THE NOVOZYMES PRIZE

PROFESSOR
JENS NIELSEN

2016

NOMINATION OF JENS NIELSEN

The 2016 Novozymes Prize is being awarded to Jens Nielsen for his scientific breakthrough within systems biology and his extensive pioneering efforts relating to the biotechnological use of systems biology methods to construct cell factories for the biosynthesis of chemicals.

Jens Nielsen studied chemical engineering and biochemical engineering at the Technical University of Denmark (DTU). He received an MSc degree in 1986, a PhD in 1989 and Doctor of Technology in 1995. Following postdoctoral positions in Canada and Germany, he was appointed as a Research Associate Professor in the Department of Biotechnology at DTU in 1990. A permanent position of Associate Professor in the Department followed in 1996. A visiting professorship position at the Massachusetts Institute of Technology from 1995 to 1996 strongly influenced his orientation towards systems biology. In 1998, Jens Nielsen was appointed Professor at the newly established BioCentrum at DTU, which included the three former Departments of Biotechnology, Microbiology and Biochemistry and Nutrition.

Until 2008, Jens Nielsen established an outstanding research environment in bioengineering that attracted substantial funding for research on microbial biotechnology. Jens Nielsen founded the Center for Microbial Biotechnology at DTU and headed it from 2004 to 2008. It was a unique research centre that positioned systems biology at the heart of future biotechnological advances. In 2008, Jens Nielsen left DTU to take up a professorship in the Department of Chemical and Biological Engineering at Chalmers University of Technology in Göteborg, Sweden. There he built up a major international research and education environment for bioengineers. Today, this is considered a world leader in systems and synthetic biology focusing on designing efficient biosynthesis processes. In 2011, Jens Nielsen joined the newly established Novo Nordisk Foundation Center for Biosustainability, where he is now Chief Scientific Officer. In 2015, he was instrumental in establishing the new Department of Biology and Biological Engineering at Chalmers.

The development of gene technology techniques in the 1970s changed the science of biology and the resulting use of biotechnology overnight. In the following years, many ingenious genetic tools and methods were developed while bioindustry applied these for specific uses focusing on biosynthesizing pharmaceutically relevant proteins and also, later, technical enzymes. However, the biosynthesis of proteins comprises only a small part of the ambitions related to the industrial use of gene technology. The real breakthrough would be constructing cell factories designed to biosynthesize chemicals based on reconstructing synthetic pathways in the selected production organism.

Jens Nielsen embarked on this extremely ambitious project at an early stage. He has contributed to this in a distinguished manner by combining molecular genetics with metabolic flux analysis and genome-based metabolic models, leading to targeted metabolic engineering methods. He had an optimal education and research background in mathematics, reaction and fermentation science and data integration, combined with rapidly acquired insight and experience in modern microbial genetics. He was therefore able to make several breakthroughs in systems biology in connection with his work with fungi (yeasts and filamentous fungi).

Jens Nielsen's pioneering work with genome-scale metabolic network models for yeast and subsequently other fungi was the first of its type for higher organisms. These models have greatly contributed to producing fungal cell factories for industrial use. By combining the models with metabolic engineering in connection with designing specific production organisms, Jens Nielsen has shown how the interaction between the desire to produce a chemical biosynthetically, the genetic reconstruction of the required synthesis pathways in cells and the models for metabolism can lead to the rapid and result-oriented identification of bottleneck problems in biosynthesis and can indicate solutions to rectify them. Jens Nielsen has uniquely developed concepts and strategic solutions involving advanced data integration for producing efficient cell factories that are now used in research laboratories and biotechnology companies worldwide.

Parallel to his pioneering work in strategic biotechnology, Jens Nielsen has contributed to basic biology. By using the developed models creatively and intuitively, he has contributed significantly to the basic understanding of the physiology of microorganisms. Similarly, he has also produced organisms in the laboratory with completely new and useful properties in response to the handicaps every natural organism has if it is to be tailored to biosynthetic production. Such initiatives can only be carried out by someone with in-depth understanding of the biology of organisms. Jens Nielsen has this understanding, and he has extensively contributed to improving the knowledge of other biologists.

Jens Nielsen's production of scientific articles is impressive. This reflects both his incredible strengths as a research leader and his ability to identify challenges and how to solve them. He has commendably served as a key resource person internationally within a key scientific and technological field with enormous future potential. He is in great demand as an adviser and speaker with broad perspectives by the scientific community and the bioindustrial complex. Jens Nielsen has been awarded numerous honours and prizes for his scientific breakthroughs, and he has continually expanded his fields of interest in an incredibly creative manner.

Jens Nielsen's mentoring activities especially illustrate his significance. He has advised about 70 PhD students and about 70 postdoctoral fellows and senior researchers. Most of these have served as successful ambassadors for the type of thinking they developed during their scientific education as part of his research group. This testifies to Jens Nielsen's unique accomplishments in biotechnology.

In conclusion, Jens Nielsen's original work in systems biology and the concept of metabolic engineering represents a landmark breakthrough for the potential of using cell factories for the biotechnological production of chemicals. He has thus demonstrated that the biosynthesis of chemicals is a realistic industrial platform that may contribute significantly to future sustainable solutions to several global problems. Based on this, Jens Nielsen is an obvious and worthy recipient of the 2016 Novozymes Prize.

CURRICULUM VITAE

JENS NIELSEN

PROFESSOR, DIRECTOR
BORN 17 NOVEMBER 1962, HORSENS, DENMARK

2015	Founding Head of Department, Department of Biology and Biological Engineering, Chalmers University of Technology, Sweden
2012	Nature Award for Mentoring in Science, Nature Publishing Group, UK
2011	Professor, Novo Nordisk Foundation Centre for Biosustainability, DTU, Denmark
2008	Professor, Department of Chemical and Biological Engineering, Chalmers University of Technology, Sweden
2004	Founding Director, Center for Microbial Biotechnology, DTU, Denmark
1995	Deputy Director, Center for Process Biotechnology, DTU, Denmark
1995	Visiting Professor, Department of Chemical Engineering, Massachusetts Institute of Technology, United States
1994	Founding Chairman, Danish Biotechnological Forum, Denmark
1986	MSc in Chemical Engineering, DTU, Denmark

Professor Jens Nielsen has 535 publications and an h-index of 67; >18000 citations.

The scientific world must never close in on itself. It should exist in constant interaction and balance with society and industry. Jens Nielsen has devoted his scientific career to creating this symbiosis. He hopes he can help to build a sustainable future for our planet.

A SCIENTIST OF SUSTAINABILITY

BY MORTEN BUSCH

Fungi and bacteria will help save us from global climate change.

Such a statement sounds like science fiction or pure nonsense for many people. For Jens Nielsen, Professor of Biological Engineering at Chalmers University of Technology in Göteborg, Sweden and Chief Scientific Officer and Professor at the Novo Nordisk Foundation Center for Biosustainability, this is just an ambitious objective that drives him in his everyday work as a researcher. His dream is a world in which oil-based products have a much less significant role.

"We will not run out of oil any time soon, but my research focuses on improving the environment. We will find a way to produce all the chemicals and fuels that we use today in a renewable and sustainable manner," explains Jens Nielsen.

Scientists have already succeeded in using yeast in large-scale production of bioethanol, proving that bioethanol can be produced much more rapidly and less expensively this way. This should reduce the need for fossil fuels.

"Our research indicates that microorganisms are part of making energy supply more sustainable. There are some obvious barriers. Oil is very inexpensive, and if you have to compete, then you should indeed be cost-competitive. There is a giant leap from developing a proof-of-principle process in which a microorganism can produce milligrams of a compound to achieving a process that can work in large-scale industry."

The researchers therefore focus on two different principles – and two phases – within systems biology. In the first part of the process, synthetic

biology, they strive to get an organism to produce a substance it does not normally produce. In the next phase, metabolic regulation, they strive to optimize the organism so it produces even more of the new substance.

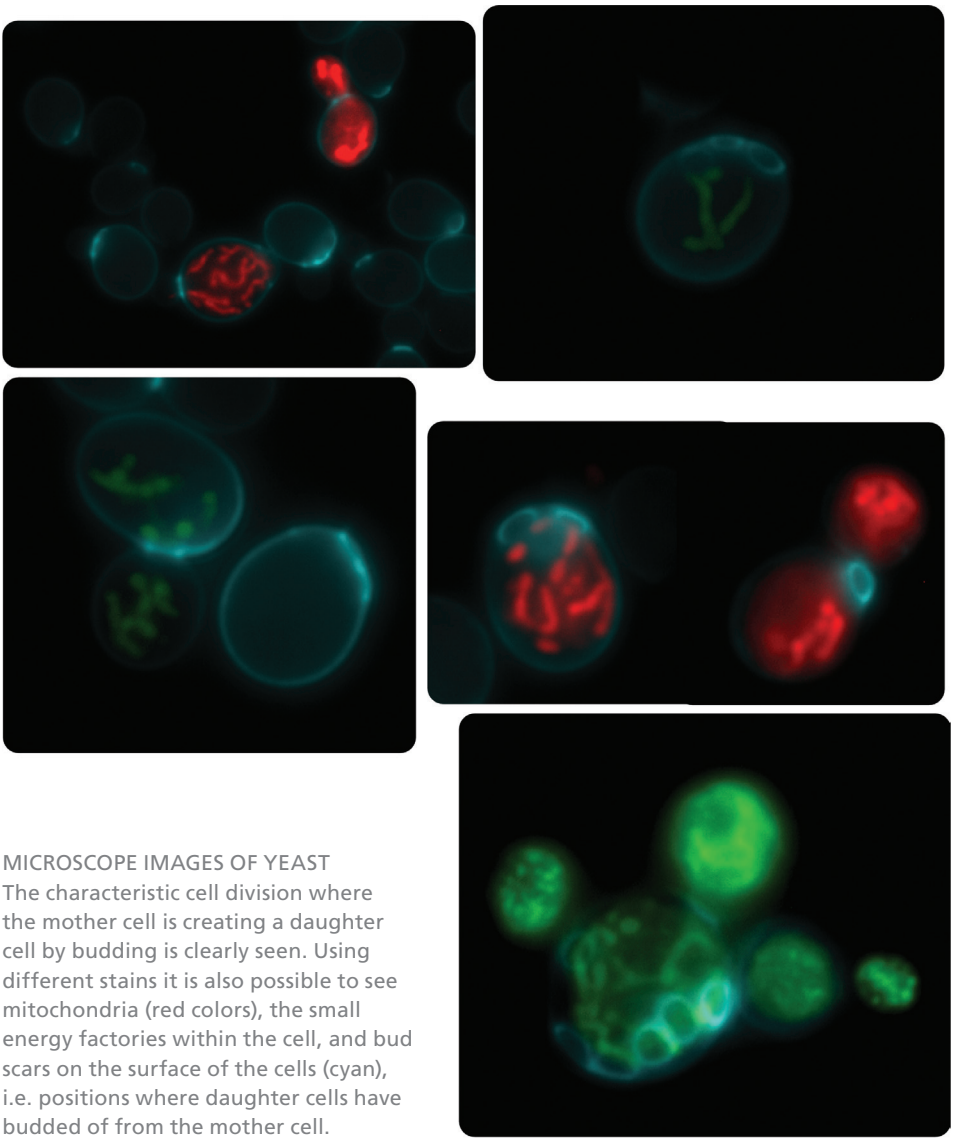
"I had a great interest in basic science, but it had to be application-oriented to motivate me."

"Typically, we take some genes from microorganisms or plants and splice them into yeast and then try to get them to work in the context of a pathway. If we succeed in establishing a new pathway that works, this typically only results in very small amounts of the product. Yeasts are evolutionarily selected to be really good at producing ethanol, so their whole metabolism has developed this way. So if we want to change yeast metabolism, we are up against this evolution."

MAKING A DIFFERENCE

The effort to transform yeast cells into bio-based cell factories is a balancing act, and the code word is sustainability, since optimal performance requires optimally balanced yeast cells. Sustainability is a recurring theme throughout Jens Nielsen's scientific work – and not just the sustainability of the planet or yeast cells. He focuses on scientific sustainability – and how to ensure that science benefits society and industry. This has always been close to his heart, even when he did not know that science would be the centre of his professional career.

"I come from a family with no academic background. I never thought I would become a professor. In fact, I barely knew what it meant to be a professor. I started out at the Technical University of Denmark (DTU), because it seemed to be a good, solid place to be. There you could become an engineer and could get a job in industry. I was sure that I would work at Novo Nordisk or somewhere else in industry where I could make a difference."



MICROSCOPE IMAGES OF YEAST
The characteristic cell division where the mother cell is creating a daughter cell by budding is clearly seen. Using different stains it is also possible to see mitochondria (red colors), the small energy factories within the cell, and bud scars on the surface of the cells (cyan), i.e. positions where daughter cells have budded of from the mother cell.

Things did not quite turn out this way. Jens Nielsen's supervisor, John Villadsen, convinced him that he belonged in the world of research and that he should continue his research career after finishing his PhD studies. However, Jens Nielsen had one condition.

"I requested that my project had some connection to industry if I were to continue to do research. I had a great interest in basic science, but it had to be application-oriented to motivate me. Otherwise, I could not see myself continuing to conduct research for the rest of my life."

Jens Nielsen and his supervisor therefore approached Novo Nordisk, which at that time wanted to expand their production of penicillin and wanted more basic scientific knowledge related to the processes to scale up production.

"They had created a five-year development project. It was a great partnership, because they respected the academic world and because they had a vision and had the courage to think strategically and long term. This approach is important for success in the bioindustry. If you do not understand the basic science, the idea of optimizing processes in bioindustry will not work."

WHEN KNOWLEDGE ADDS VALUE

Novo Nordisk stopped producing penicillin in the mid-1990s, since producing both insulin and penicillin in the same cultivation tanks was too difficult logistically. Instead of ending in defeat, the change turned into a victory for Jens Nielsen. Before long, there was international demand for Jens Nielsen's expertise; DSM, a penicillin-producing company headquartered in the Netherlands, contacted him.

"It was both very surprising and stimulating to be approached by a large international company. And it was a sign that my work had been noticed and what I had been doing was relevant in a broader sense. We started collaborating, and I worked for them as a consultant for many years."

Jens Nielsen's educational and research background turned out to fit perfectly into the dramatic revolution in biology that happened in those years. Many new genetic methods were developed in parallel with several new biotech companies being started, focusing on the design of cell factories for biosynthesizing proteins, enzymes and chemicals.

"I soon realized that finding the balance between academic and industrial issues is important. Academia should not start optimizing the things that industry is adept at doing. Researchers may make a real difference by developing methods, concepts and principles, which can provide general insight but can also create value for businesses. Collaboration that succeeds in finding this balance is usually the most durable and successful."

Jens Nielsen delivered ground-breaking work in the next few years by combining the molecular genetics of metabolic models with reconstructing metabolic pathways and developing new methods for metabolic regulation in yeast that have greatly contributed to the use of fungal-based cell factories for industry.

"What may seem to be an industrial optimization process is in fact pure basic research. It is fascinating to see what happens when we begin to adjust some of the cellular mechanisms. There are always some unexpected things, and every time we learn something fundamental about the organisms through the development-oriented work."

AN EYE-OPENER

Jens Nielsen could easily have continued his career in the secure setting of DTU. He had discovered his niche and knew the methods and processes. However, for the first time in his career, he decided to surprise both his colleagues and even himself.

"After 5–6 years at DTU I was an example of a good locally bred researcher in Denmark. Instead of continuing where I had left off, I decided to challenge myself. I was awarded a Fulbright Scholarship and went to the Massachusetts Institute of Technology (MIT) – a visit that changed my career and especially my outlook on research forever."

The MIT posting was inspiring; Jens Nielsen worked with Greg Stephanopoulos, an MIT professor, with whom he co-authored the first textbook on metabolic engineering in 1998. The visit primarily gave him an opportunity to do something more far reaching, especially reflecting on which direction he would take his research.

"It was an eye-opening stay in all respects. I mainly learned to set more challenging goals for myself. This taught me to dare to take more risks. It was important to examine things more fundamentally at a point in my career when I thought that I had everything under control."

When he returned to DTU, he was appointed professor. One research group with which he began working was a bioinformatics group led by Søren Brunak. Together, they started collaborating around functional genomics – a discipline in which researchers attempted to deduce a gene's function from its DNA sequences. Over the next years, he became deputy director and then director of the Center for Process Biotechnology until 2004, when he founded the Center for Microbial Biotechnology at DTU.

"The visit to MIT taught me to think on a larger scale. And even though I am not necessarily the best example of this, I always try to instil in my students the importance of learning how things are done in other parts of the world, so that they are inspired and dare to set ambitious goals and seek alternative paths."

THE ECOSYSTEM OF SCIENCE

Jens Nielsen has more than 50 patents to his name, has co-authored more than 500 articles and 40 books, has been cited more than 18,000 times and has attracted almost DKK 200 million in venture capital. Nevertheless, he considers his students to be the best benefit of his job.

"Every day, I get to collaborate with and serve as a mentor to my students. They all have incredibly different personalities and I like these differences. They bring their drive and good ideas. They are smart, exciting and challenging and they dare to explore new territory. I sometimes joke that I learn more from them than they learn from me, but there is much truth in this. I get the latest scientific input and new talent into our research group through them."

Jens Nielsen has mentored an extraordinary number of students. He has supervised about 70 PhD students and around 70 postdoctoral fellows and senior researchers. For his enormous efforts, Jens Nielsen received the 2012 Nature Award for Mentoring in Science. However, he believes that his true reward is that his students act as ambassadors for the way of thinking his group has developed.

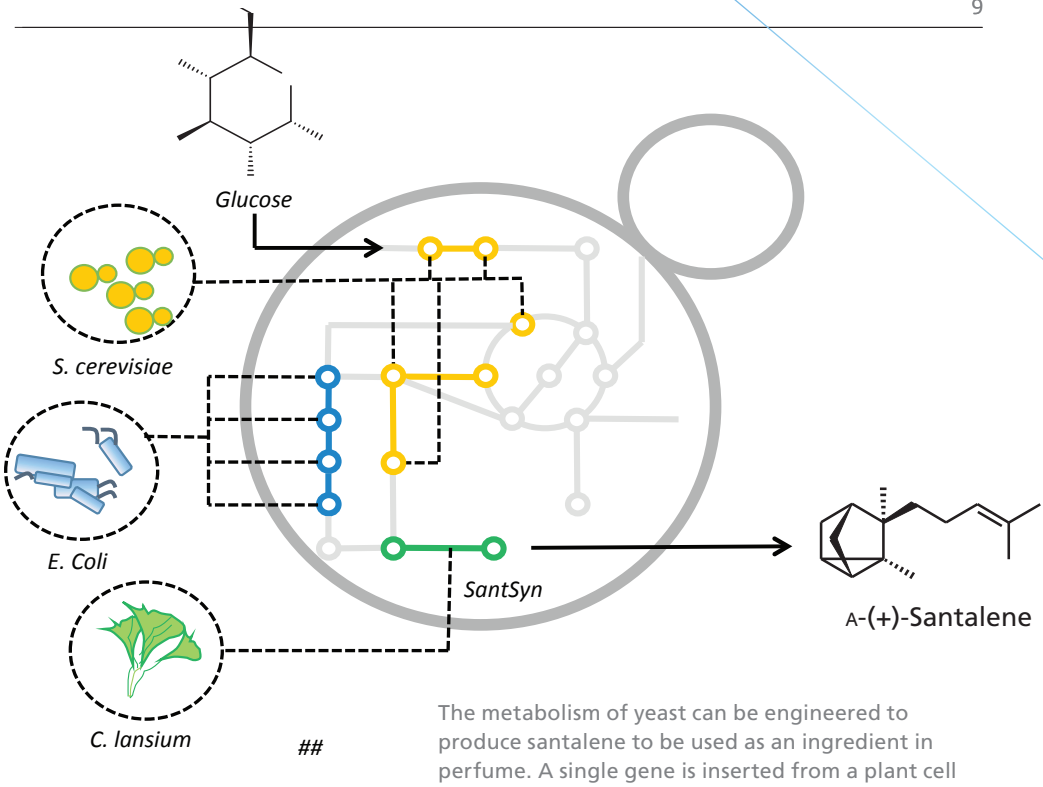
"Our primary purpose in academia is to educate young people. Keeping that in mind is important. I believe that the best way to educate them is by carrying out top research that has extremely ambitious objectives. This challenges young students. An interesting by-product is producing things that are relevant to industry and that can be patented."

Thus, although Jens Nielsen's PhD students typically work at the crossroads between academia and industry, the projects are always rooted in the academic challenges. However, the possible applications of this new world are also important because they can also help to motivate students.

"However, keeping the priorities straight is vital, because the most important ones are education and mentoring. Similar to my mentor, John Villadsen, I also give my students considerable freedom and let them participate in developing and designing projects. I can contribute through my experience, which enables me to advise them on which challenges are likely to arise. But they need to be allowed to try. This is how they learn."

THE PROFESSOR FROM SWEDEN

In 2007, after 10 years as professor in Denmark, Jens Nielsen surprised his colleagues again, resigning his professorship at DTU to build a completely new laboratory: the Division of Systems and Synthetic Biology at Chalmers University of Technology in Göteborg, Sweden.



The metabolism of yeast can be engineered to produce santalene to be used as an ingredient in perfume. A single gene is inserted from a plant cell whereas other genes are transferred from bacteria. Finally some of yeasts own genes are manipulated in order to ensure efficient production of santalene from glucose.

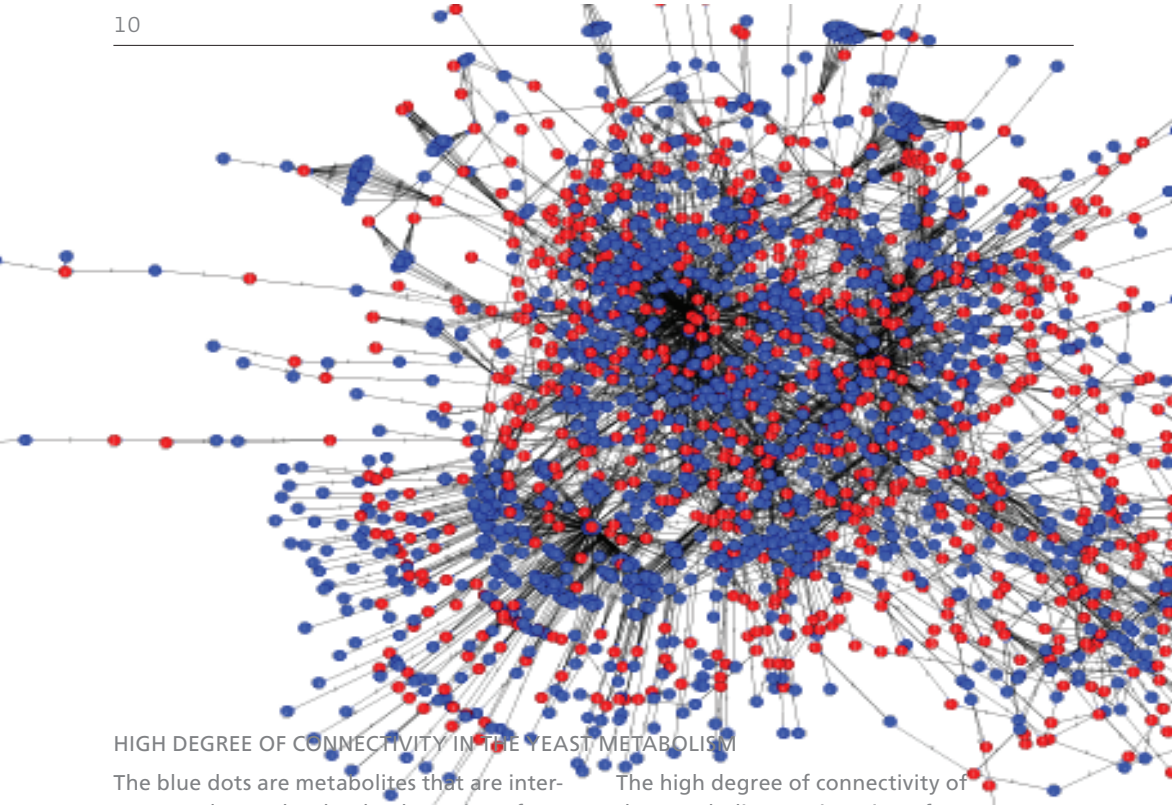
"Most of my colleagues and friends couldn't understand why I would move to Sweden since I was so well established at DTU. However, similar to my journey to MIT, the time was right to challenge myself, and I was given a unique opportunity to build something new from the ground up."

The research at DTU had been spread over many fields, but Jens Nielsen decided that his new laboratory would become the world leader within research into the metabolism of yeast. Since he was able to start completely from scratch, there was one simple question: what was needed to accomplish this?

"I was able to proceed systematically. For example, we had to master the latest methods within genetic modification. We needed to procure the appropriate computer equipment, and so on. And I was really fantastic ally received here. Whereas everyone in Denmark knew me and had for years, in Sweden I was treated like the new professor from abroad who was an expert in creating metabolic models."

While he was in Denmark, Jens Nielsen had tried to get collaboration partners from outside his usual field to use his models but without great success. He believed that these models could be used in other settings, such as in studies of diseases, including cancer and diabetes.

"I think that people in small countries tend to see what someone has accomplished rather than what they can achieve: putting people in a box. I could escape from this box in my new position in Sweden. You could say that I went from being a person who was known for merely examining bioprocesses to a person who knew something about metabolism in general. Further, I wasn't a young Danish professor but a well-respected professor from abroad."



HIGH DEGREE OF CONNECTIVITY IN THE YEAST METABOLISM

The blue dots are metabolites that are interconverted to each other by the action of enzymes (red dots). Each enzyme is encoded by a gene and thus it is possible to engineer the metabolic network by removing or adding genes to the yeast chromosome.

The high degree of connectivity of the metabolism engineering of one part of the metabolism will influence many other parts, and therefore computer models are necessary to predict efficient design strategies

According to Jens Nielsen, Sweden seems to understand the value of research differently. More people get advanced degrees in Sweden, and science is celebrated totally differently in Sweden: for example, when Nobel Prizes are awarded.

"It's a festive day in Sweden, with everyone waiting excitedly to find out who will win the prizes. Research is far more accepted in Sweden, and at present getting funding for research is also easier."

During the past eight years, Jens Nielsen has developed a major international research and education community at Chalmers with 60 employees that is considered a world leader in systems and synthetic biology focusing on designing efficient biosynthesis processes.

"The strange thing is that, since I moved to Sweden, I have established fantastic new collaboration within the studies of human disease in Denmark: for example, with Rigshospitalet – Copenhagen University Hospital. I am extremely pleased that our research, which started with studies of the metabolism of yeast, can be applied to research on how cancer and diabetes develop in collaboration with some of the best researchers in Denmark and abroad."

THE SUSTAINABLE FUTURE

The other collaboration opportunity with Denmark arose in 2011 when DTU contacted Jens Nielsen about its plans to establish a centre for biosustainability with support from the Novo Nordisk Foundation. Together with Professor Bernhard Palsson and other researchers, including Professor Søren Molin from DTU, funding was obtained for the major new centre, at which Jens Nielsen now operates as Chief Scientific Officer.

"This is a brilliant set-up. The Center is intended to be the world leader within designing, constructing and testing cell factories. By expanding the spectrum of chemical compounds and protein-based products that can be produced biologically, our ambition is to play a part in steering global industry towards a more sustainable society in the future."

According to Jens Nielsen, this future may arrive sooner than we think. His research group in Sweden in collaboration with the Novo Nordisk Foundation Center for Biosustainability are working intensively on creating cell-factory platforms that can provide greater flexibility in constructing new cell factories.

"The idea is to optimize yeast cells in producing a specific class of chemical compounds. Yeast cells usually produce considerable ethanol, but their metabolism can be reconstructed so that they produce, for example, more fatty acids or aromatic amino acids instead. Accomplishing this can create a platform for many other cell factories."

Creating a stable and viable platform for new cell factories will subsequently enable biological production lines to be added in a factory – depending on which specific chemical compounds are desired.

"There is great interest in many chemical substances that can be derived from fatty acids. One example is alkanes, which can be used as biofuel, and are directly compatible with existing oil compounds and work better in many respects than bioethanol, for example. Alkanes are denser and can be used as jet fuel. However, there is still some way to go before this becomes economically viable, because we can still only produce alkanes in small quantities."

Chalmers has major collaboration with Total, an energy company headquartered in France, on implementing this platform, but this is still a huge challenge because the result has to be extremely inexpensive to compete with oil. However, cell factories are already being used in a broad spectrum of other applications, for example within cosmetics.

"Adding other slightly different chemical groups to fatty acids enables other compounds to be created that are of great commercial interest, such as jojoba oil or sandalwood oil. We can thus use the same yeast cell factory platform for creating individual cell factories that can be used for the production of different final products having different applications."

The ideas for new discoveries often arise at the crossroads between industry and research institutions. Industry often starts the process by having a need. Research then has to ensure that new knowledge is created and not merely optimize an industrial process. According to Jens Nielsen, this balance is decisive and is the foundation of good sustainable collaboration.

Nevertheless, Jens Nielsen is not prepared to speculate on what the future will bring.

"Right now I enjoy the best of both worlds, both at Chalmers and at the Novo Nordisk Foundation Center for Biosustainability at DTU. So even though I like to challenge and surprise myself, it is rather difficult to imagine where I might have better opportunities for my research to make a difference in improving the future."

THE NOVOZYMES PRIZE COMMITTEE

The Novozymes Prize is a new European research award instituted by the Novo Nordisk Foundation. The Novozymes Prize is awarded in the name and with the funds of the Foundation. The purpose of the Prize is to raise awareness of basic and applied biotechnology research.

The Novozymes Prize is awarded to recognize outstanding research or technology contributions that benefit the development of biotechnological science for innovative solutions. It consists of a funding amount for the Prize recipient's research of DKK 2.5 million, and a personal award of DKK 0.5 million. An additional element of the Prize is an international symposium within the Prize recipient's field of research.

Prize recipients must have a current position at a public or non-profit research institution in a European country. They can previously have worked anywhere and have any nationality.

The Novozymes Prize is awarded by a prize committee that selects the successful candidate based on scientific achievements after a confidential nomination and review process.

The members of the Novozymes Prize Committee are appointed by the Novo Nordisk Foundation Board of Directors, and presently the committee consists of 6 members:

- Søren Molin, professor, chairman
- Henrik Callesen, professor
- Liisa Viikari, professor emeritus
- Claus Hviid Christensen, director R&D
- Michael Broberg Palmgren, professor
- Birgitte Nauntofte, CEO

The award event takes place in the spring at the Novo Nordisk Foundation Prize Celebration, at which the Novo Nordisk Prize is also awarded.

In addition, in celebration of the award, the awardee gives a lecture lasting about 1 hour at his or her workplace. Before the end of the year, the recipient and the Foundation arrange an international symposium within the scientific field of the prize winner.

Candidates for the Novozymes Prize can be nominated by the prize committee and former prize winners.

Additionally a "Call for nominations" is published in the Spring and candidates can be nominated on the basis of this call.

At the committee meetings the nominated candidates are thoroughly discussed with regard to their research contribution and impact, and a comprehensive bibliometric report is produced. A limited number of candidates are then selected for a thorough international peer review. On the basis of the international peer reviews the committee reaches a decision about the year's prize winner.

PREVIOUS RECIPIENT OF THE NOVOZYMES PRIZE

2015 PROFESSOR, DIRECTOR BERNARD HENRISSAT

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