish financial market regarding science-based firms that have a long product-development cycle and require a significant amount of money.

As is possible to see, between 2010 and 2013, investments were at a very low level. During this timeframe (from 2007 to 2013), there were three private investors. In addition, there may have been some venture capitalists and VC investments in these categories that are not documented in the statistics. From the documented ones, the only currently active private investor has in its portfolio, pharmaceutical companies, biotechnology companies and medical device companies but in recent years has had very modest follow-up investment rounds in the portfolio companies.
3.4.2 Potential Finnish RM cell therapy financial market

Figure 3-3 presents the distribution of these investments between public, private and foreign investors. Even though the amount of investments is similar between private, public and foreign investors, the public investors' average investment size is only 0.27 M€. In the private sector, the average investment size is 0.74 M€, and the foreign investors' average investment size is 1.23 M€. However, the average investment size does not automatically indicate how much firms actually receive from the investment round, because several investors might have invested in the firm. The overall picture of the Finnish financial market in this sphere is not spectacular and it is crucial for the future of Finland, somehow, to foster the growth in this financial market.

3.4.3 Local ecosystem in Tampere, Finland

The RM cell therapy ecosystem in Tampere is based mainly on the research and product development projects in BioMediTech. There are a few small biotechnology-related firms in the Tampere region, but most of them have no tight linkage with BioMediTech, even though there are some exceptions. In the biomaterial field, some of the companies in the region have been successful, but most of them have not been able to grow further. There are some exceptions, though. In 1997, a company from Tampere had an IPO in New York, and a few years later, another company acquired it. Later in 2004, another company in Tampere had an IPO in London, but later this company had to branch out from the stock market. Hence, there has been some experience with industrial success, but the experience has not stimulated the growth of the local ecosystem. One of the challenges is insufficient funding; hence, potential new business ideas just stay untouched, as there are no resources to push these forward.

In the RM cell therapy field, the strength of BioMediTech is that it is interdisciplinary and combines expertise and competencies from several disciplines. In 2011, BioMediTech got a significant research grant from the Finnish Funding Agency for Technology and Innovation (TEKES) for several years in order to develop novel solutions in different needs of healthcare, focusing on strategic research, which combines both basic research and translational research focus on innovations. BioMediTech chose four technology groups and four stem cell groups for this research program with an aim to develop new therapies, drugs and technologies. Even though new therapies were the goal, along the way, they have developed technologies and tools that have commercial potential as well. Many technological concepts co-evolve with stem cell research, and there is a strong feedback loop in the development of these tools and technologies. Regionally, there have been significant investments in research facilities in BioMediTech and its predecessors, e.g., in the form of the GMP-level laboratory.

The combination of stem cells and biomaterials was an advantage in the Tampere region and for the predecessors of BioMediTech. Based on these strengths, already in 2007, there was a experimental clinical therapy that was based on the early stem cell-based innovations to grow cranial bone and place it into defect sites. These cranial bones were cultivated inside a titanium cage in a rectus abdominis to get blood vessels to grow, too. R&D for this therapy was carried out in academia, and currently there are over 25 treatments conducted within the regulatory framework of an advanced therapy medicinal products (ATMP) hospital exemption without any commercial entities. An ATMP hospital exemption requires that treatment must be a non-routine treatment and conducted under the exclusive responsibility of a medical practitioner. Thus, no clinical trials have been conducted for this therapy. However, because of several treatments conducted under ATMP hospital exemption, there is knowledge about clinical effectiveness. To get this therapy approved and commercialised, first pre-clinical studies have to be conducted with animal models, which take about three years to complete. Then clinical trials must be started, and altogether, over 200 patients need to be involved. After clinical trials, it is possible to get product approval from the public authority. Thus, even though the scientific level is high and real patients have been treated, the path for commercial products is still long.
Scientific research is dependent on public sector grants. In addition to scientific research, there have been many internal projects in BioMediTech that aim to initiate commercialisation of developed technology, tools or therapies and develop a proof of concept for them. The funding for these projects is through public grants received mainly from TEKES. The aim of the proof of concepts is to study market and commercialisation avenues for potential innovation from university R&D. In the case of therapy development, getting financing is not easy, and collaboration with foreign parties is initiated to conduct pre-clinical trials. Even though BioMediTech gets enough funding for pre-clinical trials, it is still uncertain if there will be enough funding for clinical trials. It is also always uncertain if pre-clinical trials or clinical trials will produce wanted results. The advantage for BioMediTech is that they have conducted several treatments in Finnish hospitals and the latest in Tampere, hence, they have been able to get feedback and gain experience.

BioMediTech is a research institute, even though it has a strong commercial aim and an entrepreneurial attitude. However, they currently have no entrepreneurs identified in BioMediTech who could take a product concept and bring it to the market. For those projects that aim for proof of concept development, business experts are employed from outside the BioMediTech. Local firms are loosely connected to BioMediTech, and most of them are very small. In Finland, start-up companies are able to get public financing, but in general, the amount of funding is relatively small, and VC is a scarce resource, as was shown in the previous chapter. In the case of therapies, it is not reasonable to expect that enough financing would be found solely from Finland to conduct clinical trials. Also, there are not many relevant industrialists in the ecosystem that could develop products into full-scale production. Lack of industrialists is a problem, so BioMediTech is forced to find partners from abroad as well. It is critical for the future of the Tampere region that entrepreneurs are able to do IPO and to become large enough to act in the future as industrialists.

In Finland, according to the last chapter’s history data, only a few venture capitalists would be ready to invest in RM cell therapies. If therapy for bone growth is taken, for example, finding financiers who are able to invest in a firm that continues the development is uncertain. The challenge is that it is nearly impossible for BioMediTech to conduct clinical trials for phase III, and it is difficult to find enough investments locally for a firm to continue the development. Another challenge is that there are no entrepreneurs readily available in the RM cell therapy ecosystem that could raise VC for the new company and take R&D efforts with BioMediTech further. Thus, in BioMediTech, the main route for commercialisation of research is seen to be through technology transfer to an existing company, even though partners must be found from abroad. Currently, regarding those product ideas that are not RM cell therapies, start-ups were not seen as relevant partners, as they have no established sales channels. In addition, the potential market for some product ideas from BioMediTech is seen to be too small for them. In the future for upcoming technologies, the situation might be different, even though in these cases, a product is not necessarily an RM cell-therapy product. However, the emergence of potential start-ups and entrepreneurs is necessary if venture capitalists want to start investing in the ecosystem.

3.5 Discussion

The important questions are how European firms are able to grow and especially how university-based R&D can be exploited in the market. Hale and Apotheker (2006) point out the significant difference in the VC industry between Europe and the US: European venture capitalists more often drip-feed VC over several rounds, while in the US, investors are willing to fund firms longer at early phases, which allows time for a company to develop a major product. Even though their observations concerned software industry, similar piecemeal-funding practice seems to happen, at least in Finland in studied pharmaceutical and drug development company investments. Small average investment size means that there may not be enough operating capital for firms. It would be interesting to see what the situation is in the RM cell therapy industry and VC investment between Europe and the US. Financial data of different continents are not readily available regarding RM cell therapy industry.

Competence bloc presents an ideal model of how new businesses emerge from inventions. However, in the case region of this study, this competence bloc is not developed in terms of actors, which implies that resource allocation is not efficiently done. Regarding RM cell therapy sector, innovators produce high-level research and innovations with public grants. Bone growth therapy is even used in public hospitals and has demonstrated its usefulness. Some of the innovations are in the proof of concept phase in academia, but commercial products have not appeared through entrepreneurs. In the region, there are mostly small companies that are not focused on RM cell therapies and are loosely integrated to BioMediTech in this field. Because of this, only a few companies would be potential industrialists for some RM technologies. For RM cell therapies, no potential local industrialists were identified locally. Potential entrepreneurs are not actively identified in BioMediTech, which means that potential venture capitalists have no potential firms to invest. As RM is an emerging field, no venture capitalists are focusing on it. Based on the studied Finnish financial market in the pharmaceutical and biopharmaceutical fields, it is possible that RM cell therapies are not vivid investment
targets anyway, but supporting technologies could be. Lack of entrepreneurs and venture capitalists means that there is no vivid exit-market either, but historically, there are few examples of IPOs in the foreign stock markets.

Another question is if potential RM cell therapy industry is appropriate for Finland. It seems that there is not enough funding in Finland for growth companies in this sphere, so international connections are important. Thus, in the long term, potential RM cell therapies need new investors in Finland for the development of this industry, if this is the desired path for Finland and Tampere to take. In general, the lack of venture capitalists leads to situations where competent entrepreneurs may not be recognised. It is also an important question whether universities will be able to identify commercially potential innovations and develop those further, as universities in general are not commercially competent. Without competent entrepreneurs, it is also impossible for venture capitalists to show up. Hence, the situation is currently in deadlock, and emergence of both entrepreneurs and venture capitalists is needed simultaneously.

3.6 Conclusion

The aim of this study focused on the global RM cell therapy financial market, its corresponding local financial market in Finland and a local ecosystem in Tampere, Finland. This study combines a local ecosystem, national financial market and global financial market, because the whole industry is just beginning to emerge, and there is a limited amount of relevant investors, even globally. Thus, it is important to understand from a local ecosystem viewpoint what the situation of the financial market in Finland is and how it relates to the global financial market. At the same time, it seems to be difficult for the national financial market to develop or grow if there is no viable ecosystem of firms.

It is evident that the global financial market for RM cell therapy and gene therapy is growing lately, including growth in partnership milestone payments that are four-fold, which is consistent with the general change in life science-investor landscape, in which pharmaceutical companies invest in the earlier phases of product development. In Finland, the situation is very different. Venture capital investments and average investment sizes in pharmaceutical and drug development companies between 2007 and 2013 were at a very low level.

From a science and technology point of view, the RM cell therapy industry is fascinating and full of promises. However, locally it is difficult to have start-ups in RM cell therapies, as needed financing is enormous. Thus, partnership with established companies seems to be one of the only possibilities to develop these university-based technologies and commercialise them. In the in long-term there is a need for investments in firms in the local ecosystem to develop it further and achieve sustainability through growth of these companies. As RM cell therapy products must be developed in academia longer, it should be financed, somehow. As these investments are mostly national, emerging firms should also be viable and able to raise funding from financial markets so that national investments in university R&D will return to the economy. However, the financial market in Finland is not highly supportive, and thus, currently it is not viable to spin out new RM cell therapy companies from academia. To change this, growth in the financial market is highly needed.

<table>
<thead>
<tr>
<th>RM cell therapy in Tampere</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Innovators</strong></td>
</tr>
<tr>
<td>- High level research</td>
</tr>
<tr>
<td>- Developed applications in cell therapy (bone growth), technology and tools</td>
</tr>
<tr>
<td>- Proof of concept development</td>
</tr>
<tr>
<td>- Public financial market</td>
</tr>
<tr>
<td>- Experience from university hospitals (RM cell therapy)</td>
</tr>
<tr>
<td><strong>Entrepreneurs</strong></td>
</tr>
<tr>
<td>- Small companies, not focused on RM cell therapies</td>
</tr>
<tr>
<td>- No potential entrepreneurs identified in BioMediTech</td>
</tr>
<tr>
<td>- Local companies loosely integrated to BioMediTech</td>
</tr>
<tr>
<td>- Financial market does not support emergence of entrepreneurs</td>
</tr>
<tr>
<td><strong>Venture capitalist</strong></td>
</tr>
<tr>
<td>- There are not specialised venture capitalists</td>
</tr>
<tr>
<td>- Limited connections abroad</td>
</tr>
<tr>
<td>- Limited amount of VC available</td>
</tr>
<tr>
<td><strong>Exit market</strong></td>
</tr>
<tr>
<td>- In history a few IPOs in London and New York, even though not in RM cell therapy field</td>
</tr>
<tr>
<td><strong>Industrialist</strong></td>
</tr>
<tr>
<td>- Few (if no) relevant industrialists in the local ecosystem</td>
</tr>
<tr>
<td>- Partners have to be sought from abroad (EU, USA)</td>
</tr>
</tbody>
</table>
REFERENCES


4.1 Introduction

Cutting-edge science is particularly interesting, because, as W. Brian Arthur points out, it discovers new phenomena, all of which, in principle, have the potential to be harnessed to create an effect. Unfortunately, knowing in advance which effect will have commercial application is always uncertain and the more basic the research (closer to discovery) is, the more difficult it is to know which research-discovered phenomena will have commercial application and, if there are applications, where they will be and how significant they will be, that is whether the scientific understanding can be transformed into a technology and business opportunity. These are the existential questions that should and do concern researchers, science policy makers, venture capitalists, and potential entrepreneurs. Moreover, all of these decisions are always buffeted by the vagaries of politics, emotion, hope, and hype.

Commercializing new research technologies invariably requires repurposing existing infrastructures and institutions or, what management scholars term “complementary assets” and, sometimes, constructing new ones (Hargadon & Douglass, 2001; Teece, 1986). This paper examines the efforts by a wide variety of actors, with remarkably different motives for commercializing human stem cell (HSC) technologies. As with many new technologies, HSC has both supporters and detractors, and was, almost immediately, from its inception embroiled in a political struggle regarding the use of human embryos as research and potentially as inputs to production. While the controversies over human embryonic stem cell (HESC) research attracted the greatest attention, HSC research, which has a long history, as a whole, became a topic of interest to the general public, health research advocacy groups, investors, and, of course, the stem cell researchers, themselves.

It is now accepted that new technologies can disrupt old industries and even lead to regions developing entirely new industries. Perhaps, since the formation of the biotechnology industry, scientists meeting social resistance have increasingly found it useful to appeal to the commercial potential inherent in their research (Kenney, 1988) to overcome that resistance and appeal for more government funding. In recent years, a number of new technologies have been heralded with enormous hype regarding their disruptive potential (Brown, 2003; Geels & Smit, 2000). It has been observed that with the increased interest in the commercialization of basic science the announcement of scientific success in news media has been used to improve funding or IPO chances for a startup. (Cooke, 2004). While some of these hyped technologies have been successfully commercialized, others, such as superconductivity and cold fusion failed to have the promised impact. Despite the interest, there have been remarkably few ex post evaluations of the results of what often have been major allocations of public funding to these highly promoted research fields.

Today, policy-makers and others are vitally concerned with the economic impact of scientific research. University research particularly in biology and engineering has been an important contributor to development of regional technology clusters and for some jurisdictions such as the state of California are important sources of jobs and taxes. One of the most controversial hailed, reviled, and hyped technology developed in the last three decades is human stem cell (HSC) science (Benjamin, 2013; Thompson, 2013). HSCs are particularly interesting because governments globally came to believe that HSCs had fantastic therapeutic and economic potential and, as a result, have made massive investments in what was still a very basic technology (Salter, 2007).

This paper uses California as a case study to examine the tenets of such a targeted local science policy, the fit of HSC technology with the current biotechnology commercialization model, the ability of government initiatives to create markets, and the economic geography of private sector investments in stem cell commercialization. In the first section, we briefly review the history of HSC science...
and discuss California’s Proposition 71 that led to the creation of the California Institute for Regenerative Medicine (CIRM), which was formed with the express purpose of accelerating the development and commercialization of HSC science. The next section uses a value chain perspective to the difficulties of SC commercialization when compared to traditional biotechnology. This is followed by a brief description of the methodology used to collect the data presented. The economic measures are meant to measure the impact CIRM has had on HSC research and commercialization in California. The section begins by measuring the furthest most upstream with the possible effect on NIH funding. This is followed by examining SC patenting, SBIR funding, venture capital investment, and then ending with clinical trials. There are not yet any therapies on the market. The geography of SC commercialization is compared with that of existing biotechnology industry to see if there are any apparent differences. The discussion reflects upon the lessons regarding the impact of CIRM and the difficulties of governmental entities face when evaluating investments based upon hype and blue-sky promises from researchers. In the conclusion, we suggest further promising avenues for research.

4.2 The Historical Context

Interest in biological approaches to creating body replacement parts can be dated back to the 1930s, but it was only in the 1970s that research increased significantly. By the late 1980s, the term “tissue engineering” came into usage as the belief that it might be possible to produce living replacement “parts” grew (Nerem, 2010, 1). The term “stem cells” has a long history first being used in 1868 to describe the origin of multicellular organisms for a unicellular organism (Gallicano, no date), but fixing a single date for the discovery of SCs may be impossible due to the enormous variety of SCs in the body – a variety that complicates the delineation of the “stem cell” industry. By this definition, human embryonic stem cells (HESCs), which have received the greatest attention, are only one of the many types of SCs that have received commercial attention. In this paper, when studying commercialization we will include all SC-related firms and clinical trials, though much of the discussion will focus on human pluripotent SCs, of which because HESCs have received the greatest attention and promised the most radical new therapies.

During the 1970s and 1980s, there was significant progress in research on manipulating animal embryonic stem cells particularly those of mice and there was very little controversy. With the progress in animal embryonic research, there was a natural curiosity with whether the discoveries were applicable to humans and, by extension, could lead to human therapies. Of course, to extend the research to humans it was necessary use human embryos. In the United States, the use of human embryos became entangled in the religio-ethical debates concerning abortion and at what point a fetus should be considered a human being. In 1998 University of Wisconsin researchers funded by the California firm, Geron Corporation used fetal cells to clone HESCs. These embryonic SCs in theory could be grown in vitro into any other cell or cell mass such as organs. The promise of replacement organs or cells appeared to be within reach.

And yet, research using human embryos was soon caught up in the ongoing abortion controversy. In response to the impassioned reaction of anti-abortion activists, in 2001, then President George W. Bush announced more stringent limits on Federal research funding using human embryos. One stipulation in particular was especially vexing, namely federal funds could no longer be used to fund research on newly developed cell lines – the logic was existing cell lines were excluded because those embryos had already been destroyed, but no funds would be granted in the future to destroy embryos.

President Bush’s action raised a firestorm of controversy in the scientific community that claimed this was an attack upon scientific freedom. The alluring promise that HESCs that could be grown into any type of cell gave rise to the belief that a new era of "cellular therapy" was imminent. Particularly, in states where for many other reasons, Bush was already very unpopular there was significant potential for backlash. In California, a coalition of HESC researchers, patient advocate groups, Hollywood actors, and investors secured a sufficient number of signatures to get a proposition (Benjamin, 2013)3, which came to known as Proposition 71, on to the November 2004 ballot. Proposition 71 was passed with almost 60% of the vote.

The proposition mandated the formation of a California Institute for Regenerative Medicine (CIRM) with the authority to issue $3 billion in state bonds4 over 10 years to fund SC research and develop and commercialize the results. The distribution of grants began in earnest in 2007. The research field to be funded by the state was narrow and unequivocal. There could be no reallocation, if more promising fields of biology emerged, even within the larger regenerative medicine and stem cell fields there would be no flexibility. CIRM was designed by SC researchers and their supporters to optimize their own agenda. Proposition 71 stated that it

3 For a discussion of this campaign and the compromises one of the leading stem cell scientists made to advocate and secure passage, see Goldstein (2010, 2011).
4 The actual cost in terms of interest and principal would be approximately $5 billion.
would, “maximize the use of research funds by giving priority to stem cell research that has the greatest potential for therapies and cures, specifically focused on pluripotent stem cell and progenitor (code term for “embryonic”) cell research among other vital research opportunities that cannot, or are unlikely to, receive timely or sufficient federal funding, unencumbered by limitations that would impede the research.” While SC researchers and others knew that any benefits were far in the future, the Proposition 71 text claimed that that HESC research would result in a wide number of therapies for numerous ailments and that enormous benefits in terms of health care savings and the creation of a new industry would accrue to California.

4.3 The Stem Cell Value Chain

In the U.S. context, newly developed health therapies are commercialized by firms. Of course, as many scholars have pointed out, the research is almost invariably funded by the federal government (Block & Keller 2009; Mazzucato, 2013), and this is particularly true in the case of the biotechnologies (for an early discussion, see Kenney, 1986). What this means is that in the U.S. (and most of the OECD nations) private investors, be they financiers, most often, venture capitalists, or large pharmaceutical firms must be convinced that there is the opportunity of significant financial returns or they will not invest the necessary capital to develop the invention. If a new technology requires a new value chain, then it will have to be assembled prior to successful commercialization. The difficulties that SC firms face in commercialization can be understood when compared to the traditional biotechnology small molecule value chain. This is illustrated in figure 4-1, which depicts a stylized product development value chains for a biotechnology and stem cell product. As with any new product, in particular, class of products, a value chain must be assembled. To illustrate, in 1973 when the first article was published showing that DNA recombination was possible, a controversy about its possible dangers broke out almost immediately (Krimsky, 1982). Genentech, the first recombinant DNA firm was established in 1976 during the controversy, but rather rapidly the controversy subsided and what became the biotechnology industry was formed (Kenney 1986). While the economics of the industry have been criticized (Pisano, 2006), a significant industry with a particular economic and financial model was created (Padgett & Powell, 2012). As the upper panel in Figure 4-1 shows there is a funding sequence that, if the small startups are successful ends in an acquisition by big pharma, or, much more rarely in an IPO. There is a now a known and accepted format for drug approval and, in general, insurance companies with pay the doctors and pharmacy for prescriptions. Of course, this infrastructure did not exist in 1976, but the success of Genentech and other firms provided the financial rewards that permitted the creation of the model – a model that over time would transform the pharmaceutical industry to one in which research was increasingly done in universities and then commercialized by a venture capital-financed startup, and ultimately many of the successful startups were acquired by a big pharmaceutical firm (see, for example, Rothaermel & Deeds, 2004).

The HSC industry, thus far, has been conceptualized by the participants as being similar to the biotechnology value chain. Thus far, there have been a few SC firms that have been able to raise large amounts of capital, conduct an IPO or experience a successful acquisition. The literature has identified a number of obstacles to building a successful industry. A new industry that cannot mimic an existing well-understood industry has greater difficulty. To do this, HSC firms have tried to use the biotechnology university spinoff model to raise capital and build their firms. The university spinoff model is predicated upon investors seeing a significant return on their investment. Unfortunately, HSC technologies have not provided significant returns to these investors. For example, Dodson and Levine (2015) examine seven cellular therapies and despite large investments, none of them have provided significant returns.

The difficulties can be grouped into three categories that are illustrated in Figure 4-1 and, unfortunately, the problems interact in ways that may make them intractable. The first issue is the lengthy development period that is the case for all pharmaceuticals also applies to SC therapies. During the development period, there is little income unless a sponsor usually an established pharmaceutical firm, can be found. Not surprisingly, the private investors to such a high-risk development process demand out-sized returns so that the income from the successes can cover the failures. These speculative undertakings require that investors believe that there is a future return – in a quite distant future. Hype and excitement can affect investors’ decision-making processes, but in the longer term, there must be visible returns to encourage a continuing flow of capital.

---

5 Charis Thompson (2013) points out that the initiative backers used “progenitor,” because they were trying to avoid the politically charged word “embryo.”

6 CIRM has expended significant funds on training grants, clinical trials, and various other downstream activities that are normally funded by the private sector.

7 In return for funding, the large pharmaceutical firms receive various rights to any drugs that may be developed at concessional prices. Unless extremely well managed, these rights limit the possible returns for the startup.
The HSC industry, thus far, has been conceptualized by the participants as being similar to the biotechnology value chain. Thus far, there have been a few SC firms that have been able to raise large amounts of capital, conduct an IPO or experience a successful acquisition. The literature has identified a number of obstacles to building a successful industry. A new industry that cannot mimic an existing well-understood industry has greater difficulty. To do this, HSC firms have tried to use the biotechnology university spinoff model to raise capital and build their firms. The university spinoff model is predicated upon investors seeing a significant return on their investment. Unfortunately, HSC technologies have not provided significant returns to these investors. For example, Dodson and Levine (2015) examine seven cellular therapies and despite large investments, none of them have provided significant returns.

The difficulties can be grouped into three categories that are illustrated in Figure 1-4 and, unfortunately, the problems interact in ways that may make them intractable. The first issue is the lengthy development period that is the case for all pharmaceuticals also applies to SC therapies. During the development period, there is little income unless a sponsor usually an established pharmaceutical firm, can be found. Not surprisingly, the private investors to such a high-risk development process demand outsized returns so that the income from the successes can cover the failures. These speculative undertakings require that investors believe that there is a future return – in a quite distant future. Hype and excitement can affect investors.

7 In return for funding, the large pharmaceutical firms receive various rights to any drugs that may be developed at concessional prices. Unless extremely well managed, these rights limit the possible returns for the startup.
For any new technology there are obstacles to adoption. In the field of medical products there are regulatory authorities that have standardized approval processes for therapeutic molecules and mechanical medical devices. However, cellular therapies, of which SCs are a type, require injecting or using living cells in human beings, thereby creating significant complications. Because of the differences between traditional biotechnology drugs and SC therapies, the approval protocols are still unclear. Without approval the new inventions cannot be marketed (Dodson & Levine, 2015; Rao, 2011). Because very few SC-based therapies have been approved and there are few on the market, the regulatory process has not been normalized creating greater uncertainty for investors.

While it is natural to see the invention progressing through stages that eventually lead to approval, manufacturing and usage, at each stage progress to successful introduction can be stymied. Ultimately, usage, which means sales are critical for the success of any product. If there is no market or costs exceed the sales price, then in a capitalist system; the product has no value and the market is signaling that the producers should stop. In the U.S., the market decision is largely left to Medicare and private insurers. Prior to discussing this, it is important to consider how prices for a pharmaceutical product are set. As we have shown, there is a long development cycle for pharmaceuticals, during which, in most cases, there is little income and thus the expenditures are capitalized. Eventually, the product must be manufactured. SC products are different from biotechnology pharmaceuticals as the SCs must be grown in vitro. Because this is also a new technology, at least initially or until it becomes standardized this is likely to be difficult and very expensive. However, it is in the promise of SC therapy that a conundrum emerges. The pharmaceutical industry is based upon the production of large quantities of extremely standardized products and dosages. Growing living cells for insertion or application to human beings is extremely challenging and thus costly as it is necessary to ensure that their function is entirely predictable as complications could be catastrophic. Thus mass production may not be possible and is likely to be expensive. Moreover, if the cells are mass produced they will have to be transported from the patient to the factory and then back again – a serious logistics challenge. Alternatively, the production can be at the treatment site, but then the advantages of centralization, economies of scale, and specialization will be lost.

The true promise of SC therapies is personalized medicine. The drawback is, the converse of the advantage, namely extracting and reproducing an individual’s cells is, almost certain to be extremely expensive as it is by its nature a batch process more akin to purchasing a “bespoke” or hand-made suit versus buying one off-the-shelf. The fit of the bespoke suit is superb, but the cost for most consumers is prohibitive. Even assuming that everyone’s cells will perform similarly in vitro, personalized medicine, by definition, will be costly even if a standardized batch process can be developed. Ultimately, the consummation of the value chain will depend upon whether insurers are willing to reimburse a sufficient number of patients to cover the development, capital, and variable cost of the therapy. One possibility is that the therapies will only become available to the wealthiest able to pay sufficient insurance premiums for the treatments or can bear the costs out-of-pocket.

The final issue that Dodson and Levine (2015) raise is that the medical delivery system is not yet prepared for SC therapies that have different administration protocols than the current system. These range from having a medical system optimized for standardized delivery, the fact that SC therapies are predicated upon living cells and organisms that will be implanted into a person, etc. To illustrate the difference, the biotechnology industry was born predicated upon accepting the existing pharmaceutical value chain, but segmenting it into research-intensive startups commercializing university research (Kenney 1988), it was not a disruption of the entire model. As with any social organization, new innovations are most easily adopted when they fit within the existing system, rather than require it to be transformed.

The value chain for SC therapies today has a number of missing and unstable segments, namely the manufacturing, reimbursement, and clinical segments. These uncertainties reverberate into the upstream segments. For example, if the large pharmaceutical firms are uncertain about the downstream, then they will fund fewer upstream activities at universities and particularly the expensive startups developing these new products. This is important because the current

---


9 In many respects, the necessary strict regulation of good pharmaceutical manufacturing practices forces a lack of flexibility and extreme standardization.

10 As an illustration, the Belgian firm, TiGenix, developed an autologous treatment for knee cartilage repair that was approved by European authorities in 2009. Although a few nations covered it in their national healthcare programs it was not a commercial success generating an expected net revenue of EUR 1m in 2014. One problem is the very high production costs resulting in narrow margins despite a relatively high selling price of EUR 20,000 per procedure (Seeking Alpha, 2015).
biotechnology model operates upon the premise that venture capital-based startups will either be acquired at a high multiple or make a high-multiple initial public stock offerings. Effectively, for the SC industry, there is no established value chain and, as we shall see, due the lack of a clear pathway to profitability, private sector investors are unwilling to invest in building that value chain.

4.4 Measuring the Economic Impact

The premise of most SC research initiatives is not that they will fund science, but that the research will discover new cures. Proposition 71 promised it would make California the center of a new industry. One question is if there was any chance that California would NOT become the center of the industry given its dominance in biotechnology generally. The proper comparison biotechnology cluster is the Boston area. Put in another way, did the massive investment turbocharge commercialization and propel California further ahead of Boston than it would naturally be given the size difference? California’s out-performance on every measure would be the expected outcome.

Since the California initiative only began disbursing funds in 2007, but because SC commercialization was already underway, it is possible to establish a baseline including patents granted, SBIR grants, and venture capital invested prior to this date and then examine whether there has been an acceleration in California versus our control, Boston. The two controls are activity prior to the inception of CIRM funding in 2007 and the general activity in the biotechnology industry in the three regions. To understand whether a SC industry is being created in California, we examine three spatial indicators of commercialization – patents, SBIRs, and venture capital investing.

4.4.1 Patenting

Patents are an indicator of whether inventors believe they have a commercially interesting technology. One of the difficulties in the SC field is that patents maybe in a wide variety of patent classifications. In the interest of simplicity, we extracted patents from the two most central classifications. We identified 2,391 U.S. SC patents whose priority date was between 2000 and 2013. California led the US with 493 (21%) patents, while Massachusetts had a total of 263 (11%) patents. However, what is more interesting is the change in the number of granted patents filed by year. Beginning in 2000 there was a dramatic increase that peaked in 2006 right when CIRM was established and then there was another peak in 2008. However, after 2008 there was a significant decline in the number of patents filed suggesting that the research, which was experiencing dramatic increases in funds, was becoming commercially less

Figure 4-2. Patent deposits through time (unit: First priority dates, from 2000 to 2013, family patent filing).
[Source: University of Bordeaux GRETHA, July 2015]

---

11 All of the patent data was collected by the University of Bordeaux Gretha researchers.
12 c12N 5/00 Undifferentiated human, animal or plant cells, e.g. cell lines; Tissues; Cultivation or maintenance thereof and cCulture media therefor. A61K 35/00 Medicinal preparations containing materials or reaction products thereof with undetermined constitution.
interesting. While California continued to be the national leader, it also experienced a marked decrease in patenting despite the fact that CIRM dramatically increased funding for California researchers with stated intention of supporting commercialization. California patenting experienced a greater drop than did the national level. There are a number of possible explanations. The least likely is that CIRM itself through its funding decisions discouraged patenting. More likely and of far greater concern is the possibility that fewer researchers, entrepreneurs, and firms see commercial opportunities in the SC field. From a scientific perspective, this is not a problem. However, this would invalidate the claims of Proposition 71 proponents that the income from SC inventions would defray the state's investment. Either the technology remains too young or the other possibility is that it simply will not produce commercializable and thus beneficial therapies. Either way, the result is a cause for concern.

It is possible that patenting in biotechnology as a whole slowed down and therefore SCs were simply reflecting a more general pattern. For this reason, we examined the national and California situation in the larger patent (435) class containing all molecular and microbiology patents. Patent class 435 is central to biotechnology industry and thus very close to SCs. The pattern does exhibit a slowdown beginning in 2000, but after 2009 patenting increased significantly. This suggests that secular decline in SCs is not part of a more general phenomenon, but unique to SCs. Patents are one of the earliest commercial stages, in the next section we turn to a next step to commercialization, SBIRs.

4.4.2 Small Business Innovation Research Grants (SBIRs)

SBIRs are a widely used source of funds for fledgling firms to support initial operations. For entrepreneurs SBIRs are particularly attractive because they are grants and thus non-dilutive. Research suggests that firms receiving SBIRs have superior performance to control groups (Audretsch et al., 2002; Lerner, 1999). SBIRs are particularly useful for academic scientists forming biomedical firms (Toole & Czarnitzki, 2007). Because SBIRs fund early-stage firms and frequently the firms are formed by academic scientists, they are early indicators of commercialization initiatives and provide an earlier indicator than venture capital funding.

There has been little research on the spatial aspects of SBIR grants. In one of the few articles, Rosenbloom (2007) found that in both per capita and in absolute terms, SBIRs were concentrated in a few cities especially Boston, Denver, New York, San Diego, San Francisco, and Washington, DC.

Mirroring both the spatial distribution of all SBIR grants (see below) and SC-related NIH funding and other indicators, SC-related SBIRs were concentrated in San Francisco (41), Boston (37), and San Diego (28). From 1998 to 2014, the number of California SC firms receiving their first SBIR grew at a CAGR of 8.71%, while the national growth was 8.17%, but Boston was only 1.01%. This suggests that California entrepreneurs continued to establish SC firms, whereas Boston researchers, as measured by SBIRs, slowed commercialization efforts substantially.
In terms of all SBIRs, California was the national leader. Further, California’s share of US SBIRs grew more rapidly than the national average, thereby increasing its national share. From 1998 to 2014, California SBIRs grew at a faster rate than the national average. Of course, SC SBIRs began from a very low base and should be expected to grow more quickly than the total SBIRs. CIRM may have contributed an increase in the knowledge base that encouraged SBIR formation. To be certain of this, it would be necessary to examine each SBIR in detail to ensure that it is related to CIRM. In the final analysis, the recent small increase in SBIRs is difficult to interpret, and could also be a response to the lack of venture capital discussed in the next section.

4.4.3 Venture Capital-Financing

The U.S. biotechnology industry was, in some respects, made possible by the availability of venture capital (Kenney 1986; in particular, for the centrality of venture capital in the San Francisco Bay Area and their role in San Diego, see Powell et al., 2002). The ability to transfer biomedical technology from U.S. universities was dependent upon having a set of financiers that were willing to take significant risks with unproven incipient technology (Thursby et al., 2001). More recently, because of the changes in the pharmaceutical research, development, and production value chain, the role of venture capital investment has become of even greater importance. Big Pharma has dramatically decreased its investment in research and even development preferring to purchase small venture capital-financed firms or license new technologies from inventors, either way this often commercializes a university invention (Kneller, 2010; Rafols, 2014). These changes suggest that venture capital-financed firms have become a critical link for the eventual commercialization of a treatment.

Stem cells have received a comparatively small amount of venture capital funding. As Figure SC Funding shows, in the 2000s California SC firms were quite successful when compared to other states. But after 2008, California’s share of total SC VC funding appears to have decreased—not what one would expect due to California researchers having greater resources than other states. The data also identifies two peaks in investment, which were also peaks of hype about SC promise. The first peak was in 2000, two years after the announcement of HESC at the University of Wisconsin. The other peak was in 2005, immediately after the hype that surrounded the effort to pass Proposition 71. However, the VC market is self-correcting and after a drop in 2006 and 2007, investment collapsed and in 2012 and 2013 there was no VC investment at all. While investment has been scattered nationally, San Francisco (21), Boston (17), San Diego (15) are the home of the largest number of venture capital-funded SC firms.
As a control, we examined whether venture capital financing for biotechnology in general decreased and therefore the decline in SC funding was part of a more general trend. When we compare SC venture investment to the total in biotechnology, it is clear that it is insignificant. This is of policy relevance, because it suggests that Proposition 71 directed funds into a field that was not an area of significant economic interest and despite the massive investments is still not of economic interest. As Figures SC BT VC show, there was a decline in VC financing for biotechnology nationally and in California after 2007, probably due to the financial crisis. And yet, funding increased significantly in 2014, while SC investment did not respond to the uptick. The data indicates that the world’s most savvy investors in new biological technologies show little interest in commercial opportunities emanating from SC research.
4.5 Discussion

Since SC research continues to progress and it is inherently impossible to predict the outcomes of basic research, this discussion and summary of what we know is provisional. There was a unique moment of fear that HSC research would be handicapped during the early 2000s, but this quickly proved not to be the case. There were wild claims that other nations such as Singapore, Korea, Japan, ad infinitum would soon surpass the U.S.; none of which would prove to be true. However, CIRM was one of the lavishly funded experiments in sub-national technology policy in U.S. history and therefore can help us sort out the impacts of such initiatives.

For any science policy that envisions commercialization as a result, understanding the technology in an industrial value chain should be a first step. If the technology is likely to fit in an existing value chain, then it is more likely that commercialization will be predictable and rapid. If, however, like SCs it will require constructing a new value chain, adoption speed is likely to be slowed. As a result, if commercialization is even possible, it will take longer and require more capital. Depending upon the degree of increase, the technology may be prohibitive for existing commercial funding agents such as venture capital.

The record in terms of patents was interesting. Despite increased funding from CIRM and reinforced by the Federal government, the number of patents decreased, even while the biotechnology patents nationally and in California increased. This suggests that despite increased funding, the knowledge that researchers believed could be commercially valuable decreased. Whether this is an indicator of decreasing returns, an evaluation by knowledgeable parties that there was not significant commercial value in the research results, or some other factor; because patents would be the first indicator of commercialization, we see little evidence of success as measured by increasing numbers of patents that could signal greater interest in SCs.

The next step in commercialization is raising financial support for spinoff firms – this is particularly important in SCs, because established pharmaceutical firms are doing little commercialization. We measured two funding mechanisms, SBIRs and venture capital funding. We found some evidence that there were more SBIRs founded in California, it is difficult to attribute this to CIRM and the overall number were quite low. Venture capital investment in SCs has completely collapsed throughout the U.S., but particularly in Boston and California. Effectively, in two markets with the most sophisticated venture capitalists, the investment decreased the most. CIRM appears to have had no impact at all on building an active venture capital-funded cluster of firms.

Given the unproven value chain for SC products, it is not surprising that the now nearly $2 billion dollars expended by CIRM has not had any discernable commercial impact. Of course, CIRM continues to fund SC research and increasingly is responding to the market’s lack of interest in commercialization by moving further down the R&D continuum. Unfortunately, as it does so it must make progressively larger investments and contract with organizations from outside California thereby reinforcing them. The risks will grow commensurately, and if there is little success, then research will be truncated for no apparent gain.

Thus far the massive investments by both CIRM and the federal government have had few commercial outcomes. Were it not for the extravagant claims and massive investment, it would natural to conclude that it is still quite early to expect significant results. However, the unwillingness of the venture capitalists to invest in the technology hints that the technology is either far from significant commercial results or more worrisome SCs will not yield significant commercial results. If this were the case, California taxpayers would have made a very large wager and received little return.

4.6 Conclusion

In recent years, national and sub-national governments and, in the case of California convinced the electorate, that various newly announced “scientific breakthroughs” could lead to cures for disease or initiate significant economic growth. CIRM was the largest and most ambitious of all such sub-national programs and was fed by a belief that hESC offered the potential for “miracle” cures and would lead to massive economic benefits for the state.13 It is far too early to conclude that the CIRM project is a failure. However, it is not too early to draw some tentative conclusions.

On a more speculative note, Proposition 71 was launched early in the development of HESC technologies. The sponsors appear to have been convinced by a group of researchers that HESC technology was the best strategy for producing therapies. This is a remarkably early picking of winners, thereby precluding a more diversified investment strategy. Moreover, there was a clause stating that CIRM would favor hESC research. Whether this encouraged California researchers to go down the HESC path and discouraged research on animal models and HiSC technologies is uncertain, but it raises the question of whether setting research priorities on the basis of hype and anti-George Bush sentiment is a wise strategy.

13 After passage, there were already a number of economic analyzes that were quite skeptical of many of the economic promises made by supporters of the initiative (Noll, 2006; Gilbert, 2006).
From a policy perspective and an interest in advancing biomedical science and human therapies the selection of a single unproven technology made little sense. Selecting a single winning technology on the basis of emotion, politics or anti-politics, and the bold claims of self-interested scientists is risky. This type of target selection is even more risky when the technology is still very basic and the direction of progress is still unknowable. Promising favorable economic outcomes is particularly rash so early in the life-cycle of a research field. For policy-makers, it is important to carefully evaluate all claims from activists and academics.

Technology commercialization is under all conditions difficult and generally should be undertaken by commercial entities. In cases where massive public investment is targeted at producing real-world therapies, it would seem particularly important to consider whether there are complementary assets that could be mobilized to facilitate commercialization. If there are no such assets or pathways to commercialization, then even interesting results are likely to languish unused. CIRM’s response has been to try to build these assets and assemble a supply chain – an unusual and risky strategy for public entity.

A final consideration, from a policy perspective, is whether such a massive influx of capital in a specific research field creates field-specific assets that cannot be easily redeployed, if and when, funding for that specific field declines or ends entirely. The biomedical sciences as a whole are facing exactly this situation, as federal funding stagnates and may, in fact, decline (Alberts 2014). SC research is likely to face a similar situation if Proposition 71’s funding is not renewed. In the case of SC, with its training programs, targeted at producing real-world therapies, it would seem risky. This type of target selection is even more risky from a policy perspective and an interest in advancing biomedical science and human therapies.

REFERENCES


5

Venture Capital Ecosystem in Finland – Fragile and Thin

Pasi Sorvisto & Markku Sotarauta

5.1 Introduction

Finland has been among the most competitive countries for some time, according to the World Economic Forum (2015) and the IMD Business School (Pajarinen & Rouvinen, 2014). Finland’s economic competitiveness is based on a relatively small number of large corporations, and thus, Finland is not only competitive but also vulnerable. It has been argued that a versatile business sector with several strongholds and a vibrant start-up scene significantly strengthens both the competitiveness and resilience of any country. In the many efforts to boost economic performance, a venture capital ecosystem often plays a vital role in securing both of these aims (Lerner, 2010; Samila & Sorenson, 2011). So far, the Finnish venture capital industry has not been able to support the Finnish start-ups in the best possible way (Saarikoski et al, 2014). The evolutionary perspective on the Finnish economy suggests there may be dynamic system failures blocking the emergence of an efficient venture capital market and associated business development. Therefore, to secure a well-functioning economy in Finland, there is an increased need to focus on the co-evolution of venture capital and the start-up community (see for more, Avnimelech & Teubal, 2006; Avnimelech & Teubal, 2008a; Colombo et al., 2010; Rosiello et al., 2011).

The three interrelated research questions addressed in this Chapter are: (a) How has the Finnish venture capital (VC) ecosystem performed in 2007–2014; (b) what are the main bottlenecks in the Finnish VC ecosystem; and (c) what policy recommendations have been raised during the last two decades to boost its performance? This chapter should be read as a summary and conclusion of a broader study to be reported more extensively in other forums.

5.2 Venture finance and innovation ecosystems

Venture finance as a whole comprises several sources and instruments of finance for early stage companies. These include such traditional sources as public grants and subsidies, bank loans, lines of credit, angel finance and venture capital, and non-traditional sources such as crowdfunding. We may call the system of providers of these instruments a venture finance ecosystem. It is generally acknowledged that a well-functioning innovation ecosystem requires competent venture financiers, who recognize the most prominent companies and teams, finance them, bring added value to their management (networks, competencies, etc.), and thereby enable companies and teams to capture the underlying value of their businesses. Understanding how capital markets affect the growth and survival of nascent firms is among the central questions of venture finance. The promotion of new high-potential business ventures and venture capital are of critical importance to economic growth, as venture capital has repeatedly been shown to be a major contributor to the emergence of new industries and the emergence of highly successful start-ups. It has been observed that an increase in the supply of venture capital affects firm start-ups, employment, and aggregate income positively (Samila & Sorenson, 2011). Financiers indeed play an important role in the selection of winning ideas, products, and services.

The impact of venture capital has been one of the most investigated topics related to financing nascent companies. Venture capital (VC) refers to “the professional asset management activity that invests funds raised from institutional investors, or wealthy individuals, into promising new ventures with a high growth potential” (Da Rin et al., 2013). Venture capital seems also to have a relatively wide positive impact in those regions where venture capital investment activity is high. By using the panel data of the U.S. metropolitan areas, Samila and Sorenson (2011) show that an increase in the supply of venture capital positively affects the establishment of firms, employment, and aggregate income. For their part, Lerner (1999) and Gompers and Lerner (2001) show that there is a strong correlation between the local venture capital ecosystem and the expanding business ecosystem. They also observe that, in the US, from 1985 to 1995 such companies that received the Small Business Innovation Research (SBIR) R&D grants and were located in a VC-active region experienced faster employ-
ment growth than those located in a non-VC active region (Gompers & Lerner, 2001; Lerner, 1999). Luukkonen’s study on Finnish pre-seed and seed stage finance reveals that the Finnish system seems to be better equipped for promoting a diversity of ideas, inventions, and ventures than supporting them to compete in the markets (Luukkonen, 2010).

Venture capital fertilizes the soil where new firms are established, even more so than only the new firms it funds directly, as the expanding venture capital supply increases the possibilities of would-be entrepreneurs to secure funding for their ventures. Moreover, expertise on how to acquire funding and launch a new venture is disseminated inside firms, and also more widely in the local ecosystem. So, the demonstration effects support the establishment of new venture capital backed firms, which again encourages other active individuals to become entrepreneurs.

5.3 Methodology and data

The data used in the study consist of three interrelated sources that are as follows: (1) statistics of the European Private Equity & Venture Capital Association (EVCA) and the Finnish Venture Capital Association, (2) secondary data, and (3) interview data.

Descriptive statistical analysis is based on the statistical data on venture finances from the Finnish Venture Capital Association (FVCA) and the European Private Equity & Venture Capital Association (EVCA), Avera, Finnish Industry Investment (TESI), and the Finnish Funding Agency for Innovation (Tekes). The descriptive statistical analysis focuses on the following: (1) venture capital investments made by the Finnish and European venture capitalists, (2) the total amounts of venture capital raised by Finnish companies, and (3) capital flows to new venture capital funds.

For the analysis of the secondary data on the policy discussions related to the venture capital industry in Finland a dataset on the Finnish venture finance-related studies and evaluations was collected. The dataset comprises 164 reports from 1987 to 2014. To identify relevant reports, we used the search terms ‘venture capital’, ‘VC’, and ‘venture finance’. The reports were collected from organisations that have been actively involved in the Finnish debates on venture capital, the venture finance industry, and high growth venturing as a whole (see Figure 5-1). These organisations are the Ministry of Employment and the Economy and its predecessor, the Finnish Innovation Fund (Sitra), the Research Institute of the Finnish Economy (Etla), the Finnish Funding Agency for Innovation (Tekes), the Ministry of Finance (MoF), and the Prime Minister’s Office. Also, the

---

Figure 5-1. Annual amount of venture capital-related reports in Finland during 1987–2014 by a publishing organization (MEE = Ministry of Employment and the Economy; MTI = Ministry of Trade and Industry; MoF = Ministry of Finance; Tekes = the Finnish Funding Agency for Innovation; ETLA = Research Institute of the Finnish Economy).
Finnish Venture Capital Association (FVCA) was acknowledged as a highly relevant stakeholder in the field, but, as it is also a lobbying organization, its reports were left out from the dataset. We also excluded (a) the financial and annual reports of the selected organizations, as they treat venture finance-related issues only in general terms, and (b) studies focusing on the venture finance market in some other countries. The selected reports represent as comprehensively, professionally, and independently as possible the overall status of the Finnish venture capital ecosystem. These studies also deal with the fundability of the Finnish companies and hence provide this study with an overview of the financial markets more generally from the standpoint of early-stage companies in Finland.

In the interviews, the main aim was to construct an understanding of the state of the art, the challenges of the Finnish venture capital industry in the global context, and the ways public policies and initiatives may enhance venture finance ecosystem. In total, 55 interviews were carried out in Finland, six in the USA, and five in Israel. Interviewees were business executives, venture capitalists, and representatives of public development agencies and the FVCA, as well as innovation and commercialization experts from academic institutions.

5.4 The big picture: The performance of the venture capital ecosystem

According to the statistics of the Finnish Venture Capital Association (FVCA), the venture capital investments made by the Finnish private equity firms have remained roughly at the same level since 2008. They are at a significantly lower level than in 2007, which represents the second highest peak after the short boom period of 2000–2001 (Figure 5-2). Overall, Finland is not alone with its stagnating venture capital ecosystem. It follows European trends quite systematically in the volume of new money raised for the venture capital funds (Figure 5-3).

From 2007 to 2014, the flow of private investments to the venture capital funds has decreased both in Europe as a whole and in Finland. According to the FVCA’s statistics, in Finland, the total amount in 2014 was €63 million, which resembles the figures of the situation after the financial crisis in 2008/09. As a comparison, according to the IVC Research Center (2015), in Israel the respective figure was USD 914 million (appr. €740 million). Additionally, there has been a remarkable downward trend in private investments to the venture capital funds in Europe and even more notably in Finland (Figures 5-4 and 5-5; Tables 5-1 and 5-2). New pri-
Private investments to the Finnish VC funds have decreased tremendously, and thus the share of the government agencies is conspicuously high (Figure 5-6). It seems obvious that Finland has not been able to provide private investors with an attractive landscape to invest in new venture capital funds. The only positive sign is a growing number of private individuals investing in the venture capital funds (Table 5-1).

Figure 5-3. Volume of raised VC funds in Europe and Finland 2007–2014. (EVCA, 2015)

![Graph showing volume of raised VC funds in Europe and Finland 2007–2014.](image)

Figure 5-4. Investors (LPs) to the European VC funds in 2007 and 2014. (EVCA, 2015)

![Bar chart showing investors (LPs) to European VC funds in 2007 and 2014.](image)

<table>
<thead>
<tr>
<th>Million €</th>
<th>2007</th>
<th>2009</th>
<th>2011</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic institutions</td>
<td>0.10</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Banks</td>
<td>13.50</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.20</td>
</tr>
<tr>
<td>Capital markets</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Corporate investors</td>
<td>42.21</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Endowments and foundations</td>
<td>0.00</td>
<td>0.00</td>
<td>12.00</td>
<td>3.15</td>
<td>0.00</td>
</tr>
<tr>
<td>Family offices</td>
<td>1.00</td>
<td>2.44</td>
<td>2.00</td>
<td>5.15</td>
<td>0.00</td>
</tr>
<tr>
<td>Fund of funds</td>
<td>10.33</td>
<td>10.00</td>
<td>20.50</td>
<td>15.50</td>
<td>0.50</td>
</tr>
<tr>
<td>Government agencies</td>
<td>58.43</td>
<td>37.22</td>
<td>55.92</td>
<td>49.75</td>
<td>20.29</td>
</tr>
<tr>
<td>Insurance companies</td>
<td>32.00</td>
<td>0.00</td>
<td>3.00</td>
<td>0.60</td>
<td>0.00</td>
</tr>
<tr>
<td>Other asset managers</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>2.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Pension funds</td>
<td>70.00</td>
<td>0.00</td>
<td>10.00</td>
<td>5.38</td>
<td>0.00</td>
</tr>
<tr>
<td>Private individuals</td>
<td>6.00</td>
<td>0.00</td>
<td>11.50</td>
<td>6.05</td>
<td>16.90</td>
</tr>
<tr>
<td>Sovereign wealth funds</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Unclassified</td>
<td>25.27</td>
<td>7.32</td>
<td>14.30</td>
<td>1.50</td>
<td>24.90</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>258.84</strong></td>
<td><strong>56.98</strong></td>
<td><strong>129.22</strong></td>
<td><strong>89.08</strong></td>
<td><strong>62.79</strong></td>
</tr>
</tbody>
</table>
Table 5-2. Shares (%) of the main investor groups of the investments to the Finnish VC-funds in 2007, 2009, 2011, 2013 and 2014. (FVCA)

<table>
<thead>
<tr>
<th>%</th>
<th>2007</th>
<th>2009</th>
<th>2011</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic institutions</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Banks</td>
<td>5.2</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.3</td>
</tr>
<tr>
<td>Capital markets</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Corporate investors</td>
<td>16.3</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Endowments and foundations</td>
<td>0.0</td>
<td>0.0</td>
<td>9.3</td>
<td>3.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Family offices</td>
<td>0.4</td>
<td>4.3</td>
<td>1.5</td>
<td>5.8</td>
<td>0.0</td>
</tr>
<tr>
<td>Fund of funds</td>
<td>4.0</td>
<td>17.6</td>
<td>15.9</td>
<td>17.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Government agencies</td>
<td>22.6</td>
<td>65.3</td>
<td>43.3</td>
<td>55.8</td>
<td>32.3</td>
</tr>
<tr>
<td>Insurance companies</td>
<td>12.4</td>
<td>0.0</td>
<td>2.3</td>
<td>0.7</td>
<td>0.0</td>
</tr>
<tr>
<td>Other asset managers</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>2.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Pension funds</td>
<td>27.0</td>
<td>0.0</td>
<td>7.7</td>
<td>6.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Private individuals</td>
<td>2.3</td>
<td>0.0</td>
<td>8.9</td>
<td>6.8</td>
<td>26.9</td>
</tr>
<tr>
<td>Sovereign wealth funds</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Unclassified</td>
<td>9.8</td>
<td>12.8</td>
<td>11.1</td>
<td>1.7</td>
<td>39.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Figure 5-6. Government agencies’ share of investments in the European and Finnish venture capital funds from 2007 to 2014. (EVCA, 2015)
5.5 The main bottlenecks: Drip-feeding, piecemeal funding and competencies

As the previous section shows, the Finnish venture capital ecosystem performs below the European average. It is below the average especially in the average size of investments made to target companies (Figure 5-7), which suggests that Finnish companies are suffering from the symptoms caused by ‘drip-feeding’ and ‘piecemeal funding’.

According to Hale (2005) and Hale and Apotheker (2006), ‘drip feeding’ or ‘piecemeal funding’ generate a vicious circle by limiting companies’ operative performance, which again decreases the ability to target major market opportunities, and which for its part decreases the ability to attract talented management (Figure 5-8). If the company has insufficient management competencies, investors become cautious and invest only small amounts in the target companies, and this again reinforces the emergence of a vicious circle generated by piecemeal funding. Piecemeal funding also has a negative effect on the valuation of the company and incentives of the founders (entrepreneurs) of companies. Investors tend to justify small investments by ‘investment risk management’ arguments, but when considering the consequences caused by piecemeal funding, it may well be that cautious risk management is causing exactly what it aims to escape.

If companies are piecemeal funded, ‘drip fed’, they need constantly to acquire new funding from investors. As the top managers of the companies are the ones who need to be personally involved in securing the funding, they end up spending too much time on things other than building up the business and related products and services. Therefore, drip-feeding narrows down companies’ abilities to exploit major opportunities and perform up to their true potential. As a consequence, companies’ valuations are kept chronically low, and the main losers are the founders (entrepreneurs) of these companies but also the venture capitalists themselves. From the founders’ (entrepreneurs’) point of view, drip-feeding may be useful in the short-term, but in the long run, in most of the cases, it may turn out to be harmful. Thus, many entrepreneurs and investors have labelled piecemeal funding as a ‘kiss of death’.

Side by side with issues arising from the vicious circle caused by piecemeal funding, according to our interviewees, an inadequate understanding of the main markets and deficiencies related to venture capital funding are among the core issues related to the future efforts to boost the Finnish economy. In Finland, there is a lack of fundable companies, on the one hand, and the capital raised for venture capital funds is insufficient, on the other hand. Also, the VC fund managers are not competent enough to convince institutional investors to invest in the funds that they manage. Moreover, international venture capitalists are hesitant to invest in Finnish companies without a Finnish cornerstone investor. All too often, Finnish companies are not able to secure a cornerstone investor. Speculatively, the reasons...
for this may be that (1) there are no dedicated venture funds in that specific field, (2) venture capital funds are too small, (3) fund managers do not understand the markets well enough, and (4) there are inadequate networks with the main global markets and thus a limited capacity to add value in the companies.

5.6 The key points of the past policy debate

The debate on how to promote the venture finance ecosystem in Finland has been active since the early 1990s. From 1987 to 2014, altogether 164 such studies or evaluations have been published that focus, one way or another, on the state of the Finnish venture capital industry, and that have been commissioned or produced by official development agencies. The analysis of the secondary data shows that during the last 25 years the main themes, key observations, and policy recommendations have mainly been repeated regardless of the analysts’ background or the agency that commissioned the study or evaluation. Some recommendations have been implemented, but many of them have not been put into practice. It also seems to be obvious that there has been plenty of information providing policy makers with food for thought and action. Consequently, the current situation should not surprise the Finnish policy makers, business community, and venture finance ecosystem; as warned, Finland is performing below the European average, and the role of the public sector in venture capital funds is excessively high. What is surprising is that, given the abundance of analyses and evidence, the corrective measures have been scarce.

In the studies and evaluations focusing on the Finnish venture finance ecosystem, the main recurrent observations are as follows: (a) In Finland, the venture capital markets and industry are small, inward looking, and fairly conservative; and (b) the role of the public sector is dominant. Many of the reports refer to severe deficiencies in the competencies of both financiers and entrepreneurs. The most important recommendation that has been repeated in many of the reports is to construct incentives for private investors for the purpose of having a more vibrant private venture capital market. In spite of the fact that the studies and evaluations have repeatedly highlighted the importance of improving the overall functionality of the private venture capital ecosystem, and especially the importance of incentives targeted at private actors, policy initiatives have fairly largely been targeted at public measures and funding. The main issues in Finland are mainly systemic but, contrarily, the interventions have mainly been focusing on isolated and individual issues. As the descriptive statistical analysis reveals, the Finnish venture finance ecosystem has not developed favourably and, in 2015, the situation corresponds to the overall picture painted in the many warnings presented in the studies and evaluations. The venture finance ecosystem is dependent on the public sector, and the share of private investments is too low, as shown in the previous section.

Over two decades of venture capital-related policy debates, as manifested in the analysed reports, the discussion has repeatedly touched upon the same issues. The most commonly presented ones are as follows:

- Venture capital plays a central role in innovation and business growth; it supports commercialization of innovations and enables companies to grow. Professional venture capitalists may add value to target companies in the form of personal networks and competencies.
- There is no lack of innovative business ideas, but only a few of them can be turned into fundable growth companies. Among entrepreneurs, there is a lack of ambition and competencies for building fundable companies.
- Finland has a small, under-developed, and too domestically dependent venture capital ecosystem. Fixing the situation requires targeted interventions by the government. There is a need to address the systemic failures and work to substantially increase the number of growth companies. All this should be set as the key target of economic policy.
- There is a lack of market driven, specialized private professional services for growth companies as well as competent and internationally connected seed and early stage financiers. Instead, there is a great number of public organizations. Their operations are criticized for being fragmented, non-efficient, and not meeting the needs of growth companies.
- Direct venture capital investments by the public sector have generally been seen as ineffective and expensive. The government should focus on indirect initiatives instead of direct funding. Public interventions ought to resolve market failures by creating favourable conditions and incentives for private investors to invest in venture capital funds and target companies. The poor alignment of incentives, vulnerability to political pressures, and lack of trained investment staff do not justify direct investment by public agents.
• The functionality of a venture capital ecosystem is also dependent on the exit market; venture capitalists need to be able to sell shares of the target firms. Incentives targeted at the private actors ought to include novel policy initiatives that would encourage companies to make initial public offerings or activate them to make acquisitions. Successful exits are the key determinant for a well-functioning VC market. Indeed, public interventions ought to focus on generating favourable conditions for well-functioning exit markets (initial public offerings and mergers and acquisitions).

All said in this Chapter points towards a need to more systematically operationalize the venture funding offerings. Traditional venture capital or R&D models do not fit well enough with the needs of early stage and growth companies. In the UK, USA, and Israel, for example, there are financial instruments that could also provide a model for the Finnish efforts to boost the venture finance ecosystem’s dynamism. These examples could be used in the construction of such operational models that fit as well as possible with the Finnish system and change it accordingly. Moreover, discussion of the competencies and abilities of the venture capital management teams and policy makers as well as ways to construct the required competencies are surprisingly limited in most of the analyses. It may be that the institutional investors (LPs) do not believe in (1) VC fund managers’ competencies to generate expected returns, and (2) target companies’ capabilities to perform in the marketplace. Moreover, it may be that (3) venture capital as an instrument is too illiquid for LPs, or (4) the other investment opportunities are just more attractive for them.

Generally speaking, the public initiatives to solve the identified problems have been narrow in their focus, target ed mainly at public operations and institutions, and targeted less on the systemic issues and providing private markets with proposed incentives. This is crucial, as, in the market economy, the major responsibility for raising new venture capital funds remains on private fund managers, and as the Finnish venture capital ecosystem has undergone major changes during recent years. In 2008, BioFund Management, the largest life science-focused venture capital management company in Finland, having 200 million euro capital under management, was acquired by a Danish firm, Capinordic Group. In 2009, British 3i announced that it shuts down its operations in Finland, and a year later Capman Plc made public that it would not continue with its technology investments. Consequently, Capman Plc significantly reduced early stage investment activities. Moreover, in 2010–2011 Sitra-based spin-off, Eqvitec Partners, (almost 500 million under management) sold its major funds to Verdane Capital Advisors (Norway) and began downscaling its operations. All these changes are reflected also in the investment volumes in Finnish companies, as shown in the previous sections.

5.7 Discussion: From traditional policy-making towards evolutionary targeting?

The Finnish venture capital and start-up ecosystem suffers from several systemic failures, introduced briefly above. As also indicated in the previous sections, many of the deficiencies are well-known, but implementing the solutions presented by a series of commentators over two decades has proven difficult. As suggested by Rosiello et al. (2011), in the many efforts to boost innovation and business ecosystems, the evolutionary perspective instead of the traditional policy-making model might serve future efforts well. Evolutionary perspectives consist of an explicit focus on competencies and not only on financial incentives and formal institutions. Rosiello et al. (2011) maintain:

“…traditional approach to venture capital policy implicitly assumes that a central problem in creating a venture capital market is overcoming pre-existing market failure in the financing of start-ups. It is implicitly assumed that the resulting market equilibrium is a desirable outcome, without consideration for its configuration, size, dynamics of emergence, and the broader objectives of innovation policy. Moreover, it is assumed that ex ante fiscal provisions (capital gains reduction) and institutional changes can push the system closer to venture capital market equilibrium. Both sets of measures seem generally applicable, regardless of the structure of the economy or its institutions. Moreover, any type of economic system, irrespective of its industrial or institutional configuration and stage of development, is expected to react positively to the setting up of new forms of intermediation and/or the eradication of barriers to entrepreneurship.”

While many studies recognize the contribution made by experienced and competent venture capitalists to entrepreneurship (Da Rin et al., 2006), most disregard the construction of competencies and such ecosystems that allow markets and/or industries to emerge and operate effectively. In the design and implementation of VC-policies, there is very little, if any, analysis of the processes linking the mechanisms overcoming market failure with the emergence of venture capital market and its subsequent growth (Rosiello et al., 2011). Becker and Hellmann (2003) maintain that also the poorly developed entrepreneurial skills and culture often cause difficulties. Indeed, one of the weaknesses, not only in Finland but also more broadly in the traditional policy approaches to venture capital, is the absence of analyses of entrepreneurial and fund management competencies. This is exactly why Finnish policy-makers, as suggested in the previous section, also ought to concentrate on generating financial incentives or institutional changes that are targeted at generating more dynamic private venture capital markets and building competencies in the long run.
Lerner (2010) maintains that well-considered public policies can profoundly influence the dynamism of the venture capital markets and related competencies, but he also maintains that many public initiatives are misguided. Lerner (1999) emphasizes that public interventions are justified if the promise is to fix market failures and generate positive externalities associated with the growth of technology-based companies. Regarding the problems faced by European countries, Bottazzi et al. (2004) and Da Rin et al. (2006) emphasize that direct public intervention is a fundamentally misleading approach for closing the funding gap. The optimal scenario is that public support to business R&D and venture capital investments complement instead of supplement each other (Lerner, 1999). This is important, as highlighted by Bottazzi et al. (2004) and Da Rin et al. (2006), who argue that the venture capital market responds to most of the public incentives but typically not to the public attempts to increase the flow of venture capital by direct investments. Even in the most favourable conditions, venture capitalists' entry into the market may require coordinated stimulation by indirect venture capital policy.

Rosiello et al. (2011) point out that even though various studies recognize that demand and supply of venture capital co-evolve, most assume that venture capital demand will automatically respond to public stimuli or institutional changes. Examples from the European countries suggest otherwise; the presence of favourable fiscal rules, institutional settings, and access to stock markets do not automatically generate the desired outcomes. This may be due to the difficulties in harnessing and developing the relevant competencies of venture capitalists and start-up firms and other related agents. Of course, as Rosiello et al. (2013) highlight, co-evolutionary processes differ from case to case as the systems differ from each other significantly; local political dynamics, industrial history, learning capacity, and economic resources are indeed different in different countries, and thus there is a need to be careful with any propositions on easy fixes and one-size-fit all policies.

The long-term ambition of any VC-related policy ought to be creating conditions for such a venture finance ecosystem in which venture capitalists specialize in investing and adding value to companies according to their specialization (Rosiello & Parris, 2009; Sorenson & Stuart, 2001), and hence, the ecosystem would support such cumulative learning, a dynamic process of accumulation of experience, and network contacts, which would upgrade an entire ecosystem up to a higher level (see Kaplan et al., 2004; Lerner, 2002; Zook, 2004). Incentives ought to be related mainly to taxation on capital gains and barriers to entrepreneurship. According to Bottazzi and Da Rin et al, excessive taxation should always be avoided as it potentially reduces investors' motivation to invest. Also, dynamic labour markets and the functioning stock markets for technology-based start-ups drive investments.

All said here highlights the significance of the formation of entrepreneurial, technological, and managerial capabilities as crucial in the generation of ‘investor-ready’ business opportunities (Mason & Harrison, 2003). Once these generic conditions are in place, the flow of venture capital more or less follows the rising demand from start-ups and generates a positive cycle that stimulates the emergence of a more dynamic co-evolutionary venture finance and start-up ecosystem (Bottazzi et al., 2004; Da Rin et al., 2006; Rosiello et al., 2011). What follows is that venture capital policy ought to strengthen pre-emergence conditions rather than immediately aim at establishing a full-fledged venture capital market, and some aspects of this strategy would require venture capital-related rather than venture capital-directed policies (Avnimelech & Teubal, 2006; Avnimelech & Teubal, 2008a). In some cases, for example Israel in the 1990s, venture capital policy aimed simultaneously to trigger and sustain the emergence of both the venture capital market and the entrepreneurial cluster. Indeed, Israel is often mentioned as a prime example of a successful evolutionary targeting of public policies.

The successful development of the Israeli venture capital and start-up ecosystem was quite largely based on the co-evolution of the venture capital system (the supply agent) and start-ups (the demand agent) (Avnimelech & Teubal, 2006). In Israel, there were approximately 300 start-ups in 1992; some of them were of high quality and undertook an initial public offering in the NASDAQ. While they, at that time, represented demand for the services of the future venture capital industry, their presence also signified excess demand. The Israeli government-led Yozma program (an investment scheme for the establishment of new VC funds and management teams) stimulated the supply of VC funds through injections of public money into VC funds of newly created private limited partner (LP) organizations. This signified the beginning of a systemic VC/SU co-evolution process and the emergence of a domestic venture capital market and entrepreneurial high-tech cluster (Avnimelech & Teubal, 2006; 2008a).

A major difference between a traditional equilibrium-oriented policy approach and an evolutionary one is their relationship to inherent uncertainty of global business (McAlfe, 1994). To minimise the side effects of uncertainty and take advantage of the suddenly emerging opportunities, policy-makers ought to be capable of defining such policy objectives and strategic priorities that provide the main private actors with as predictable and resilient playground as possible. In the middle of a mix of uncertain and confusing incidents and processes, the role of public policy is not to add institutional confusion by its own actions but to stabilise it for strategic adaptation and hence work for long-term competence-building instead of short-term gains (Sotarauta & Srinivas, 2006). As Lerner (2002) highlights, venture capital could also be seen as a form of intermediation in a long process of competence building, as there is a need to

77
solve complex (contractual) problems in the field of private equity investors and entrepreneurial ventures in a context that is characterized by high risk, information asymmetries, and moral hazards – inherent uncertainty.

Avnimelech and Teubal’s (2008b) view on evolutionary targeting summarizes the above discussion for the analyses of systemic and co-evolutionary processes in the context of a venture capital and start-up ecosystem. Their model is based on the prior work on emergence and non-emergence of venture capital industries and the conditions for the successful targeting of such industries in a wide variety of contexts. According to them, evolutionary targeting:

"... focuses on triggering, re-enforcing and sustaining market-led evolutionary processes of emergence of multi-agent structures (industries, clusters, markets, etc). A major aspect is leveraging existing successes in firms to promote emergence of such structures. This requires discrete policy interventions directed at varying areas of system/market failure, which make their appearance at different phases of the overall process".

Evolutionary targeting is based on the following notions:

- Implementation of government policy in crucial transition points of market-led development processes may have a significant influence on the effectiveness of market forces.
- In certain circumstances, a major policy objective should be targeted at the emergence of new multi-agent structures.
- Targeting is often based on leveraging the success of key market agents in a particular area.
- Often market-led pre-selection and existence of some capable market forces should be considered as necessary pre-conditions for targeting.
- In order to trigger a cumulative process of emergence, it may be important to assure a critical mass of competent market agents.
- Successful targeting should consider supply, demand, and institutional background conditions and other pre-emergence factors.

(Avnimelech & Teubal, 2008b)

All the notions listed above involves several policies and policy actions related to the multi-agent structures: (1) promotion of pre-emergence conditions to generate policy targeting candidates (variation); (2) determination of relevant criteria for socially desirable multi-agent structures and selection of those to be targeted; (3) identification of system and market failures blocking the unaided emergence of selected multi-agent structures; (4) determination of targeted policy objectives, design, timing, and implementation oriented to triggering (or reinforcing) and sustaining cumulative emergence processes; and (5) termination of targeted support. Multi-agent structures include clusters, sectors, markets, industries, product classes, and other multi-agent constellations (Avnimelech & Teubal, 2008b).

5.8 Conclusion in the form of selected policy recommendations

In Finland, the venture capital-related debates have been active for more than 25 years, and a close reading of dozens of reports reveals that there is a strong evidence base for needed improvements. It is a striking fact that policy recommendations have remained sustainably similar over the years. Consequently, or simultaneously, the Finnish venture finance ecosystem appears to be fairly stagnant and dependent on the public sector.

In sum, the document analysis suggests there should have been an adequate strategic awareness among the Finnish policymakers, who are responsible for enhancing innovation and venture capital ecosystems, of the main bottlenecks of the Finnish venture finance ecosystem and also clear recommendations of what kind of corrective measures might be needed. It seems that the Finnish policymakers, for one reason or another, have not been learning from the experiences of the other countries or experimenting with the policy recommendations that have been presented in the many studies and evaluations: many of those commissioned by the policy community itself.

The recommendations presented here are drawn from the interviews, analysed studies and evaluations, research literature, and policy briefing sessions organised by the EcoLEad –project. Here, only the most relevant of the strategic level recommendations are mentioned. They are not necessarily novel or unique, but the secondary document analysis, statistics, and interviews suggest that they need to be repeated once more.

- A development strategy with two cores. Finland’s venture capital ecosystem is to be developed side-by-side with the start-up ecosystem; they ought to be seen as one ecosystem instead of two separate ones. There is a need to enhance competencies in (1) business formation for global markets and (2) successful management of the venture capital funds in global markets. A competent firm calls for competent and sufficient funding, and money calls for productive and competent targets.
- Integrated competencies. Formation and funding growth and globally oriented business require novel sets of competencies, which again calls for (1) including venture financing among the priorities of the economic development policies in Finland; (2) integrating the core Finnish actors to the leading business and venture capital locations in the world; and (3) introducing the best possible expertise and knowledge of business formation and financing in the higher education institutions, firms, and funding bodies.
Exposing Finnish students, firms, and funding agencies to global markets as deeply and early as possible. To strengthen the competencies in Finland, students and start-up firms ought to be exposed early enough to the operational culture of the global venture capital markets and networks. Exposure enables the construction of mature market understanding, the customisation of services and product offerings to each market in the best possible way, the formulation of competitive strategies, and also the securing of venture capital to exploit novel business ideas. This kind of integrated construction of new competencies is illustrated in Figure 5-9.

Integration of theory and practice. There is no lack of studies and evaluations highlighting the need to enhance business formation and venture funding-related competencies. It would be important to establish degree and training programmes at the Finnish universities that would integrate theory and practice in the same way as is done in the education of conductors, fighter pilots, and surgeons.

Operationalization. There should be initiatives to operationalize funding and business support services novel ways for high potential start-ups and growth companies. Basically, funding instruments and business building services should clearly focus on early stage companies for (1) building the understanding of global main markets, (2) accessing the relevant networks (customers, investors, business partners, etc.) of the main markets, (3) validating the business case, and (4) making the firms fundable for the private investors and financiers.

Incentives. There should be concerted efforts to offer incentives to private and institutional investors to attract more resources to venture capital funds and other instruments targeted at start-ups. Thus, public interventions would also indirectly boost the functionality of the Finnish venture capital ecosystem. Additionally, the double taxation of foreign investors ought to be removed, which continues to be one of the bottlenecks in the Finnish system.

REFERENCES


Appendix 1. The publications produced in the EcoLead project


Publications indirectly linked to the EcoLead project


Blogs


Markku Sotarauta: Kapea Polku pohjoise (3.11.2015) http://www.saunalahti.fi/~atmaso/blog---kapea-polku-pohjoise


Markku Sotarauta: We were warned but chose not to listen (15.1.2016) http://www.saunalahti.fi/~atmaso/blog---kapea-polku-pohjoise/we-were-warned-but-choose.html
Appendix 2. Venture finances in the EU countries as a whole and in Finland in comparison

- **Insurance Companies Share as LPs/Investors to VC Funds**
- **Corporate Investors Share as LPs/Investors to VC Funds**
- **Banks Share as LPs/Investors to VC Funds**
- **Private Individuals Share as LPs/Investors to VC Funds**
- **Pension Funds Share as LPs/Investors to VC Funds**
- **Fund of Funds Share as LPs/Investors to VC Funds**
# Appendix 3. Glossary with definitions and abbreviations for stem cells and regenerative medicine (European Science Foundation, 2010)

<table>
<thead>
<tr>
<th>Term</th>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regenerative medicine</td>
<td>RM</td>
<td>Reconstruction of functionally impaired, diseased or injured tissue by activation of endogenous repair systems or by implantation of exogenous cells or combination products.</td>
</tr>
<tr>
<td>Tissue engineering</td>
<td></td>
<td>An interdisciplinary field that applies the principles of engineering and life sciences toward the development of biological substitutes that restore, maintain, or improve tissue function.</td>
</tr>
<tr>
<td>Stem cell</td>
<td>SC</td>
<td>A cell that can continuously produce unaltered daughters and also has the ability to produce daughter cells that have different, more restricted properties.</td>
</tr>
<tr>
<td>Embryonic stem cell</td>
<td>ESC</td>
<td>Pluripotent SC lines derived from early embryos before formation of the tissue germ layers.</td>
</tr>
<tr>
<td>Foetal stem cell</td>
<td>Foetal SC</td>
<td>Found in blood from the umbilical cord, in the placenta or isolated from aborted foetus.</td>
</tr>
<tr>
<td>Adult stem cell</td>
<td>Adult SC</td>
<td>May be derived from umbilical cord blood or adult tissues, among which bone marrow and fat are mostly used.</td>
</tr>
<tr>
<td>Tissue stem cell</td>
<td>Adult SC</td>
<td>A cell derived from, or resident in, a foetal or adult tissue, with potency mostly limited to that tissue. These cells sustain turnover and repair throughout life in some tissues.</td>
</tr>
<tr>
<td>Induced pluripotent stem cell</td>
<td>iPS cell</td>
<td>An adult somatic cell which is reprogrammed to become pluripotent and behave like ESCs typically, by inducing a “forced” expression of certain genes (including the master transcriptional regulators Oct-4 and Sox2).</td>
</tr>
<tr>
<td>Mesenchymal stem cell</td>
<td>MSC</td>
<td>An adult multipotent cell derived from a well-characterised population that can form fat cells, cartilage, bone, tendon and ligaments, muscle cells, skin cells and even nerve cells.</td>
</tr>
</tbody>
</table>
Tekes’ Reviews in English


328/2016  The Role of High-impact SMEs in Finland. Thommie Burström, Mikko Grönlund and Tuomas Ranti.

322/2015  Patients, business and the state – Translating health information into sustainable benefits. Policy brief for engagement practices in Canada, Finland, Iceland, Spain, UK and the US. Aaro Tupasela, Karoliina Snell and Jose A. Cañada. 51 p.


295/2012  New opportunities for China-Finland r&d&i cooperation. Jani Kaarlejärvi and Matti Hämäläinen.


Subscriptions: www.tekes.fi/english/publications