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Mathias UhlÃ©n is a world-renowned microbiology researcher at the KTH Royal Institute of Technology.

Since 2003, he has led the Human Protein Atlas (HPA) project, an international effort to systematically map the human proteome and transcriptome. Among his many other achievements,

he was also the founding director of the Science for Life Laboratory (SciLifeLab), one of the largest molecular biology research laboratories in Europe, and created 23 life sciences companies. UhlÃ©n discusses the evolution of Swedenâ??s life sciences ecosystem, the impact of the Human Protein Atlas on medical research globally, as well as the role of the SciLifeLab and strategic collaborations between the â??Stockholm trioâ?? in driving innovation in Swedish life sciences.

As a world-renowned researcher with more than 30 yearsâ?? experience in Swedish academia, how have you seen Swedenâ??s research and innovation ecosystem evolve?

From the 1950s to the 1970s, Sweden was considered a pioneer in life sciences. Many of the methods used in the pharmaceutical industry as well as medical research were developed here in Sweden. These innovations include, among others, chromatography, electrolysis and centrifugation, for which Nobel prizes were awarded. This pioneering science led to the rise of Pharmacia, Kabi and Astra, companies that were at the forefront of the biopharmaceutical revolution. For instance, Kabi collaborated with Genentech on the development of recombinant human growth hormone in the late 1970s.

In 1990, Kabi merged with Pharmacia which itself merged with US company Upjohn in 1995. However, Pharmacia retained its footprint in the country. As a result, in the 1990s, Pharmacia and Astra were the two giants driving the ecosystem. The situation drastically changed after Pharmacia-Upjohn was acquired by Pfizer and Astra merged with Zeneca. What followed was akin to a depression around the millennium. In the case of Pharmacia, Pfizer closed down most of the facilities, but retained the biomanufacturing site in StrÃ¤ngnÃ¤s. AstraZeneca closed its research operations in Lund then in SÃ¶dertÃ¤lje and only retained its Molndal site near Gothenburg.

The gap left by Pharmacia and Astra led to the emergence of an enormous amount of small and midsized biotech companies relative to the small size of the country. In 2016 for instance, Sweden ranked third in the number of life sciences companies going public with 36 IPOs, ahead of larger EU countries like France, Germany and Switzerland. In total, Sweden is home to around a thousand biotech companies. These numbers show how strong of a competitor Sweden is within the global life sciences sector.

One of the main reasons why the country churns out so many innovative biotech companies has to do with the so-called â??teacherâ??s exceptionâ?•, a concept unique to Sweden. Here, university researchers retain the intellectual property rights to their discoveries and inventions. As a result, universities are incentivized to help turn inventions into innovations, and take stakes in the companies created.

This is the reason why I have started 23 companies, almost one every year. It is extremely easy from a bureaucratic standpoint. I do not think any country in the world has an easier bureaucracy when it comes to creating a company. Moreover, a lot of funding goes into the life sciences from public sources but also from business angels and venture capital firms. In addition, whereas in the late 1990s and early 2000s biomanufacturing was moving out of Sweden, the situation has since changed. AstraZeneca is developing one of the largest biomanufacturing facilities in the world in SÃ¶dertÃ¤lje. Octapharma in Stockholm is setting up a new factory. Pfizer in also expanding its biomanufacturing plant in StrÃ¤ngnÃ¤s acquired from Pharmacia. Last but not least, GE Healthcare, is also expanding its bioprocessing site in Uppsala inherited from Pharmacia Biotech and already the companyâ??s largest life sciences site globally. Moreover, the company, in collaboration with the Swedish government, has opened the Testa Center, a large test center designed to help biotech companies bridge the gap between discovery and industrialization of biological products.

Since 2003 you have been the director of the Human Protein Atlas (HPA) project, a concerted effort to map all the human proteins. The project has resulted in over 500 publications and the launch of the Cell Atlas, Tissue Atlas and Pathology Atlas. What have been some of the most interesting developments since these three major launches?

We have spent approximately 1500-person-years on the project to date, and we have during these years employed 520 people. We have extensive collaboration with groups in China, South Korea and India. Our aim is to make a map of all the building blocks of humans. When people think about the building blocks of humans they often refer to DNA, genomics and so on. However, the real building blocks are the proteins, and more than 95 percent of the drugs produced in the world are geared towards proteins, which I am certain will remain the case in the future.

The project has received massive financial support from the Knut and Alice *Wallenberg* Foundation, about USD 150 million USD so far. With this funding, we set ourselves the task of finding out where the different proteins are around the human body. Like Lego pieces, proteins interlock to form complex structures. The difference is that humans do not only have two or three Lego pieces but 19,670 which allow us to go about our daily tasks. In a way, I think this is much more interesting than the Genome project which told us what genes and DNA are. In 2015, we published our findings in a paper in Science which became one of the most cited papers in the world that year. Furthermore, we decided to look at what proteins are inside the cell, the smallest unit in the body, which became the Cell Atlas. Finally, we asked ourselves what are the proteins that affect the survival of cancer patients which resulted in the publication of the Pathology Atlas in 2017. The applied side of the Human Protein Atlas has allowed the start-up of many companies based on the research. Four of them are on now public (on the stock market), and altogether, six clinical trials are ongoing in these companies.

Since all the data is available in open access, the HPA has become the dictionary for proteins. Every month, about 300,000 researchers from 200 countries visit the HPA. Every day, more than 10 publications are published citing the HPA. Pharmaceutical companies also visit the HPA on a daily basis as this data can be used to think of practical applications. On September 6th, 2019, we will launch three new parts to the Human Protein Atlas: the Blood Atlas, the Brain Atlas and the Metabolic Atlas. Consequently, this is the busiest time in my life!

An article published on the HPA website discusses the fact that although immunotherapy has advanced the field of cancer treatment, many patients develop a resistance to immunotherapy. What are some ways the HPA can be used to solve this problem?

Four of the companies that I founded are working in immunotherapy and a great interest of mine is moving into precision medicine by trying to use knowledge and data to predict who will become resistant and who will benefit from treatments. Every immunotherapy is based on targeting proteins in different ways, which makes it very interesting to find out where these proteins are in the human body.

Furthermore, drug development is a matter of going through clinical trials, demonstrating the effectiveness of a drug and showing that it does not have many side effects. It is important to point out that all drugs have side effects on some patients. Therefore, what we are hoping for is that a knowledge of the targets and a holistic view of the proteins in the human body make it possible to understand the symptoms and side effects in a better way.

When we spoke with Jenni Nordborg from the Life Sciences Office, she mentioned that digitalization was a focus for Swedenâ??s life science sector. How advanced is Sweden in terms of digitalization?

Ten years ago, around the same time I started the HPA, I also approached the Swedish government with two messages. The first message was that life science and medical research are driven by two separate factors. The first is expensive infrastructure which is becoming increasingly more important to generate data. The second is big data and digital health to handle large data. Together with colleagues, we convinced the government of the opportunity for Sweden to create a new national institute for big data and a life science infrastructure which was named the Science for Life Laboratory (SciLifeLab). In 2010, we started a pilot in Stockholm. The three universities are now known as the â??Stockholm Trioâ?• â?? Karolinska Institutet, the KTH Royal Institute of Technology and Stockholm University â?? came together and formed this new institute at the Karolinska campus in Solna. I was the Founding Director for the SciLifeLab for six years until 2015. In 2013, as Uppsala University joined, we created a national infrastructure, securing funding from the government of about USD 30 million per year, a large sum of money in a small country like Sweden. With this funding, we moved into two new buildings. I was the first employee and after six years we were 600 employees in Stockholm and another 400 people in Uppsala, 200 of which are focused on bioinformatics. This shows our focus on digital health within this national infrastructure.

How do you believe this will continue to contribute towards putting Sweden on the worldâ??s radar as a frontrunner in the life sciences industry?

The vision ten years ago was that infrastructure and big data were important in life science and medical research. I think it is even more true today. Obviously, I think that this quest for expensive infrastructure to generate data is important but more importantly there is a need to have solid infrastructure to take care of the data. We have had a few excellent pilot programs. One of them has been run by a researcher called Anna Wedell. Anna has begun to study genomics focusing on metabolic diseases in children, which has quickly moved from basic research into clinical practice.

How have collaborations and connections between KTH, the Karolinska Institutet and Stockholm University allowed yourself and your peers to progress your research both nationally and internationally?

In the last decade, much of the medical research has become technology and data-driven and therefore there are incredible benefits in the collaboration between the medical faculty at Karolinska, the technical faculty at KTH and the natural science of Stockholm University. This was the idea behind the SciLifeLab, putting a group together in order to form something strong. Before the SciLifeLab, there were very few collaborations, and although I am a little biased, I think the SciLifeLab is a great way of bringing the Stockholm trio together and formalizing a centre of excellence. Furthermore, in the SciLifeLab building, we have 14 floors and my hope is for every floor to have at least some scientists from each of the universities. It is clear that in order to be competitive on an international scale we need to collaborate between the faculties.

The Karolinska Institute recently announced a strategic collaboration in microbiome research which you have been appointed to lead alongside Lars Engstrand. So far, no therapy has been developed as a result of microbiome research. What do you see as the potential of microbiome research for the development of new breakthrough therapies in different therapeutic areas?

I see the microbiome as an unexplored area where there are many myths and uncertainties. It will be a systematic effort where we will be starting with 10,000 patients. In the future, we would like to expand up to one million, partnering with the Chinese and other international collaborators. It is an interesting question as I do not know quite where it will lead us. However, we will definitely find out a lot of new information about the way people react to drugs depending on the bacteria present in the gut. The project has two objectives. The first is to learn how to treat people with drugs targeting the microbiome and the second is to follow people who have gut problems. The collaboration has only just started but it is for the long term. We have a similar process with a cancer group where we are looking at around 1,000 cancer patients in Sweden together with the BGI in China, performing whole-genome sequencing, which is very expensive, in order to analyze ways to predict how these patients should be treated in the best way.

What is your future outlook for research and innovation in Sweden?

Sweden has always been great at developing and using modern technologies, which has resulted in the creation of many small innovative life sciences companies. I am optimistic that many of these companies will grow and begin to merge together to create the next generation of national champions within the next ten years.

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