Stockholm/Uppsala – Strengthening and Enhancing Its Position as an Emerging Neurotechnology Cluster

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Jesper Ericsson

Mikael Nygård

Minrui Zheng

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Abstract

Neurotechnology represents various aspects of analyzing and influencing the nervous system and especially the brain. Given the massive unmet market for brain-related illnesses, the commercial opportunities within the global neurotechnology industry are enormous.

In a recent global ranking Stockholm/Uppsala was considered to be the 10th leading Neurotechnology cluster. In this report we have tried to analyze factors that have been important in establishing this position and tried to pinpoint the most significant current efforts within this cluster today and some of the challenges that the cluster is facing.

Based on literature studies and in-depth interviews we have identified the basic neuroscience research within the region as one of the foundations of the progress of the cluster. This, in combination with the fast growth experienced in the Swedish venture capital market in the last decade, the high quality of the Swedish educational system, and the aggregation of these factors in especially the metropolitan Stockholm/Uppsala region, has determined the progress of the neurotechnology cluster to this point.

Currently there are several initiatives in the region which have the potential of maintaining or enhancing the international competitiveness of the Stockholm/Uppsala neurotechnology cluster. Some big consortia have been formed within specific areas of neuroscience that seem highly competitive, and there are several efforts made to enhance the innovation system on a national and regional level. However, a number of challenges were also identified, the most serious being the draining of academic research with increased costs and lack of public funding. Other major challenges include for example the entrepreneurial climate and financial environment and also the geographical separation between Stockholm and Uppsala, issues which need to be addressed to promote a successful development of the cluster.

Considering the currently existing excellent scientific base and promising initiatives, the Stockholm/Uppsala neurotechnology cluster has a good chance of future success in this global industry, but it is crucial to address the issues raised to be able to stand up to the fierce international competition.

Contents

1 Purpose of the Study

Globalization increases the demands on local economies to adapt and to exploit their local advantages and areas of excellence. Sweden has a unique history of excellence in the field of neuroscience and the Stockholm region was in a recent global analysis listed as the 10th leading neurotechnology cluster worldwide (NeuroInsights, 2005a).

The aim of this study is to investigate the factors that have contributed to the successful development of the Stockholm/Uppsala neurotechnology cluster to see if these factors still contribute and what efforts should be made to preserve, enhance or change them. Future potential factors that may enhance and strengthen the position of the cluster will also be investigated.

We also aim to identify current and future challenges experienced by actors from different branches in the Stockholm/Uppsala neurotechnology cluster and identify efforts that have been made, or should be made to overcome such challenges. In some cases these challenges will be specific for the Stockholm/Uppsala region or the neurotechnology sector, whereas other issues will be of general interest for the biotechnology market in Sweden.

2 Introduction

2.1 The Neurotechnology Industry

The main science and technology fields that are critical in the development of and drive the neurotechnology industry include bioscience, information science, nanotechnology and neuroscience. Innovations within neurotechnology with a commercial application generally need input from more than one of these areas of science, which indicates the need for good networks and collaborations to achieve a successful venture.

The neurotechnology industry comprises three major sectors: the neuropharmaceutical, the neurodevice and the neurodiagnostics sector (NeuroInsights, 2005a).

2.1.1 Neuropharmaceutical Sector

This sector includes companies that develop pharmaceuticals and therapies for psychiatric and neurological illness. Within this sector three major markets can be discerned; the memory and attention related illnesses such as Alzheimer's disease and mild cognitive impairment; the mood-related disorders such as depression and anxiety and also the sensory and motor-system disorders e.g. pain and Parkinson's disease. There is a great need for innovative treatment within many of these areas depending on the low efficacy and side effects associated with current treatment and also with an increasing life expectancy of the general population. Taken together this creates enormous present and future market opportunities within this sector.

2.1.2 Neurodevice Sector

Companies that develop medical devices to treat brain illness are included in this sector. A major driving force in the sector is the technological advancement, which can be implemented in illnesses where the neuropharmaceutical sector has failed in developing efficient therapies. Markets included in the sector are: neuroprosthetics, including e.g. cochlear implants; stimulation devices to restore lost functions; neurosurgical devices including radiosurgery; neurofeedback solutions such as software to treat e.g. memory decline.

2.1.3 Neurodiagnostic Sector

This sector includes companies that provide tools to monitor and diagnose brain illness. Included markets are neuroimaging e.g. position emission tomography (PET), in vitro diagnostics including biomarker assays and genetic testing and also neuroinformatics.

2.2 Significance of the Neurotechnology Industry Worldwide

Already today brain-related illness generates more healthcare costs than any other therapeutic area, estimated at 1,0 trillion USD annually worldwide and 350 billion USD annually in the U.S (NeuroInsights, 2005a). There are two major factors that together create an even larger future market potential for the neurotechnology industry. Firstly, the general population is getting older. The proportion of the world population over age 60 is forecasted by the WHO to double between 2000 and 2050. This shift in the population

will result in increases in age-related diseases such as Alzheimer's disease, Parkinson's disease and many other illnesses related to the nervous system. Secondly, the currently available therapies are leaving room for new treatments since many of today's neuropharmaceutical products are associated with low efficacy and side effects. Besides the neuropharmaceutical field the neurodevice and neurodiagnostics sectors are emerging fields with great opportunities and with continued advances in technology these both sectors hold great future potential.

2.3 The Cluster Concept

The concept of a cluster is based on the presence of companies, suppliers and institutions within a geographically defined area that have mutual benefits from this proximity (VINNOVA, Nyckelbegrepp, 2005). The benefits of a cluster are many and include facilitation of e.g. labor specialization, specialized merchandise/service development, transfer of technology, knowledge and information (VINNOVA, Nyckelbegrepp, 2005). Clusters also increase and retain angel and venture capital, as well as increased partnerships, corporate investments, and national and international investments (Walshok M, 2006). Within a functional cluster there is also usually a well-developed triple-helix system, which helps connecting basic science to high tech and biotech business development (see below).

2.4 Major Actors in the Innovation System – the Triple-helix Model

An innovation system consists of all the factors that affect the development, spread and use of innovations (VINNOVA webpage, 2006). These factors can broadly be divided into three groups that traditionally have been very much separate: public research, business and government. These three spheres are now increasingly working together in the process of innovations and capitalization of knowledge and these interactions, which are a necessity in a successful innovation system, is usually described as the triple-helix model to illustrate the reciprocal relationships between these actors.

2.5 Overview of the Stockholm/Uppsala Neurotechnology Cluster

There are different ways to define the Stockholm/Uppsala region and in this report we generally refer to the geographical region along Uppsala, Stockholm, Södertälje, and Strängnäs. Swedish biotechnology is at the global forefront in the world and is listed among the top four countries in Europe (SwedenBIO, 2003). The Stockholm/Uppsala region contains about 60 percent of Sweden's about 800 pharmaceutical, biotechnology, and medical technology companies (Dolk T and Sandström A, 2005) and is the strongest region in general but especially in the field of neurotechnology (Neuroinsigths, 2005a; the Boston Consulting Group, 2001).

2.5.1 Academic Institutions and Universities

There are a total of 26 institutions for higher education in the Stockholm/Uppsala region (OECD, 2006). Below is a short description of the four most influential in science and engineering.

Karolinska Institutet

Karolinska Institutet is one of the world's leading and most respected medical universities and was listed on fourth position on the list of the 100 best medical universities in the world (Times Higher Education Supplement, 2005). It is Sweden's major research university and has the prestigious responsibility for awarding the Nobel Prize in Physiology or Medicine. Five Swedish neuroscientists have received the Nobel Prize over the years (Figure 2).

Karolinska Institutet is very strong in nearly all areas of both basic and clinical neuroscience and key departments include the Department of Neuroscience, Department of Clinical Neuroscience, Department of Cell and Molecular biology, and NEUROTEC.

Some of the strongest research areas include Alzheimer's disease, stem cell research, neurocognitive research, neurophysiology, histology/neurochemistry, and neuropharmacology.

Royal Institute of Technology

The Royal Institute of Technology is the largest university of technology in Sweden and internationally acknowledged for its leading education and research. It has very strong research in computational neuroscience, robotics, artificial vision, human-machine interaction and bioinformatics.

Stockholm University

Stockholm University is one of Sweden's primary academic institutions and is recognized for its strong education and research. It is world leading in its membrane protein research and bioinformatics, and has strong psychology and neurochemistry research.

Uppsala University

Uppsala University is one of Europe's leading centers of research in biomedicine and biotechnology. It has strong research in imaging, molecular engineering, gene technology, molecular medicine and drug development.

2.5.2 Consortia and Science Parks

Swedish Brain Power

Swedish Brain Power is a national consortium with some of the worlds leading researchers in neurodegenerative diseases and one of the largest medical research investments in Sweden. The consortium realizes a new concept of interdisciplinary research between academia, healthcare and industry mainly within the areas of Alzheimer's disease, dementia and stroke. The consortium is lead by Professor Bengt Winblad at Karolinska Institutet in Huddinge and the goal is to create better healthcare

and treatments for these neurological diseases and drive innovative drug discovery programs in this area of research.

Stockholm Brain Institute

Stockholm Brain Institute (SBI) is a newly formed consortium for cognitive and computational neuroscience and includes some of the internationally leading academic research groups in this field as well as strong industrial partners: AstraZeneca, Carlsson Research, Elekta, IBM and CogMed. SBI is led by Professor Hans Forssberg and Professor Martin Ingvar at Karolinska Institutet and the other academic scientists are from Karolinska Institutet, the Royal Institute of Technology and Stockholm University and the clinical research partners are from Stockholms läns landsting (Stockholm County Council) and the Karolinska Hospital. The goal of SBI is to understand the biological correlates of cognitive functions and associated brain disorders and thereby develop new approaches for prevention and treatment of these disorders. They also aim to decrease the gap between bioscience scientists and computer scientists and thereby foster a new generation of leaders and scientists in cognitive and computational neuroscience.

Stockholm Bioscience

Stockholm Bioscience is a joint venture by three of Sweden's leading universities: Karolinska Institutet, the Royal Institute of Technology and Stockholm University. It aims to increase the competitiveness of the universities within the life sciences and create a vibrant arena for bioscience to promote regional growth. It is now in its start-up phase but will in the future include facilities that could accommodate up to 200 companies and has received strong support from the Swedish government.

Novum Research Park

Novum was the first Swedish science park that was purely focused on the biomedical sector and has become one of the leading international biomedical incubators in Europe. Novum is known for its successful integration of basic, clinical and industrial research in the field of drug discovery. Some of the research areas are Alzheimers's disease, Multiple Sclerosis, and depression and companies such as KASPAC, Medivir, and Karo Bio are located here. Novum is planning to expand even more over the next few years to further develop their successful concept.

Uppsala Science Park

Uppsala Science Park is characterized by the closeness to academic research in Uppsala and has approximately 150 companies within the life science field.

Campus Uppsala

Campus Uppsala is located in one of Sweden's most knowledge based environments and through collaborations with academic research departments and innovative companies this is one of the strongest science parks in the Stockholm/Uppsala region and contains for instance GE Healthcare.

Karolinska Science Park

Karolinska Science Park was initiated by Karolinska Institutet in order for both small start-up companies and more mature companies to establish in close proximity to the

academic research. The vision is to create a research and innovation community that will increase the success of the companies as well as the academic research through collaborations and exchange of ideas. Karolinska Institutet Innovations AB and Neuro Therapeutics AB are some of the actors in this science park.

Teknikhöjden

Teknikhöjden is a joint venture between the Royal Institute of Technology and Stockholm University to promote and facilitate the commercialization of their research.

2.5.3 Public Actors with a Focus on Innovation and Entrepreneurship

There are a number of governmental agencies that act at different levels in the process of innovation. They mostly work on a national level but also have more specific programs to promote a certain region or topic. The national innovation policy for Sweden is stated in the document "Innovative Sweden" which is a strategy on how to achieve growth through innovation (The Ministry of Education, 2004). This national focus on innovation is a rather new phenomenon as are some the institutions that are to realize this.

VINNOVA (Swedish Agency for Innovation Systems) was established in 2001 and promotes innovation in different sectors as well as different regions of the country. One program within the Biotechnology sector that is co-financed by VINNOVA is the before mentioned "Swedish Brain Power". The regional innovation programs are called VINNVÄXT one of which is "Uppsala Bio" which is a regional biotechnology program.

Innovationsbron (the Innovation Bridge) is a state financed organization with the purpose to aid in the commercialization of research-based and knowledge-intense business ideas by providing seed-capital and management. Innovationsbron is also running the National Incubator program, which supports in the Stockholm Uppsala region e.g. Karolinska Institutet Innovations, Uppsala Innovation Centre and STING (Stockholm Innovation and Growth).

NUTEK (the Swedish Business Development Agency) works as a general entrepreneurship promoter on a national level.

Industrifonden invests in all kinds of technology companies. Investments are usually not in the very early stages and the fund therefore has a role that is similar to a private venture capitalist.

ALMI is a similar state financed organization with a more local focus that helps small companies with financing and business consulting.

The Invest in Sweden Agency (ISA) assists and informs foreign investors about business opportunities in Sweden. ISA is also a co-financer of Swedish Brain Power.

2.5.4 The Neurotechnology Industry

Sweden has excellent neuroscience research, which has led to several successful neurotech start-ups as well as a strong international interest from leading pharmaceutical

and other neurotech companies to increasingly turn to Sweden for innovative drug discovery and important collaborations.

AstraZeneca is today one of the leading and most successful pharmaceutical companies in the world and employs over 60,000 people worldwide, of which 11,000 are employed in Sweden with over 4,000 employees in R&D. AstraZeneca has invested substantially in both production and research facilities in the Stockholm/Uppsala region and recently invested an additional 60 MUSD in their CNS (central nervous system) research unit in Södertälje (the Boston Consulting Group, 2001).

Below is a list of some of the companies within the region. There are however many more companies within the region and also most of the larger international neurotech companies use Stockholm as their Nordic sales and marketing city.

Table 1: Selected companies with research and/or development within the neuroscience field in the Stockholm/Uppsala neurotechnology cluster. For detailed information on most neurotechnology and biotechnology companies within the region and Sweden, see reference section from *Biotech Sweden, 2006* and *Scandinavian Life Science Database, 2006*.

Company	Business Area
AcurePharma Consulting AB	Drug discovery consultancy
Actar	Drug discovery
AstraZeneca	Pharmaceuticals
BioArctic Neuroscience AB	Pharmaceutical company focusing on Alzheimer's disease
CMA Microdialysis AB	Development and marketing of microdialysis products
Cogmed	Software-based cognitive training
Elekta Instruments AB	Advanced medical technology company for minimally invasive neurosurgery
HUBIN	Neuroinformatics
Karolinska Development I and II	Seed investment companies
KASPAC	Pharmaceutical company focusing on Alzheimer's disease
Medivir AB	Pharmaceuticals
Neuronova AB	Pharmaceuticals for neurogenesis
Neurotherapeutics	Pharmaceuticals for stem cells/Parkinson's disease
Oasmia	Pharmaceuticals (mainly cancer, but also neurology)
Sangtec Medical AB	Medical diagnostics in oncology and neurology
Sanofil-Synthelabo AB	Pharmaceutical company performing clinical trials in Sweden
Uppsala Universitet Utveckling AB	Uppsala University Holding Company
Visionar Biomedical AB	Contract research organization

Sweden is the largest pharmaceutical and clinical trial market in northern Europe with over 40 companies performing studies on Swedish patients in 2004 (Business Arena Stockholm, 2004). Some leading pharmaceutical companies that choose Sweden for R&D in neuroscience include Eli Lily (US), Merck (US), Lundbeck (Denmark), Sumitomo Pharmaceuticals (Japan), Tanabe Seiyaku (Japan) etc. (Invest in Sweden Agency, 2004).

2.5.5 International Rankings of Sweden

Several benchmarking studies of different biotech and neurotech parameters have been made in both Europe and internationally and Sweden is ranked in the very top of most of these studies. Figure 1 summarizes most of these parameters.

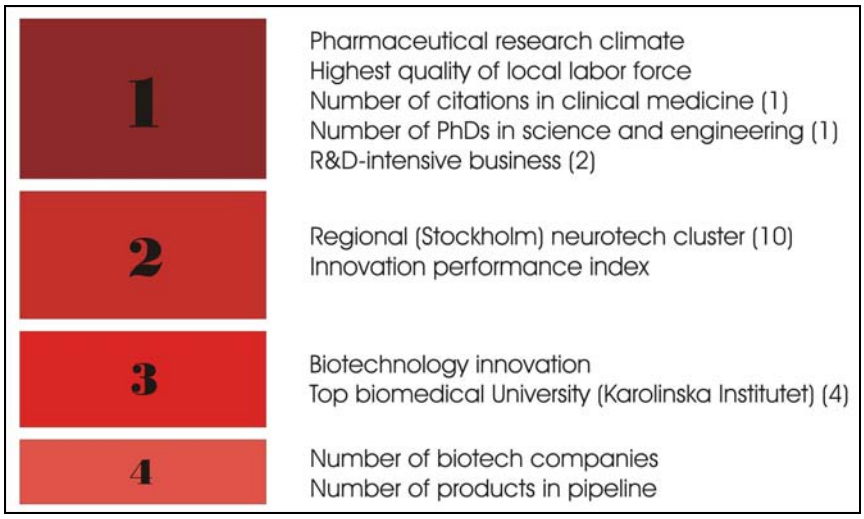

Figure 1: European rankings and known international rankings in parenthesis of Sweden, unless otherwise specified. Figure modified from *Business Arena Stockholm, 2004*.

2.6 A Global View of Neurotechnology Clusters

In 2005, NeuroInsights published a regional and economic analysis of the global neurotechnology industry and listed 15 leading regional economic clusters in neurotechnology. NeuroInsights is an American based neurotechnology-analysis firm that assists investors, industry executives and the public to understand and profit from the rapidly growing nervous system related market. The regional and economic analysis that was published is based on the more comprehensive report “The Neurotechnology Industry 2005” (NeuroInsights, 2005b) and also on specific regional investigations.

A neurotech cluster was defined as a geographic concentration of interconnected companies, suppliers and service providers as well as associated institutions within the field. These clusters were categorized as established, emerging or nascent based on the quality of research facilities, educated workforce, venture capital, experienced managers

and proximity of supplier networks (see below). 20 regions were evaluated worldwide on three main factors: the number of neurotechnology companies, access to risk capital, and social infrastructure (universities and research institutions). It is not stated in the report exactly how they investigated the "social infrastructure" which makes it hard to evaluate the value of this complex factor.

The three categories of neurotechnology clusters were defined in the following manner:

Established Cluster: This denotes a region where neurotechnology firms and academic research have a high innovative technological convergence, specialized workforce and risk capital networks, resulting in specialized and translational firms with economic returns and a strengthened regional growth.

Emerging Cluster: This denotes a region where neurotechnology firms have strong technological innovation but currently lag behind established regions in technological convergence as well as labor strength and risk capital, resulting in fewer innovative start-ups and decreased competitive advantage.

Nascent Cluster: This denotes a region where neurotechnology firms and/or academic research have strong technological innovation and partial convergence but currently lack major components of labor strength and risk capital. These regions may have few start-ups but strong governmental institutional support.

Table 2: NeuroInsights' neurotechnology nexus ranking.

Category	Global Rank	Regional Neurotech Cluster	Neurotech Companies (Rank)	Social Infrastructure (Rank)	Risk Capital (Rank)
Established	1	San Francisco Bay	1	2	1
Established	2	Greater Boston	3	1	2
Established	3	San Diego	2	3	3
Established	4	London-Cambridge	5	4/5	4/5
Established	5	Greater New York	4	4/5	6
Emerging	6	Raleigh-Durham	8	6	4/5
Emerging	7	LA-Irvine	9	7	7
Emerging	8	Greater Philadelphia	6	10	9
Emerging	9	Shanghai, China	13	8	8
Emerging	**10**	**Stockholm, Sweden**	**10**	**9**	**11**
Nascent	-	Munich, Germany	-	-	-
Nascent	-	Montreal, Canada	-	-	-
Nascent	-	Singapore	-	-	-
Nascent	-	Tokyo, Japan	-	-	-

Nascent	-	Melbourne, Australia	-	-	-

Table modified from *NeuroInsights, 2005a*

Stockholm is discussed in short terms in the NeuroInsights report, and they especially mention the “Swedish Brain Power” project, the five Swedish Nobel Laureates in neuroscience, Karolinska Institutet, Karolinska Institutet Innovations, Neuronova and the new OECD Neuroinformatics Center (decided during the spring of 2006) at Karolinska Institutet and the Royal Institute of Technology.

3 Research Questions

3.1 How Did Stockholm/Uppsala Become an Emerging Neurotechnology Cluster?

As stated above, the Stockholm/Uppsala region was in a recent investigation categorized as an emerging neurotechnology cluster and was ranked on 10th place globally (NeuroInsights, 2005a). We attempt to analyze the three factors that this ranking was based upon and other relevant factors in the Stockholm/Uppsala region to evaluate if this is a correct judgment, and if so what factors have played an important role in facilitating the development of this cluster.

3.2 What Should be Done to Further Strengthen and Enhance This Cluster?

In order to enhance the competitiveness of this cluster the weaknesses need to be identified. According to the report by NeuroInsights the emerging neurotechnology clusters, in comparison to the established ones, "lag behind with respect to technological convergence and specific inter-firm regional linkages resulting in lower positive network effects, fewer innovative startups and decreased competitive advantages" (NeuroInsights, 2005a). In analyzing the characteristics of the Stockholm/Uppsala neurotech cluster we aim to identify in more detail the specific factors that need to be improved to further promote the development of the cluster.

4 Methods

In order to answer the questions outlined above we need to identify the factors that are crucial for the development of a successful cluster in general. We also have to identify specific factors that have been and will be of importance for the neurotechnology field in general and for the Stockholm/Uppsala region in particular. The information will be gathered using two main approaches:

I. Literature search and analysis.

II. Interviews with persons representing the different main actors in the Stockholm/Uppsala neurotechnology cluster, including the venture capital market, neurotechnology companies, academic research institutes, financial organizations and major consortia:

- Professor Sten Grillner; Chairman, OECD Neuroinformatics Network
- Professor Hans Wigzell; Chairman, Karolinska Institutet Innovations; Scientific Advisor to the Swedish government
- Mats Berggren; SwedenBIO
- Professor Erna Möller; Executive Director, Knut and Alice Wallenbergs Foundation
- Professor Bengt Winblad; Director, Swedish Brain Power
- Kai Hammerich; Director-General, Invest in Sweden Agency
- Ylva Williams; Director, Life Science, Invest in Sweden Agency
- Professor Jonas Frisén; Board Member, Co-founder, Neuronova AB
- Sören Johansson; Vice President, Business Development, Elekta
- Gösta Jonsson; Former (April 2006) Vice President of Global Discovery Affairs, AstraZeneca
- Dr Johan Christenson; Partner, HealthCap
- Professor Hans Forssberg; Director, Stockholm Brain Institute and Vice President of Karolinska Institutet
- Professor Martin Ingvar; Chairman at the Department of Clinical Neuroscience, Karolinska Institutet; Faculty Member, Stockholm Brain Institute
- Dr Lars Öjefors; Chairman, CONNECT Sweden; former CEO, Industrifonden
- Jonas Jendi; Managing Director, CogMed Cognitive Medical Systems AB
- Alvaro Fernandez; Managing Director, SharpBrains Inc

5 Status of the Stockholm/Uppsala Neurotechnology Cluster

From the conducted interviews, many agree that the 10th position for the Stockholm/Uppsala neurotechnology cluster ranked by NeuroInsights in 2005 is fairly reasonable, although two interviewees argued that the cluster has certain significant advantages over its competitors and should have a better position. In this chapter, the Stockholm/Uppsala neurotechnology cluster is reviewed and key findings, such as contributions to the cluster's development in the past, current efforts that enhance the cluster and existing problems and contentious issues are presented.

5.1 Key Contributions to the Development of the Cluster

The foundation for the development of the Stockholm/Uppsala region as a neurotechnology cluster is the long history of strong and world leading academic neuroscience research in Sweden in general and Stockholm/Uppsala in particular. Equally important is that many of the leading neuroscientists have also been entrepreneurs. As mentioned in chapter 2.5.4, Sweden has also had some very strong pharmaceutical companies over the years, such as Astra and Pharmacia, as well as other successful neurotech companies like Elekta, CMA Microdialysis, Neuronova, CogMed etc. which all have contributed to the success of the region.

Important are also other factors such as the high degree of well-educated people and the high level of labour force quality (chapter 5.1.2; figure 1), infrastructure and strong social security system.

5.1.1 Sweden's Strong Neuroscience Research

The strong research environment in Sweden was much created during the 1950's through generous funding by the Swedish Medical Research Council. The strong position that Sweden today has in basic and clinical neuroscience is much thanks to some influential strong pioneers in this field, that all made groundbreaking discoveries (see Figure 2). Their scientific impact can be seen in the number of citations their work has resulted in (see Table 3). Several of these people also received a Nobel Prize (see Figure 2) for their excellent research, and maybe some of today's strong researchers are tomorrows Nobel Prize Laureates.

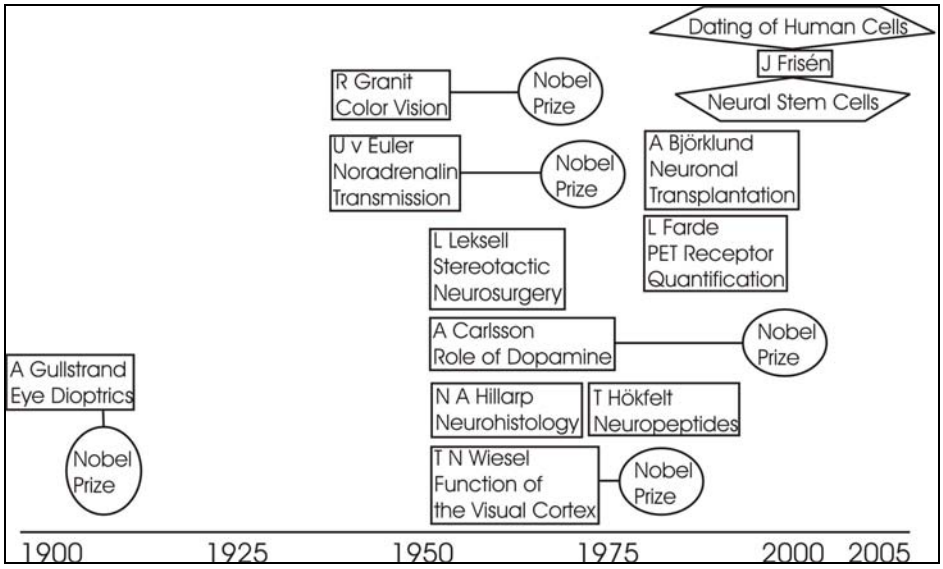

Figure 2: Swedish Nobel Laureates within the neuroscience field as well as some other historical achievements by Swedish neuroscientists. Figure modified from *the Boston Consulting Group, 2001*.

Table 3: An analysis among the 298 most highly cited scientists for the period 1981-1999 within neuroscience (*Thomson Scientific, 2002*) identifies 10 Swedish scientists of which 7 are from the Stockholm/Uppsala region (indicated in dark grey) and 3 from southern Sweden (indicated in light grey).

Scientist	Institution	Research Area
Björklund, Anders	Lunds Universitet	Neuroscience
Brundin, Patrik	Wallenberg Neuroscience Center	Neuroscience
Fuxe, Kjell Gunnar	Karolinska Institutet	Neuroscience
Hökfelt, Tomas	Karolinska Institutet	Neuroscience
Lindvall, Olle	Lunds Universitet	Neuroscience
Lundberg, Jan M.	AstraZeneca	Biology & Biochemistry, Pharmacol Neuroscience
Olson, Olof Lars	Karolinska Institutet	Neuroscience
Terenius, Lars	Karolinska Institutet	Neuroscience
Ungerstedt, Urban	Karolinska Institutet	Neuroscience
Winblad, Bengt	Karolinska Institutet	Neuroscience, Social Sciences, General

Some of the mentioned researchers have also been successful entrepreneurs which has been an important factor for the development of the Stockholm/Uppsala neurotechnology cluster. For instance Lars Leksell, one of Sweden's most talented clinical neuroscientists, who was a professor in neurosurgery at Karolinska Institutet, founded the medical-technology company Elekta in 1972 based on his scientific work. Other scientists like Göran Sedvall, Lars Farde and Torgny Greitz were among the first to develop applications with the PET technology. Professor Jonas Frisén at Karolinska Institutet was one of the co-founders of Neuronova in 1998, a promising young neurotechnology company that develop drugs to stimulate neurogenesis within the brain. Professor Patrik Ernfors, also at Karolinska Institutet, was one of the co-founders of Global Genomics in 2000 and this company was aquired by Genizon in 2005. Professor Urban Ungerstedt started CMA Microdialysis already in 1984, which is now the leading company developing and marketing microdialysis products. Dr Torkel Klingberg at Karolinska Institutet was one of the co-founders of CogMed in 2001, a software based neurotechnology company providing working memory training products. CogMed is based on innovative basic research and has been very successful in translating their research results into clinically and commercially viable products to improve quality of life for people with serious attention deficits.

Sweden has also been successful in applied neuroscience, as in Human-Machine-Interface (HMI) together with companies like Volvo and Saab. Another example is the Center for Technology and Health at the Royal Institute of Technology and Karolinska Institutet headed by Professor Hans von Holst. At the center scientists are performing interdisciplinary research between medicine and technology with several different projects such as neuronal implants and advanced head and brain protection.

In drug development Sweden has had a strong position in neurophsyciatric diseases since the 1940's with Astra (AstraZeneca since 1999) and Pharmacia (today Pfizer) as key companies. Also, Jan Lundberg who is Executive Vice-President of AstraZeneca and Head of Discovery Research, is a former professor from the Department of Pharmacology at Karolinska Institutet and one of Sweden's most cited neuroscientists (see table 3).

A strong and unique feature in Sweden is the open access to medical records in the Swedish health care system. This provides clinical researchers with very good patient material, extensive biobanks and comprehensive and organized databases. The bioethical regulations are also very good in Sweden and have contributed to a strong position internationally in several areas, but especially in embryonic stem cell research.

A recent investigation of the neuroscience field in Sweden was performed by the Boston Consulting Group for the Swedish Brain Power project, and identified some strong research groups which are listed in table 4. It should be mentioned that the list is not comprehensive and there are many more very strong and influential research groups within the Stockholm/Uppsala region. However, the mentioned groups are based upon in depth interviews with more than 200 Swedish and international researchers (the Boston Consulting Group, 2001).

Table 4: Strong research groups within the Stockholm/Uppsala neurotechnology cluster.

Basic/Clinical Neuroscience	Applied Neuroscience
Laura Fratiglioni (Epidemiology)	Lars Bäckman (Imaging)
Jonas Frisén (Molecular neurobiology)	Henrik Christensen (Neurobotics)
Sten Grillner (Neurophysiology)	Jan-Olof Eklundh (Artificial Vision)
Tomas Hökfelt (Histology/Neurochemistry)	Kerstin Sevrinson Eklundh (HMI)
Carlos Ibáñes (Molecular neurobiology)	Anders Lansner (Computational neuroscience)
Lars Lannfelt (Genetics)	Lars-Göran Nilsson (Psychology and memory)
Bengt Långström (Imaging)	Yngve Sundblad (HMI)
Lars Olsson (Histology/Neurochemistry)	
Lars Terenius (Clinical genetics)	
Bengt Winblad (Alzheimer research)	
Martin Ingvar (Imaging)	

Table modified from *the Boston Consulting Group, 2001*

Some of the above mentioned researchers that are and have been Swedish pioneers within neuroscience are approaching retirement age, which could be seen as a risk for the continuation of their research. However, there is a strong regrowth of younger researchers within these groups and in other areas of neuroscience (general opinion by interviewees). Sweden seems to be especially competitive within molecular neurobiology, imaging, spinal cord research, Alzheimer's disease and Parkinson's disease, bioinformatics, genetics, learning and cognition.

5.1.2 Labor Quality

Labor quality is of great importance in the life science industry in general because of the high demands of specific knowledge and skills not only in R&D but also in areas such as intellectual property protection and regulatory affairs. For R&D intensive companies the local research climate and availability of high quality universities is of special importance both for attracting workforce and for collaborations. Labor quality in Sweden is generally characterized by high standard and was recently listed as the best in the EU when the "average number of education years" and "percentage of population with tertiary education" was evaluated (Cap Gemini Ernst & Young, 2004, figure 1). Also when looking at more specialized education Sweden holds a very strong position with regard to

the number of graduated PhD's in relation to population where Sweden is ranked first among the Organization for Economic Cooperation and Development (OECD) countries both in total number of PhD's and PhD's in science and engineering (OECD, 2003, see figure 1). All these factors can be assumed to be especially strong in the metropolitan Stockholm/Uppsala region, which is characterized by very high educational level because of the density of strong academic institutions. In a global comparison of regions of knowledge, Stockholm received the highest "knowledge competitiveness" score in Europe and was ranked number 15 globally (worth noting is that all the 14 first regions were located in the US) (Robert Huggins, 2004). Sweden is also characterized by relatively low wages for highly educated labor. These factors have likely been important historically and contributed to the progress of especially the big pharmaceutical companies such as AstraZeneca and the former Pharmacia (OECD, 2006; Interview with Gösta Jonsson) and thereby promoted the development of the neurotechnology cluster.

5.1.3 The Teacher's Exemption

By law, researchers in Sweden maintain the rights to the intellectual property related to their research results (the Teacher's Exemption). Whether this system promotes innovation or not is a topic currently under debate, and in a recent proposition from the government it was suggested that it should be taken away or changed to aid the commercialization of research (Regeringens proposition 2004/05:80), an issue that is now being investigated. Some claim that the Teacher's Exemption encourages researchers to search for commercial opportunities (Nilsson et al., 2006; VINNOVA, 2005; the Boston Consulting Group, 2001). Since this arrangement is rather unique internationally this would be a competitive advantage that can attract good scientists to Sweden. This issue is complex and during our interviews the opinions "keep it" and "remove it" and everything in between was heard. On the negative side was mentioned that a lot of the basic science is publicly funded and the university/state therefore should get something back from a profitable invention. Others claimed that the Teacher's Exemption has been very important in creating the present biotech market in Sweden. Since the technology transfer (TT) offices at the universities were established only recently in Sweden, the Teacher's Exemption has been important since it has given researchers the option to commercialize their ideas via other channels instead of having the idea "getting stuck" at the university. So with the Teacher's Exemption the researcher may choose the best agent on the market instead of being forced to stick with the university's own TT office. The TT offices in Sweden have since their establishment undergone substantial development, however both VINNOVA and SwedenBIO suggest that the infrastructure around the universities need to be even further developed to become more professional and competitive before the Teacher's Exemption can be changed or removed (VINNOVA, 2005; SwedenBIO, 2005). It should be mentioned that the TT office at Karolinska Institutet, the Karolinska Institutet Innovations, is an exception and a pioneer within the TT office infrastructure in Sweden and has been very successful, with international experts visiting to study and learn from this unit to improve their own TT offices.

5.1.4 Venture Capital

Venture capital (VC) is important to facilitate the linkage between the private sector and research institutions. Sweden has a larger share of VC in gross domestic product (GDP)

compared to other OECD countries and a larger share of total VC in biotechnology (OECD, 2006). Sweden also scores high when the availability of VC is compared to other European countries (Cap Gemini Ernst & Young, 2004). Between 1995 and 2000 Sweden was home to the fastest growing VC market in the world, much of which was directed at the life science sector (Business Arena Stockholm, 2004). Although the VC market has experienced hardened conditions in the last years both in Sweden and other countries, it is likely that these "golden years" contributed significantly to the growth of the biotech industry in general in Sweden. It also seems that the Swedish VC market has recovered quicker than the rest of EU (Table 5). HealthCap is the largest VC firm within life sciences in the Nordic countries and one of the largest independent actors in the sector in Europe with committed capital exceeding MEUR 660. Many of the major Swedish VC companies, including HealthCap, are located in the Stockholm/Uppsala region (Table 6), which probably has contributed significantly to the regional growth in the life science field.

Table 5: Early stage venture capital expressed as percentage of GDP.

	1998	**1999**	**2000**	**2001**	**2002**	**2003**
Sweden	0.007	0.057	0.095	0.093	0.097	0.081
EU average	-	0.029	0.057	0.060	0.037	0.025
Sweden relative to EU (%)	-	195	168	154	262	322

Data from *European Commission, 2003a*

Table 6: Major biotechnology VCs in the Stockholm Uppsala Bioregion.

HealthCap
H&B Capital
Innovationskapital
Investor Growth Capital
Karolinska Investment Management
Scandinavian Life Science
SEB Företagsinvest
Swedfund

Table modified from *Business Arena Stockholm, 2004*

5.1.5 The Metropolitan Stockholm/Uppsala Region

In Sweden, 94% of the people employed in the pharmaceutical, biotechnological and medical-technological industries are located in one of the 3 major metropolitan areas in Sweden and the Stockholm/Uppsala region alone accounts for 58% (VINNOVA, 2005). This is to a high degree correlated to the location of research institutes and highlights the dominance of the metropolitan regions in this field. The Stockholm region is economically very successful and competitive and ranks high in quality of life measures much because of strong public health performance, high educational attainment and low poverty levels which are amongst the best in the world (OECD, 2006). This has most likely contributed to the positive development of the cluster. There are 26 institutions for higher education in the region and they account for 48% of all university-based spending in Sweden. The quality of these institutions can be seen in the strong net-inflow of undergraduates and PhD students both domestically and from abroad (OECD, 2006). The Stockholm metropolitan region was until recently the same as Stockholm County. However, a recent reassessment shows that the labour market area has expanded, and it now encompasses almost the entire Uppsala County with a total population of 1.94 million inhabitants, 21.5% of the Swedish total population, (OECD, 2006).

The Stockholm region is characterized by competitive and innovative industry clusters (OECD, 2006). A mapping shows that the there is a domination by a few clusters that account for the majority of jobs and in which Stockholm has a regional competitive advantage in Sweden including biopharmaceuticals, financial and business services, transport and logistics, information and communication technology (ICT) and analytical instruments (Fördel Stockholm Mälarregionen, 2004). One of the most expansive of these clusters is biotechnology in which the number of employees grew by 68% between 1990 and 2001 (Fördel Stockholm Mälarregionen, 2004).

5.2 Current Efforts

5.2.1 Stockholm Brain Institute

As described in chapter 2.5.2, Stockholm Brain Institute (SBI) is a rather new consortium but with great potential. Several of the research groups within SBI are excellent on the brain imaging side and together with the expertise and state of the art imaging technologies at AstraZeneca this research will be even stronger. Also, the increased collaboration with computational neuroscientists should increase the impact and success of the research. Within this framework AstraZeneca recently signed an agreement with the Karolinska Intitutet positrion emission tomography (PET)-center to invest SEK 80 million over the next five years.

The tight collaboration with several strategic industrial partners is positive in many aspects: it provides a solid and stable financial situation for the research projects and from a company perspective it of course strengthens the companies' potential in finding new and innovative drug candidates, treatments and diagnostics in the specific field of research. Also, the industrial-academic partnership strengthens the progress of fostering academic scientists that also have an understanding of the process of commercialization of research results. This is good for the region in general, but the Swedish society in

particular since this will probably increase the number of commercially valuable research results and thereby the number of university spin-off companies which increases the wealth of the society.

Big constellations like SBI are also important in the aspect of attracting external money from the European Union and other sources and within complex fields such as cognition, it is also important to form these constellations in order to cover all levels and aspects of the research – from cell to systems level and from molecular neurobiology to imaging and computational neuroscience (general opinion from several interviewees). All these aspects will increase the success of the research and the high international position of the research groups within SBI.

5.2.2 Swedish Brain Power

The Swedish Brain Power project is an initiative to strengthen neuroscience in Sweden and is strategically focused on a small number of prioritized projects. The global management consulting firm Boston Consulting Group was hired to analyze Swedish brain science in a strategic perspective. This was performed by identifying areas in which Sweden is internationally leading scientifically, and analyzing the market potential of these areas (the Boston Consulting Group, 2001).

The analysis showed that there was much strength in Swedish brain science today but pointed out that Sweden's strong position has slipped during the last decade and due to the limited recourses there is a need for strategic focus. It was found that Sweden's health and medical care systems offers unique conditions for testing and evaluation of drugs and other treatment methods for neurodegenerative diseases and for projects aimed at understanding such diseases. A number of specific project proposals were later evaluated and a project led by Professor Bengt Winblad at Karolinska Institutet, Huddinge Hospital, was chosen. The ultimate goal of the project is "to improve early diagnosis, treatment and care of subjects affected by neurodegenerative diseases" *(http://swedishbrainpower.se)*.

There are two unique aspects of the project. One is the funding, which is a joint effort from the Invest in Sweden Agency (ISA), and five major Swedish research-founding institutions: the Knut and Alice Wallenberg Foundation (KAW), the Swedish Foundation for Health Care Sciences and Allergy Research (Vårdalstiftelsen), the Swedish Knowledge Foundation (KKS), the Swedish Foundation for Strategic Research (SSF) and VINNOVA. The other is the multidisciplinary approach of the project. The goal is to establish a centre built on Sweden's strengths in neuroscience and related disciplines with representation from all key organizations: the pharma and biotech industry, regulatory authorities, primary and municipal care, and research institutes. The project seems to be a good implementation of the triple-helix model (see 2.4) and holds great potential.

5.2.3 Stockholm BioScience

The project was initialized in 1999 and originated from the Centre for Medical Innovations at Karolinska Institutet and was the idea of Professor John Skår and the Karolinska Institutet president at that time, Professor Hans Wigzell. It is a joint project between Karolinska Institutet, the Royal Institute of Technology and Stockholm

University and the initial founding of the project came from Stockholm Foundation for Technology Transfer (Innovationsbron Stockholm).

The aim of the project is to "create new and exciting opportunities for breakthroughs in bioscience based on world-class multidisciplinary research" (Ola Björkman, 2005). This will be accomplished through the formation of a new city section, the "Norra Station", close to the universities and the university hospital, which would significantly strengthen the scientific profile of Stockholm. The development of this infrastructure is in an advanced planning stage (Stockholm BioScience, 2005). However, this seemingly huge project is very complex and will likely need some time before it can actually bear fruit.

Another task of Stockholm BioScience is to catalyze collaborative academic research programs integrating the three universities mentioned above and support these in an early phase to initiate collaborations and thereby strengthen the cluster. One such program, "NeurITe – Center for integrative brain research", was previously initiated and formed between the three universities. This is now part of the later formed Stockholm Brain Institute (see above).

The "Norra Station" project seems to have very strong support from academia, as well as the private and public sector and therefore has all the possibilities to succeed. With the regional density of excellent research as well as bioscience companies, the area has the potential to become a very attractive location for researchers and biotech companies.

5.2.4 The OECD International Neuroinformatics Coordinating Facility

An OECD (Organisation for Economic Co-operation and Development) network for neuroinformatics research (Professor Sten Grillner, Chairman) recently decided to place the headquarters of the organization at Karolinska Institutet in Stockholm. This will be a coordinating facility headed by Professor Jan G Bjaalie who will build up the organization of this center that will lead and coordinate neuroinformatics research within the 10 participating countries so far. Neuroinformatics is the merging of neuroscience with information science, and the goal of the facility is to create a resource where the enormous amount of research data can be efficiently stored, integrated and used. The idea is to do this through the creation and use of (I) neuroscience data and knowledge databases, (II) analytical and modeling tools, (III) computational models (OECD, 2005).

For the Stockholm/Uppsala region it is a recognition of the excellent neuroscience and information science in the cluster, to be selected as the host of a new international research center. The center will except from the in house expertise of the center, also strengthen the region through the symposiums that will be arranged together with leading researchers in specific fields of neuroscience (Interview with Professor Sten Grillner).

5.2.5 Karolinska Institutet Innovations

Karolinska Institutet Innovations was founded in December 1996 with the purpose of providing KI's researchers professional support in commercializing academic inventions. Professor Hans Wigzell, president of KI at that time, was the person with the vision to establish this professional university technology transfer office. In 2006 the name was

changed from Karolinska Innovations AB to Karolinska Institutet Innovations (KI Innovations).

KI Innovations evaluates incoming projects both from KI and other universities across the Nordic region. The evaluation is performed through a systematic stepwise procedure with the goal of identifying high-potential inventions and the risks associated with them. When a project makes it through the evaluation, a project group is assigned to manage preparatory activities.

Pre-seed funding of SEK 50,000 – 250,000 is allocated through Karolinska Development[1] for further analysis, protection of intellectual property rights and to eliminate certain risk components. KI Innovations also assesses the possibility of complementing the initial invention or bundling technologies to create a highly competitive project. On top of that, KI Innovations offers project management, legal advice and business development. The process is directed, depending on circumstances, towards either creation of a new spin-out company or transfer to the industry directly through a license agreement.

To date KI Innovations has

- Reviewed more than 650 academic inventions
- Created 35 start-up companies
- Closed 25 license agreements

Below is a partial list of companies co-founded by KI Innovations.

Table 7: A partial list of companies co-founded by KI Innovations.

Actar	Cogmed	MCe Med
Antrad Medical	Dilafor	NephroGenex
Aprea	DustGun	Neuro Therapeutics
Athera Biotechnologies	Genordia	Oncopeptides
Avaris	Global Genomics	HBV Theranostica
Axelar	IMED	Sidec Technologies
Bioneris	InDex Pharmaceuticals	SpectraCure
Calabar	Lipopeptide	Triple Crown
CENSdelivery	CarbGraft	SoftCure

Table modified from *www.karolinskainnovations.ki.se, 2006*

KI Innovations is also working with VINNOVA to extend the collaboration between the Swedish universities and industry.

[1] There are two investment companies, namely: Karolinska Development AB (KD I) and Karolinska Development II AB (KD II). Karolinska Development III AB is currently in the pipeline.

5.2.6 CONNECT Sweden

According to Dr Lars Öjefors, chairman of CONNECT Sweden (*http://www.connectsverige.se*), many start-up entrepreneurs need assistance in evaluation of their business ideas, as well guidance in improving the packaging and presentation of their ideas and business proposals. In 1997 a group from the Royal Swedish Academy of Engineering Sciences (IVA) and the Swedish Venture Capital Association came in contact with CONNECT in California and decided to adapt the American model to Swedish conditions. In the CONNECT model there are extensive preparations together with the start-up companies and entrepreneurs so that they are coached on how to meet and act with venture capital firms.

Today there are a great number of activities with several regional networks existing around the country. The most important activity are springboards in which a panel of experts assists entrepreneurs in solving business problems, identifying possibilities and gives practical advices on how to move the company forward. Other important activities include:

- Meet a researcher – PUB (Partnership University Business) evening
- Meet an entrepreneur
- Financial Forums
- Partnership Forums
- Business Angel Networks
- Seminars and educational courses

Professional people from service providers, industrial companies, universities and venture capital firms participate in these activities in order to consolidate the entrepreneurs' business ideas in the best possible way so that the ideas can be developed into successful companies.

5.3 Challenges and Problems Together with Suggestions

In this section, an attempt is made to list out and discuss some of the challenges and problems currently encountered in the development of the Stockholm/Uppsala neurotechnology cluster. Arguments from various aspects gathered from conducted interviews are presented and suggestions to some of the issues are also included.

5.3.1 Insufficient Public Funding for Academic Research

Although public funding for academic research has been identified in earlier sections as one of the current efforts in the development of the Stockholm/Uppsala neurotechnology cluster, the responses from conducted interviews and many recent reports still stress that much more should be done. In "A National Biotech Agenda for Growth" published in 2004 by SwedenBIO, 100 suggestions of different improvements for the Swedish biotechnology climate is listed. The most highly prioritized point is to strengthen the science and knowledge base in Sweden through increased funding for competitive biomedical R&D projects. In a survey performed by journalists at Swedish Radio P1 where 2100 Swedish professors were asked about financing and the research climate in

Sweden, over 50 % claimed that their research is financed to 2/3 by non-public money (Anna Jaktén, 2006). The survey shows a general view of the Swedish research climate in terms of financing which is very troublesome and where many professors claim that they spend more time on applying for money rather than on actually using the small amount of money received to conduct research. Below is a directly translated quote from Arvid Carlsson, the Swedish Nobel Laureate in medicine in 2000, on the question "Do you think you could have had your success in today's system?" – quote: "No, I am absolutely sure that I would never have had the opportunity to receive a Nobel Prize".

The Swedish government often stresses the fact that Sweden has a high input per capita in R&D. In 2001 Swedish R&D expenditure totaled 4.3% of GDP, putting the country number one among the 29 countries of the OECD, however the higher education sector accounted for only 19% of that (The Swedish Institute, 2004). So in practice the funding to basic research is not that impressive and as long as the goal is to be a leading nation of knowledge the infrastructure for basic research needs to be improved and we therefore stress that the government should increase the public funding for this purpose.

The situation in clinical research with a constant lack of money is also confirmed during the interview with Martin Ingvar, Chairman at the Department of Clinical Neuroscience, Karolinska Institutet. He is also deeply critical to how the government systematically describes the financing of basic science in flattering terms. Also, Sören Johansson from Elekta is very critical to the possibilities of today to collaborate with both the healthcare as well as clinical researchers. This problem is also confirmed by Jonas Jendi from CogMed, and it seems that in comparison to the US, Swedish healthcare professionals could greatly improve their collaborative efforts and attitude towards life science companies. Throughout the interviews there has also been a general consensus that several actors within academia and healthcare regard companies as something suspicious to collaborate and work with. This may halt both the willingness of companies to support academic research as well as weakening the region in general since existing companies may instead go abroad to other collaborative partners.

Many of the interviewees mentioned the power of large research consortia as a competitive advantage when attracting funding. It was also mentioned that in certain scientific areas where multiple disciplines are needed such consortia are necessary to keep a high international position. However, during some interviews it was also brought up that the useful interactions occur elsewhere and these networks are more of political constructions. As pointed out in section 5.1.1 it is the excellence related to a few individuals that has been important for the progress of Swedish neuroscience. It is therefore somewhat contradictory that public funding is directed so much towards big consortia rather than individual grants.

Two main reasons justify the necessity of increased public funding for basic research. Firstly, there is a general acceptance that knowledge is the primary resource which enables innovation and that innovation is what drives economic growth through creating new industries, new jobs and new wealth for regions and nations. Research is a primary source of this new knowledge (Walshok M, 2006). Secondly, basic research activities are crucial from the strategic aspect of sustainable development for a region and as a solid platform of knowledge for both companies to access through collaborations as well as for education of students. The diversified and high-volume basic research activities will

prepare a region better in times of change, such as a shift in the industry pattern or the creation of new industries. With the groundwork being carried out, the region will be quick to respond and can always maintain an edge over and take the lead from its competitors.

5.3.2 High Rental Costs for Swedish Universities

Related to the public funding of academic research are the increasing rental costs at Swedish universities due to the monopoly-like situation of Akademiska Hus (property company in Sweden owing almost all of the university buildings, research institutions etc.). Through the interviews it has been confirmed that the current situation with Akademiska Hus is threatening the research in Sweden through substantial draining of the acquired funding of individual research groups. The net profit after tax for Akademiska Hus for the year of 2005 was SEK 6,654 million (Akademiska Hus Year-end Report, 2005), which could be compared to the total public research budget for 2005 of about SEK 4,400 million (Regeringens proposition, 2004/05:80). The absurd situation was also confirmed during the above mentioned survey involving 2100 Swedish professors, where researchers at the Royal Institute of Technology in Stockholm had put notes on the doors of small storage rooms in their basement that showed how much money the departments had saved by terminating their rental agreement of these small storage rooms: 87,305; 15,431; 31,466 SEK, etc.

During a recent debate (Research Debate, May 2006) about the research politics in Sweden, when all major political parties in Sweden were represented, it was suggested by Carl Bennet (Chairman of the IVA and NUTEK project: “framtidens näringsliv”, translated to “the future business world”) that the public research budget should be increased through reinvestments of part of the profit of public companies. This is an excellent proposition and we suggest that the total profit from Akademiska Hus be directly reinvested into the public funding of academic research.

5.3.3 Lack of Management Competence

There is a general acknowledgement from the interviewees that management competence of especially small and medium sized biotechnology companies is lacking in the Stockholm/Uppsala cluster. As several of them have pointed out, the biotechnology management competence in Sweden is largely established from big companies, the number of which is limited compared to the number of small startup companies. Also, the management skills needed in small and medium sized biotechnology companies differs from those in larger biotech companies. On top of that, it is not common for managers from big companies to leave their positions and join small startup companies as salaries and social security are normally not as good in the smaller firms. As a result, there is a lack of management competence, especially small-scale management for startup companies. So, as mentioned by Alvaro Fernandez from SharpBrains Inc., in order to attract good people to lead the small startup companies one must be able to offer very attractive equity and stock option packages, to compensate for lower salaries and benefits compared to larger, established companies.

Several interviewees claim that most failures of startup companies are caused by poor management and stress the importance of the availability of strong management and their

crucial role. Management competence is based on practical experience, not theoretical studies, so in order to keep and increase the amount of great management there is a need of a vibrant and growing company-environment. It has also been discussed during interviews how important it is for small biotech startup companies to be dynamic throughout the progress of the company and choose the most suitable management teams and executives for different phases of development.

5.3.4 The Teacher's Exemption Re-visited

The Teacher's Exemption has been a topic of recent debate. The advantages of this contentious policy have been presented in 5.1.3. In summary, the Teacher's Exemption encourages researchers to make inventions and may also attract top scientists from all over the world to come to Sweden to do their research where they own the rights to their discoveries. It also helps to create competition among venture capital firms and other actors, when each individual researcher can freely choose whom to partner with, which seems better compared to a monopoly situation where the university owns all the patents.

However, the Teacher's Exemption also has its drawbacks, one being the difficulty of obtaining a patent and the almost impossible task of defending the patent if you do not have the backup from a large company or substantial assets.

However, we share the view of most of the interviewees, of keeping the Teacher's Exemption for the time being. When the system of university technology transfer offices becomes more mature in the future, a change of the Teacher's Exemption could then be considered.

5.3.5 Inadequate Levels of Trust between Scientists and Venture Capitalists

There is a general feeling among the interviewees that scientists do not fully trust the venture capitalists and they believe venture capitalists are "too greedy". This situation may have arisen because the venture capital market in Sweden still shows signs of immaturity and also because of lack of knowledge by scientists regarding the venture capital business. Although the VC market has grown rapidly in Sweden compared to other countries and is quite prosperous, the number of companies on the market is still rather low. Sometimes a competitive situation is turned into a collaborative situation which increases the market power of VC companies.

Therefore, we would like to see increased competition in the venture capital market brought about either by the emergence of new players or by legislative efforts. Another solution could be by further strengthening university technology transfer offices, such as KI Innovation. These technology transfer offices are located on-campus close to scientists, and at the same time are parts of the university. It is noted that scientists generally accept universities more than venture capital companies; therefore this may be a better approach. However, it is crucial that such technology transfer offices are equally competent to ordinary VC companies.

5.3.6 Lack of Local Loyal Capital and Serial Entrepreneurs

Professor Hans Wigzell, chairman of Karolinska Institutet Innovations, commented that there is a lack of local loyal capital in the Stockholm/Uppsala neurotechnology cluster.

Local loyal capital refers to the money raised in such a way that the owners have a long-term interest in the region. In such cases, companies are most often characterized by having their headquarters located within the region, and this increases the overall level of business activities in the region and its attraction to investors dramatically. In order to raise the level of local loyal capital, appropriate incentives should be introduced by the government, for instance various tax incentives.

Another area that the Stockholm/Uppsala neurotechnology cluster is lacking is serial entrepreneurship. As pointed out by Dr Johan Christensson, partner of HealthCap, many Swedish entrepreneurs do not move to new ventures and do it all over again after their initial success. In sharp contrast, serial entrepreneurship is very common in the USA. This is probably mainly due to lack of financial incentives and tax relieves for individuals to reinvest their earned wealth into new ventures and companies, but may also be related to Swedish culture which is not as business driven as for instance in the USA. This is also confirmed by Alvaro Fernandez from SharpBrains Inc. who sees a lack of entrepreneurial equity culture in Sweden. In order to promote serial entrepreneurship, the government should introduce relevant incentives for successful entrepreneurs to continue new ventures.

5.3.7 Geographical Separation between Stockholm and Uppsala

The geographical fact of a linear distance of 70 kilometer between Stockholm and Uppsala has posed some problems for the cluster. Presently, Stockholm and Uppsala still exist to a certain extent as two separate cities instead of a joined cluster. Interviewees indicate that Uppsala has stayed outside the Stockholm locality.

One problem arising from the geographical separation is the low level of intra-cluster communication. Many interviewees agree that once outside the Stockholm locality, Uppsala is not different from Lund or New York. People from these two cities do not meet as often, and some unhealthy competitions have been observed between Stockholm and Uppsala. One worrying sign is that Uppsala is now trying to brand itself in the international field instead of uniting with Stockholm. The Vinnväxt program introduced by VINNOVA supported only one biotech cluster in the region, which was in Uppsala, and therefore had the effect of fragmenting the Stockholm/Uppsala cluster instead of initiating collaboration (OECD, 2006).

In order to bridge the distance between Stockholm and Uppsala, there have been calls for a better transportation system between the two cities, such as a new express railway system that could possibly compress the travel time from 40 minutes as of today to 20 minutes in the future. In this context the issue of infrastructure should also be considered in the planning of the Stockholm BioScience project “Norra Station” (discussed in 5.2.3). We believe that both Stockholm and Uppsala should do their outermost in creating a collaborative environment in terms of urban planning, regional promotion, research and company collaborations etc.

5.3.8 Entrepreneurial Climate

Sweden has the highest number of biotechnology companies per capita in Europe and is in fourth place in Europe when it comes to absolute numbers of biotech firms. However, many of these are spin-outs from former Pharmacia and there are worrying reports about

the low level of entrepreneurial activity in Sweden (OECD, 2006). The report shows that within the life science industry, AstraZeneca and Pfizer have an overwhelming domination. These firms are of course crucial assets to the region, but in a longer perspective Swedish policymakers need to ensure a better mix of large, old companies and new fast growing firms. This is also confirmed from the interview with Gösta Jonsson, former Vice President of Global Discovery Affairs at AstraZeneca, that Sweden's possibilities to compete with the US and Asia in creating new, large global pharmaceutical companies has passed. It also seems that the future within the pharmaceutical industry is based on small, innovative and highly specific R&D intense companies that may license out or collaborate with the big pharmaceutical companies. Also for the big pharmaceutical companies it is becoming increasingly important to both in-license and out-license projects. In a report by Henreksen in 2002, there is an increased demand for differentiated products, which points to a greater role for small and new companies as engines of entrepreneurial activity. Although the Swedish innovation system is considered highly sophisticated in an international perspective it might not be as effective as it could be. The high R&D expenditures are coupled with comparatively low long term economic growth (Sweden's GDP per capita dropped from fourth to fifteenth place among OECD countries between 1970 and 2003) which is known as the so-called "the Swedish paradox" (OECD, 2006).

5.3.9 Financial Environment

The biotech market is characterized globally by large investments into companies and academic research and many countries have implemented aggressive growth strategies. Sweden has however only implemented few changes and is not focusing on such strategies, while countries like Canada, Singapore, France and UK are aggressively competing to attract external investments (SwedenBIO, 2004) as well as increasing their own investments and actions within biotechnology. The analysis from SwedenBIO has also shown that the USA has by far the best environment for the research-intensive biotechnology industry. Also, in 2004 Stockholm was listed on 15th place in Europe in a survey investigating the best cities to locate business in (Cushman et al., 2004) which is a very negative sign for the region. This is mainly due to the disadvantaging tax burdens in Sweden and overall weak incentive structures for especially developing companies while corporate tax is still quite competitive (OECD, 2006). In the OECD report they particularly mention the marginal effective tax rate of different investments, distortions from the tax treatment of different forms of financing, and high taxation on income and wealth. Also, in SwedenBIO's 100 suggestions of improvements for the growth of the biotech industry (SwedenBIO, 2004) they list the stimulation of R&D investments through directed tax incentives as the second most important measure to be taken. This is also confirmed in the interview with Mats Berggren at SwedenBIO who lists 3 main factors in achieving a strong cluster:

- Excellent science – according to our report fulfilled
- Great surrounding environment – since the market is global it needs to be better or at least as good as other clusters, especially the financial market
- National ambition supporting growth – where tax incentives to stimulate investments is one factor supporting growth

Also Professor Hans Wigzell at Karolinska Institutet Innovations, Dr Johan Christensen at HealthCap, Sören Johansson at Elekta and Dr Lörs Öjefors at CONNECT and former president of Industrifonden believe that the lacking Swedish tax incentives are hindering growth and development of the biotechnology industry.

It is also harder for Sweden to directly attract foreign investors to invest in Sweden because they would then have to pay the internationally relatively high Swedish tax on their profit, so from a tax point of view foreign investors are reluctant to put money in Swedish funds. Instead foreign investors put their money in a Swedish VC firm that is also represented abroad where the tax system is more favourable, so in the end the external investments may still be invested in Swedish companies, but the Swedish system does not facilitate the attraction of foreign capital and Sweden as a country loses a business opportunity. Another condition that Sören Johansson, and several other actors such as SwedenBIO and AstraZeneca, stresses is the tax brake for foreign specialists and management which they believe should be extended to five years. Sören Johansson believes that this should not only be true for specialist functions, but should be available without restrictions. Another innovative suggestion to improve Swedish competitiveness was made by Professor Jan Lundberg (Executive Vice-President and Head of Discovery Research at AstraZeneca) where he suggested that people with a PhD should pay less tax (Research Debate, March 2006). This could work as an encouragement to brilliant students to conduct doctoral studies and thereby increase the competitiveness of Sweden. Professor Lundberg also advocated for a substantially higher aim for the public research budget than today's budget goal which is set to 1% of GDP.

5.3.10 Other Challenges for the Development of the Cluster

In addition to the above-discussed areas, there are two other major challenges for the development of the Stockholm/Uppsala neurotechnology cluster.

Firstly, Swedes are very well known as inventors, but they are relatively poor marketers and business developers. Therefore, there is a challenge of having increased level of business development and marketing expertise in general. Especially the knowledge about and how to access the US market seems to need strong improvements since this is often the largest market for small startup neurotechnology companies. Some interviewees expressed optimism about this issue though and Dr Lars Öjefors has commented that this is the better situation than the opposite case, when basic science and creativity are lacking.

Secondly, with high living standards and fantastic social welfare systems, Sweden has been considered as a paradise country to live in and there is a lack of self-criticism in general. This may potentially lead to, or is already the case, a layback situation. Therefore, the challenge is for the society as a whole to stimulate entrepreneurship, innovation and growth of the business climate.

6 Conclusions

Swedish neuroscience is characterized by excellence in research, and this is the very foundation of the neurotechnology industry. The Stockholm/Uppsala cluster is the strongest region in Sweden and several outstanding research groups have been identified in basic, clinical and applied neuroscience at especially three main universities: Karolinska Institutet, the Royal Institute of Technology, and Uppsala University. There was a general agreement throughout the interviews that the ranking by NeuroInsights in 2005 that listed Stockholm/Uppsala as the 10th strongest neurotechnology cluster in the world was a good and fair judgment, and some even advocated that the cluster was stronger and should be ranked higher.

In addition to academic research, the ranking was also based on the regions access to venture capital as well as the number neurotechnology companies. The venture capital business in Sweden appears to be strong, especially in comparison to other EU countries, and there are several life science specialized firms within the region with HealthCap as the largest actor. There is also an increased activity by foreign venture capital firms that wants to access the Swedish life science sector and invest at early stage in start-ups (Interviews with Ylva Williams and Kai Hammerich, ISA).

The amount of neurotechnology companies appears to be fairly large, with several small R&D intensive companies, but the large pharmaceutical company AstraZeneca that has the majority of R&D within neuroscience situated in Stockholm dominates the region in size and R&D activity.

There is however also several worrying signs within the region that are mainly concerned with the inadequate measures taken by the government to increase the growth rate of the neurotechnology sector and the region in general. Within academia, there is a growing and alarming concern about the halting funding of research together with growing costs in terms of rent and administration.

In small companies in general and developing R&D intensive companies in particular, there is an acute need of improvements of rules and regulations concerning mainly taxes and financial incentives in order to facilitate investments and growth.

There is a concern that the high rankings presented in this article may be the results of previous efforts and successes within Sweden and that today's situation is actually in alarming need of swift and thorough actions in order to secure the success of the region and the neurotechnology and life science industry.

However, in recent years there has been an increased activity from the government in trying to improve entrepreneurship and innovation in Sweden which is a step in the right direction. Some improvements can also be seen with regard to tax regulations, but the general view is that the measurements must be much more aggressive. During recent months there has also been increased activity from politicians and other players within the society in bringing research questions on to the political agenda (2006 is election year in Sweden). This is positive and research should always be part of the political agenda, and the current situation creates opportunity for all involved players to advocate and debate for a strong development of the region and the lifescience industry in general.

Other initiatives and successful efforts within the region that has been crucial to the region is the Karolinska Institutet Innovations and especially its initiator Professor Hans Wigzell, who is highly involved in many of the regions strengths, both in terms of spin-off companies as well as in focused efforts in keeping the best brains and their research within the region.

The recognition of neuroscience in general as the potentially strongest area within the lifescience sector in Sweden by the Invest in Sweden Agency and others in 2001, was an important recognition of the excellence of Swedish neuroscience and later led to the establishment of Swedish Brain Power. The placement of the OECD neuroinformatics international coordinating facility in Stockholm is another important international recognition of the region. If these and other efforts such as the “Norra Station” project by Stockholm BioScience are successful they will surely contribute to the excellence of this neurotechnology cluster, which will hopefully maintain and also enhance its international competitiveness.

Our report shows that with adequate and focused measures, the Stockholm/Uppsala neurotechnology cluster has the ability not only to sustain its strong position, but to grow considerably in volume, strength and excellence.

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References

Akademiska Hus Year-End Report (2005), http://www.akademiskahus.se/fileadmin/ekonomi_finans/en/Akademiska_Hus_Year-end_report_eng.pdf

Anna Jaktén (2006), Beställningsjobb och köpt tystnad - är den fria forskningen hotad? http://www.sr.se/cgi-bin/P1/program/artikel.asp?ProgramID=1316&Artikel=855121

Biotech Sweden (2006), The Swedish Biotech Industry Guide, http://biotech.idg.se/industryguide/

Business Arena Stockholm (2004), Stockholm Uppsala Bioregion – Where science is life, http://www.uppsalabio.com/graphics/2997.pdf

Cap Gemini Ernst & Young (2004), EU Enlargement: Driving Change in the European Life Sciences Industry

Cushman, Wakefield Healey and Baker (2004), European Cities Monitor, http://www.frankfurt.de/sixcms/media.php/2000/CitiesMonitor2004.pdf

Dolk T and Sandström A (2005), Nationella och regionala klusterprofiler. Företag inom bioteknik, läkemedel och medicinsk teknik i Sverige. http://www.vinnova.se/Main.aspx?ID=0b01f8ae-24d3-44a3-8180-9154f8abcfa6

Ernst & Young (2004), Refocus: The European perspective

European Commission (2003a), European Innovation Scoreboard

European Commission (2003b), Biotechnology Innovation Scoreboard

European Commission (2005), European Innovation Scoreboard

Fördel Stockholm Mälarregionen (2004), Specialisering och tillväxt i Stockholm-Mälarregionen – Vad betyder regionens kluster?

Henreksen, M (2002), Entrepreneurship: A Weak Link in the Welfare

Invest in Sweden Agency (2004), Invest in Sweden: Neuroscience, http://www.isa.se/templates/Publications____2358.aspx

NeuroInsights (2005a), The Neurotech Nexus, http://www.neuroinsights.com/marketreports/neurotechnexus.html

NeuroInsights (2005b), The Neurotechnology Industry, http://www.neuroinsights.com/marketreports.html

Nilsson AS, Friden H, Schwaag Serger S (2006), Commercialization of life-science research at universities in the United States, Japan and China. ITPS A2006:006

OECD (2003), Science, Technology and Industry scoreboard

OECD (2005), Neuroinformatics, http://www.oecd.org/document/57/0,2340,en_2649_34319_35217721_1_1_1_1,00.html

OECD (2006), Territorial reviews, Stockholm, Sweden

Ola Björkman (2005), A new centre for bioscience in the capital of the country, Stockholm BioScience

Regeringens proposition (2004/05:80), http://www.regeringen.se/content/1/c6/04/11/35/6effb2fa.pdf

Research debate, March (2006), http://ki.se/ki/jsp/polopoly.jsp?d=135&a=10612&l=sv&newsdep=135

Research debate, May (2006), http://svt.se/svt/jsp/Crosslink.jsp?d=12094&lid=puff_488798&lpos=lasMer

Robert Huggins (2004), World knowledge competitiveness

Scandinavian Life Science Database (2006), http://www.scandinavianlifescience.org/sls/index.php

Stockholm BioScience (2005), Stockholm BioScience. Lägesrapport November 2005

SwedenBIO (2003), SwedenBIO – The Swedish Biotech Industry Association

SwedenBIO (2004), A National Biotech Agenda for Growth

SwedenBIO (2005), Abolishment of the Teachers Exemption – Consequences and Position of the Swedish Biotechnology Industry

The Boston Consulting Group (2001), Swedish Brain Power, http://www.isa.se/pdf/SwedishBrainPower.pdf

The Lancet (2004), vol. 363

The Ministry of Education (2004), Innovative Sweden – A strategy for growth through renewal, http://www.sweden.gov.se/sb/d/283/a/32462

The Swedish Institute, 2004. The Swedish research system, Classification: FS 24 r Bf/1101-6124,
Thomson Scientific (2002), ISI Highly Cited, http://www.isihighlycited.com

Times Higher Education Supplement (2005), http://www.thes.co.uk/statistics/

VINNOVA (2005), Nyckelbegrepp, http://www.vinnova.se/main.aspx?ID=4B3DCA27-2DCC-4CC1-AFA1-70D5F65BFEB2

VINNOVA (2005), Strategi för tillväxt – Bioteknik VP 2005:02

VINNOVA (2006), http://www.vinnova.se/

Walshok M (2006), lectures during SSES course “From Science to Business – Concepts in Biotechnology” http://www.sses.se

List of Interviewees

- Professor Sten Grillner; Chairman, OECD Neuroinformatics Network
- Professor Hans Wigzell; Chairman, Karolinska Institutet Innovations, Scientific Advisor to the Swedish government
- Mats Berggren; SwedenBIO
- Professor Erna Möller; Executive Director, Knut and Alice Wallenbergs Foundation
- Professor Bengt Winblad; Director, Swedish Brain Power
- Kai Hammerich; Director-General, Invest in Sweden Agency
- Ylva Williams; Director, Life Science, Invest in Sweden Agency
- Professor Jonas Frisén; Board Member, Co-founder, Neuronova
- Sören Johansson; Vice President, Business Development, Elekta
- Gösta Jonsson; Former (April 2006) Vice President of Global Discovery Affairs, AstraZeneca
- Dr Johan Christensson; Partner, HealthCap
- Professor Hans Forsberg; Director, Stockholm Brain Institute and Vice President of Karolinska Institutet
- Professor Martin Ingvar; Chairman at the Department of Clinical Neuroscience, Karolinska Institutet, Faculty Member, Stockholm Brain Institute
- Dr Lars Öjefors; Chariman CONNECT Sweden, former CEO Industrifonden
- Jonas Jendi; Managing Director, CogMed Cognitive Medical Systems AB
- Alvaro Fernandez; Managing Director, SharpBrains Inc

About the Authors

Jesper Ericsson

Jesper Ericsson is a graduate student in Neuroscience at Karolinska Institutet, Stockholm, Sweden. He studies the function of the brain in the selection process of behavior and motor learning. Jesper has a background in engineering from the Royal Institute of Technology in Stockholm and combines his graduate studies with entrepreneurial and economic studies.

Jesper serves on the board of the Graduate Students' Association, the Recruitment Committee and the Neuroscience Departmental Advisory Board at Karolinska Institutet.

Jesper Ericsson
Nobel Institute for Neurophysiology
Department of Neuroscience
Karolinska Institutet
Retzius väg 8
S-171 77 Stockholm, Sweden
Phone: +46 8 524 87362
e-mail: jesper.ericsson@ki.se
Web: http://www.neuro.ki.se/grillner/pages/jespercv.html

Mikael Nygård

Mikael Nygård is a graduate student in Neuroscience at Karolinska Institutet, Stockholm Sweden. He studies sleep and biological rhythms and disturbances of these processes during disease conditions. Mikael holds a Master of Science degree in Pharmacy from Uppsala University and has previously done research in analytical chemistry.

Mikael Nygård
Div. of Neurodegenerative Diseases
Dept. of Neuroscience
Karolinska Institutet
Retzius väg 8
S-171 77 Stockholm, Sweden
Phone +46 8 524 87873
e-mail: mikael.nygard@ki.se
Web: http://www.neuro.ki.se/kristensson/index.html

Minrui Zheng

Minrui Zheng is an undergraduate student from Singapore where he studies engineering and entrepreneurship at the National University of Singapore.

e-mail: minruiz@gmail.com
Web: http://www.nustart.sg

Glossary

Alzheimer's disease	A disease marked by the loss of cognitive ability, generally over a period of 10 to 15 years, and associated with the development of abnormal tissues and protein deposit in the cerebral cortex.
Business angel	An individual who invests his or her own money in a private company, which is typically a startup.
Cognition	The mental faculty of knowing, which includes perceiving, recognizing, conceiving, judging, reasoning, and imagining.
Entrepreneur	A person who organizes, operates, and assumes the risk for a business venture.
Fund	A comprehensive term for any money that is set aside for a particular purpose or that is accessible for the satisfaction of debts or claims.
Incubator	An organization that fosters the growth of new ideas or companies.
Intellectual property	A product of the intellect that has commercial value, including copyrighted property such as literary or artistic works, and ideational property, such as patents, appellations of origin, business methods, and industrial processes.
License	A document, contract or agreement giving permission for an individual or en entity to use, reproduce, or create an instance of the licensed work.
Neurodegenerative disease	A disease in which the nervous system progressively and irresistibly deteriorates.
Neurogenesis	Formation of nervous tissue.
Neuroscience	Any of the sciences, such as neuroanatomy and neurobiology, that deal with the nervous system.
Neurotechnology	The set of tools that analyze and influence the human nervous system, especially the brain.
Parkinson's disease	A progressive nervous disease occurring most often after the age of 50, associated with the destruction of brain cells that produce dopamine and characterized by muscular tremor, slowing of movement, partial facial paralysis, peculiarity of gait and posture, and weakness.
Science park	A property development designed for a concentration of high technology or science related business.

Serial entrepreneur	Type of entrepreneur who starts a new business after having already started and exited a previous business venture.
Technology transfer	The process of developing practical applications for the results of scientific research.
Venture capital	Money made available for investment in innovative enterprises or research, especially in high technology, in which both the risk of loss and the potential for profit may be considerable.