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2020

*Professor
Detlef Weigel*

The **Novozymes** Prize

Nomination of Detlef Weigel

The 2020 Novozymes Prize is being awarded to Professor Detlef Weigel in recognition of the outstanding research he has undertaken during the entirety of his research career, which has led not only to fundamental understanding but also to technology contributions that have had major impacts in plant biotechnology. Greater resistance to pests, less sensitivity to drought, higher yields – these are just a small selection of the requirements that crops will have to fulfil in the future. Our society needs new crops that can withstand the changes arising from global warming and can meet the growing demand for food.

Detlef Weigel started his scientific career as a PhD student at the University of Tübingen followed by postdoctoral research at Caltech. From 1993 to 2002, he was an Assistant Professor and then Associate Professor at the Salk Institute for Biological Studies in La Jolla. In 2002, he became Scientific Member and Director at the Max Planck Institute for Developmental Biology in Tübingen, where he founded the Department for Molecular Biology. He is also an Adjunct Professor at the Salk Institute and at the University of Tübingen. In 2012, Detlef Weigel co-founded the plant bioinformatics startup company Computomics in Tübingen.

In his early scientific career, Detlef Weigel went from studying how fruit flies develop to studying how flowers develop. After becoming a Max Planck Institute Director, Detlef Weigel has initiated programmes in small RNA biology focusing on microRNA identification and functional consequences, the evolution of the plant immune system, the natural variation of adaptive traits, genome evolution, epigenetic regulation, hybrid incompatibility and population genetic analysis of disease resistance. He is now investigating how plants adapt to different environments, how genetic variation is generated and maintained in nature and how

the resulting phenotypic variation allows plants to adapt to their ever-changing environment. Detlef Weigel's use of genomics technologies to study the model plant *Arabidopsis thaliana* has led to detailed understanding of the variations in plant genomes, with great potential to help prevent diseases and increase yield in crop plants.

To give one example of the biotechnological impact of the work of Detlef Weigel, an early achievement of his was the cloning of the gene *LEAFY* in 1992 and the demonstration that this gene is involved in initiation of flower development in *Arabidopsis thaliana*. *Arabidopsis thaliana* is a small weed that grows at roadsides and walkways and has no commercial value at all. How can knowledge of this plant be of any biotechnological interest?

A major goal of plant breeding efforts is to produce novel varieties that are better adapted to local environments and changing climatic conditions. For some plants, breeding attempts to achieve delayed flowering so that as much as possible green material is produced during the season. For other plants, most notably trees that normally first flower after many years of growth, the breeding

The 2020 Novozymes Prize was awarded on Friday, 27 March to Detlef Weigel, Professor, Scientific Member, and Director, Department of Molecular Biology, Max Planck Institute for Developmental Biology, Tübingen, Germany

goal is to induce flowering as early as possible. In a follow-up article 7 years later together with Ove Nilsson, a Swedish postdoctoral fellow, Detlef Weigel showed that activation of *LEAFY* in aspen caused this tree to flower already after 5 months of growth. The same system was later identified in spruce. Now the time required for breeding trees could be reduced from several decades to a few years.

This knowledge was the basis for founding the Swedish innovation and development company SweTree Technologies, which is now the leading supplier of gene technologies for forest biotechnology with an intellectual property portfolio consisting of more than 150 patents and applications active worldwide and with two spinouts, Arevo and Cellutech.

With time, *LEAFY* has been identified in one plant after the other, and everywhere it has turned out to be key for flower development. The original article on *LEAFY* from 1992 is now cited in almost 1000 publications. Articles that cite the work report on the presence and function in flower development of *LEAFY* homologues in crops such as tomatoes, rice, grapevine, tobacco, peas, alfalfa,



oilseed rape, cauliflower, cucumbers, strawberries, potatoes, onions, salvia, peppers and cotton plants, ornamentals such as petunias, chrysanthemums, impatiens, gerberas and orchids and economically important trees such as poplar, aspen, pine trees, apple, eucalyptus, almond, orange, lemon, silver birch, walnut, cedar, papaya and peach. The knowledge obtained is now used for breeding crops that can grow longer and become bigger before they get harvested.

The scientific breakthroughs of Detlef Weigel have been accompanied by technology developments that have infiltrated the whole field. These innovations have underpinned major advances in plant biotechnology. The most recent research in the Weigel lab is characterized by extensive genome and methylome analysis of *Arabidopsis thaliana* and related species. This work has involved sequencing more than 1000 complete genomes of different *Arabidopsis thaliana* individuals from all around the world. This was technically extremely challenging, and Detlef Weigel's efforts not only drove the plant field ahead but also had significant impact on genome analysis across many organisms. He pushed the frontiers in bioinformatics and brought *Arabidopsis thaliana* variants and related species to the attention of population genetics experts. A major impact of Detlef Weigel's work on biotechnology is the broad palette of genomic resources he offers to the scientific community and life science companies. Thus, the biotechnology field has relied heavily on tools he developed and information he made available.

In 2014, Detlef Weigel changed his scientific focus to study how to improve crops to adapt to effects of climate change. This work again involves *Arabidopsis thaliana*, where Detlef Weigel coordinates an international team of researchers investigating the adaptability of this model plant to climate change. They tested how individuals

collected from over 500 geographical locations in Europe respond to heat and drought by growing these plants in Spain and Germany under dry conditions. This study is a first proof of concept of the use of genome-wide environment selection models for evolution-aware predictions of climate change-associated risks for biodiversity. They observed that individuals from different parts of Europe greatly differ in their ability to withstand future climate conditions. The team's predictions indicate that many of the continent's *Arabidopsis thaliana* populations will not possess the necessary genetic mutations to survive climate change, a pattern that is probably common to many plant species across Europe. With genetic data becoming available for a growing number of crop species, it will be possible to improve predictions of where a crop species is most at risk of suffering from the consequences of climate change.

In conclusion, Detlef Weigel is one of these extraordinary scientists who has contributed to a very wide range of topics during his career. This level of output can only be achieved by an extremely high-calibre, imaginative and enthusiastic scientist. Achievement in such a wide range of topics reflects how he follows his instinct into new and interesting areas of biology, working collaboratively with other high-calibre scientists worldwide when necessary. He achieves excellence in each area through the clarity of his thinking, the excellent execution of the project, and extensive literature analysis to ensure that he approaches each topic in a scholarly fashion. His work has generated outstanding research contributions that have benefitted the development of innovative biotechnological solutions for breeding improved crops and feeding the world in the future. Detlef Weigel is therefore clearly a worthy recipient of the 2020 Novozymes Prize.



**Plants need special
help to survive
climate change**



The current trajectory of global climate change will strongly affect how well plants can adapt to their environment. Contrary to what one might think, however, the plants in the hottest regions may not be those immediately hit hardest. Experiments in central and southern Europe show that especially the plants in central Europe lack the proper genes to survive a drier and warmer climate. According to Detlef Weigel, who has studied plant development and adaptation for three decades, evolution cannot keep up and therefore needs help. To recognize outstanding research or technology contributions that benefit the development of biotechnological science for innovative solutions, Detlef Weigel is receiving the 2020 Novozymes Prize.

For most people, a red rose looks pretty much the same wherever it is found in the world, but what is invisible to our eyes is the huge genetic differences between trees, plants and flowers depending on where exactly they grow. Conversely, most people can probably see the major difference between a tree and an herb. Nevertheless, the fact that the genetics of the herb *Arabidopsis thaliana* (thale cress) is so similar to that of a tree has made it an enormously important tool for studying how trees and other plants develop and adapt to the world around them. It has even become a tool that researchers hope can inspire ideas for how to preserve green biodiversity despite climate change.

“Since it will become even drier around the Mediterranean, one might think that the Mediterranean populations are the ones that are most at risk, because the climate is going to become even more extreme there. But it turns out that the plants in central Europe are at greater risk, because they basically have no genetic toolkit to deal with drought at all. Since evolution cannot catch up, we must consider using genome editing to help plants to adapt faster. Otherwise many of them might die off,” explains Detlef Weigel.

A four-winged fly

Already in third grade, Detlef Weigel wrote in an essay that he wanted to become a professor and work in a laboratory – even though he had never visited one. He even thought he would become a plant professor – more like a wildlife biologist, since his father took him on nature trips to count ducks and herons.

“I was thinking about environmental protection and nature, so I was quite sure that I wanted to study biology at university. When I arrived, I was surprised that some of my fellow students were not so serious about studying but thought that being a budding biologist mostly meant being ‘organic.’”

Fortunately, Detlef Weigel was studying at Bielefeld University, which had a modern curriculum that exposed students early on to genetics and cloning. This was 1981, when molecular biology had just started to take off. Fascinated by the emerging field, Detlef Weigel continued at the University of Cologne – well known for excellent molecular geneticists. There he became an undergraduate under one of the leading figures in developmental genetics, José-Antonio Campos-Ortega.

“José accepted me as an undergraduate student into this lab, and I thought it was the greatest thing that I was allowed to work in the lab and use all the instruments and other resources. I was hooked, and it was clear that this was where my future was.”

One day Detlef Weigel picked up the latest issue of *Science* magazine. On the cover was a four-winged *Drosophila* fruit fly, and inside Edward B. Lewis and colleagues described the first genomic analysis of this mutant fly with four wings – now resembling a dragonfly – one of his great discoveries that would earn him the Nobel Prize in 1995.

“I was working with these small fruit flies, and this was a pivotal moment in my career: what a phenomenal time to be alive, I thought. I have learned enough biology that I can go to the library, pick up a scientific journal, understand what is written there and be inspired by the work for my own experiments. What was and is still important to me and why I love being a scientist is that it is not just about my own work. I am just as or even more fascinated by the discoveries everybody else makes. It is really about the community of researchers that together advances knowledge for all.”

Small trees in petri dishes

For his PhD work, Detlef Weigel continued to study *Drosophila* development with Herbert Jäckle at the Max Planck Institute for Developmental Biology, where he discovered the founding member of an important family of regulatory proteins, the FOX class of transcription factors, which control, for example, speech in humans. However, Detlef Weigel had his doubts about the future of the fruit flies. What was going on in *Drosophila* was great, but he was worried that the rate of new discoveries could not go on like this forever. He also knew that if he wanted to make it in science he had to go abroad, so in 1989 he moved to California Institute of Technology in the United States.



The correct timing of flowering is very important for plants. If they flower too late in the year, there is not enough time for the fruits to ripen. On the other hand, when flowers are made too early in the year, they might die because of frost.”

As a graduate student, he was working very closely with a friend named Gerd Jürgens, and he had just learned from him about the *Arabidopsis thaliana* plant, which has many attributes similar to *Drosophila*, which piqued his interest. It was a plant, but mutant screens seemed to work well, and like *Drosophila*, it could be propagated easily in the lab. And the fact that, similarly to *Drosophila*, there were *Arabidopsis* mutants in which some body parts were transformed into other body parts suggested that he could continue to apply at least some of the concepts of developmental biology the already knew.

Detlef Weigel's choice of study object turned out to be a brilliant move. Soon he and his colleagues in the laboratory of Elliot Meyerowitz at the California Institute of Technology in Pasadena discovered a master control gene that is essential for the formation of flowers in *Arabidopsis*. Because mutants have

leaves where flowers should be, they called the gene *LEAFY*. The first experiment in his own lab at the Salk Institute for Biological Studies in La Jolla, also in California, was to ask whether *LEAFY* was perhaps not only required but also sufficient to turn vegetative parts of the plant into flower.

“When I saw flowers where normally there are shoots with leaves, I was blown away. The next stroke of luck came when a postdoctoral candidate, Ove Nilsson from Umeå in northern Sweden, came for an interview. Ove had just developed methods to transform poplar trees. As we were eating lunch, looking at the ocean and musing about projects, Ove said: ‘Why don’t we just put your *LEAFY* gene into poplar trees?’ I think we both agreed that this was an extremely long shot and that probably nothing would happen.”

Even though everybody was writing in their grant proposals that *Arabidopsis thaliana* could be used as a simple model organism to learn what happens in other plants, it was unclear how far this could be stretched, especially when it came to plants with a very different body plan and lifestyle such as trees.

“Ove went back to Sweden and took a little sample of the *LEAFY* gene construct with him. I did not hear anything from him for a few months, and then all of a sudden he writes and sends these pictures with these comments: ‘You won’t believe what happened: I took your *LEAFY* gene, put it into my aspen trees and within weeks I saw flowers in my petri dish.’” Normally, aspen trees flower only after 10 years or so, and this stunning result was beyond their wildest dreams.

The early-flowering transgenic poplar trees were an important discovery for biotechnology. This was the first direct demonstration that developmental control genes from the model plant *Arabidopsis thaliana* could be used to alter the behaviour of other species in a radical manner that was

practically useful – in this case opening a door to accelerated breeding. This key experiment made it clear that *Arabidopsis thaliana* is an extremely powerful platform for biotechnological discoveries, and it has been used very effectively for this purpose ever since.

A plethora of natural variation

Although it is surprising how much is conserved over millions and millions of years of evolution, it does not mean, however, that everything is the same in all plants – not even in the same species. After having seen how *LEAFY* could turn shoots into flowers, Detlef Weigel wanted to know more about how the transition from the vegetative phase to flowering was controlled. This led initially to the discovery of the *FT* gene, which later turned out to encode the long sought-after mobile flower-inducing signal, but it also made Detlef Weigel think about the role of flowering in local adaptation.

“An obvious next step was to ask how *Arabidopsis thaliana* strains from different regions of the species range reacted to flower-inducing signals such as day length and temperature. The correct timing of flowering is very important for plants. If they flower too late in the year, there is not enough time for the fruits to ripen. On the other hand, when flowers are made too early in the year, they might die because of frost. And if plants rely on fertilization by bees or other insects, they must flower at a time when those insects are actually around. So the time when plants flower within the season is very critical.”

Detlef Weigel and his long-term collaborator Joanne Chory at the Salk Institute quickly found that *Arabidopsis thaliana* is an excellent model for studying natural variation in flowering – and also in many other traits relevant to survival in different environments. Detlef Weigel became convinced that the study of genetic variation within species was one of the next big areas of biology. The challenge was that he was widely recognized as

a developmental and molecular biologist but had no credentials in evolutionary biology, and it was unclear how he could secure funding for the new direction without being an expert in this area. “Exactly at that time, I was offered a position as a director at the Max Planck Institute for Developmental Biology in Tübingen, where I was given carte blanche to pursue whatever I thought was the most worthwhile topic. It was a no-brainer that I accepted the offer, despite the fantastic colleagues I had at the Salk Institute.”

Too much of a good thing

A great example of how the support of the Max Planck Society allowed Detlef Weigel to explore entirely new directions is his work on autoimmunity. This began when one of his graduate students at the Max Planck Institute, Janne Lempe, found two strains of *Arabidopsis thaliana* that came from the same village but flowered at different times. The researchers thought that they were probably very closely related and that perhaps just a single gene difference could be the cause. To learn whether this might indeed be the case, the first step was to cross the two strains. “To our great surprise, we got these offspring that looked really strange. At first, we did not understand what exactly was happening, but it was obvious to us that this was an unusual phenomenon that we must investigate. Later, we discovered that the poor development of the hybrid progeny came from these plants being paranoid. They behave as if they are under heavy pathogen attack, even when there are not pathogens or other parasites around. In more scientific terms: these plants suffered from autoimmunity. As in humans, an overactive immune system in plants can be fatal.”

The study of this syndrome, called hybrid necrosis because there is not only poor growth but also rampant death of tissue, turned out to reveal important lessons for understanding the plant immune system. In collaboration with Jeff Dangl, Detlef Weigel’s group demonstrated that the autoimmunity was triggered

by mismatched immune genes. Although evolution or plant breeders may want to select for as many functional immune genes as possible, there are apparently limits to this. At some point, the immune genes start to interfere with each other and activate the immune system even without an external trigger. This is a typical fitness trade-off. “This is the core of evolutionary biology. Evolution is so fascinating because it always involves trade-offs, so if an organism manages to do one thing, it often means that it cannot do something else. A lesson not only for biology, but for life in general!”

0.1% better

The move to Tübingen in 2001 also meant a move towards much more general questions of plant evolution. Microarrays had been recently invented, so suddenly plant variation across the entire genome could be investigated at the DNA sequence level. Detlef Weigel recognized that just as the first reference genome for *Arabidopsis thaliana* had revolutionized studies of mutations induced in the laboratory, so would genome sequences for additional strains revolutionize studies of mutations induced by natural processes. Detlef Weigel thus launched the first large programme on intraspecific DNA variation in plants.

“The first complete genomes of a few species became available in about 2000. The articles invariably had titles such as ‘The human genome’ or ‘The *Arabidopsis thaliana* genome’. In hindsight, a more correct title would have been ‘The first human genome’ and the ‘The first *Arabidopsis thaliana* genome’. Your genome is different from my genome, so referring to the human genome does not make a lot of sense. Of course, we knew that genomes differ, but we had no grasp of how pervasive the variation is.”

The microarray-based project used a billion distinct DNA probes to investigate DNA differences in 20 strains of *Arabidopsis thaliana* – a titanic effort at the time. The major insight from



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this study was that members of the same species can differ in the presence and functionality of hundreds, if not thousands of genes. Detlef Weigel was hooked on wanting to know in more detail how much and why genomes differ, and when new high-throughput DNA sequencing technologies became available in 2007, he immediately proposed a massive undertaking: to sequence the genomes of more than a thousand strains.

“Our colleagues working with human genomes had just started the 1000 Genomes Project for humans, so we thought it would be uninspired to do exactly the same for *Arabidopsis thaliana*. I had a sabbatical visitor, Jim Carrington, who said to me: ‘No matter what you do, you always have to be 0.1% better than the competition’, and the moniker 1001 Genomes Project was born!” The more serious side was to look at 10 individuals each from 10 populations in 10 geographical regions, in total 1000 genomes, plus the original genome as a reference. Thus 1001 – a name that stuck well and also pointed towards the future focus of Detlef Weigel’s research, although he did not stick to just *Arabidopsis thaliana*. He also helped to have the genomes of relatives sequenced, such as *Arabidopsis lyrata* and *Capsella rubella*, to provide a

new perspective for differences observed within a species by comparing them to differences found between species.

“The entire field was unaware how much variation there is both within and between species. Perhaps one of the most curious discoveries that has been made in recent years is that a substantial number of wild plants have pieces of DNA from *Agrobacterium* bacteria in them. These footprints show that nature can alter genomes using the same methods modern biotechnologists use to modify plants in the lab.”

Rain in Spain

Apart from pathogens, another major driver of plant evolution is the climate. With the resources from the 1001 Genomes Project in hand, Detlef Weigel’s group could for the first time ask what the prospects were for adaptation to a changing climate not only at one specific place but throughout the entire range of *Arabidopsis thaliana*. “We started thinking about what an altered climate will do to *Arabidopsis thaliana*, which grows in very different places, from the Mediterranean to the Arctic Circle. I was very fortunate when about 5 years ago, Moi Exposito-Alonso, then a first-year



PhD student, set up this extremely ambitious experiment in which he took hundreds of strains from the 1001 Genomes Project and grew them in both Germany or in Spain, under conditions that mimicked rainfall in a typical German year or a typical Spanish year.”

The entire lab pitched in to record the survival of the plants, which differed greatly between the two sites and the two conditions. With the data from 24,000 different pots of plants, we could not only map the exact sequence variants that help plants to survive under today’s conditions but also predict

which *Arabidopsis* populations are at the greatest risk of future extinction. One of the most important discoveries was that genes that are useful in both Germany and Spain are rare; a gene that helps a plant to survive better in Germany is typically disadvantageous in Spain. Again, trade-offs are key!

“It would be fantastic if one could breed a single variety that would be optimal everywhere, but that is not how it works. The consequence of this is more surprising, however. With climate change, we know that the area around the Mediterranean will become even drier, so you might think that the Mediterranean



plants would be the ones most at risk, but it turns out that the populations most at risk are the ones in central Europe.”

According to Detlef Weigel, these plants basically have no genetic toolkit to cope with extended drought, whereas the plants in the Mediterranean should be able to react to extended drought relatively quickly. The good news is that more and more genes and variants are being discovered that help plants to thrive in adverse conditions. This in turn has led the Intergovernmental Panel on Climate Change to specifically mention the use of modern breeding technology and genomes to help plants to adapt faster.

“Evolution may not work rapidly enough to save these plants, but we are fortunate since we now have genomic technologies that give these plants a head start. Just as genome editing is revolutionizing medicine and animal breeding, it is a revolutionary technology for plants.”

No free lunch

Since trees are still one of the best methods of removing carbon dioxide from the atmosphere, Detlef Weigel thinks it would be absolutely a shame if we did not use these modern tools to help plants deal more effectively with the consequences of climate change. As in nature, this choice is about trade-offs as well.

“I do not think we will all die of hunger if we do not use genome editing, but if we do not use it, we will probably have to increase the use of agricultural land, and the more land we use for agriculture the less land there is, for examples, for trees to grow. Just as in nature, there is no such thing as a free lunch.”

Detlef Weigel says that we have to not only explain the benefits well – either to the consumer or the environment but we also have to explain very clearly what happens when we do not use modern tools of breeding or even boosting the genetics of keystone species in the wild.

“The precautionary principle is a great achievement of European environmental regulation, but this has also led us to focus too often on potential negative consequences, even if these are exceedingly rare. We have to remind ourselves that a tomato that has not been genome edited to make its cultivation more sustainable comes with a cost. Economists know this as an opportunity cost, and the opportunity here would have been to add the gene and save fertilizers, pesticides and the environment.”

The Novozymes Prize Committee

The Novozymes Prize is a 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 may previously have worked anywhere and may 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. The 2020 Committee comprised the following seven members:

- Bernard Henrissat, professor, chair
- Jens Nielsen, professor
- Gunnar von Heijne, professor
- Henrik Callesen, professor
- Johanna Buchert, professor
- Michael Broberg Palmgren, professor
- Birgitte Nauntofte, CEO, Novo Nordisk Foundation

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 recipient 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 recipient.

Candidates for the Novozymes Prize can be nominated by the Prize Committee and former Prize recipients. In addition, a call for nominations is published in the spring, and candidates can be nominated based on this call.

The Committee meetings thoroughly discuss the nominated candidates with regard to their research contribution and impact, and a comprehensive bibliometric report is produced. A few candidates are then selected for thorough international peer review. Based on the international peer reviews, the Committee reaches a decision about the year's Prize recipient.



Previous recipients of
The Novozymes Prize
2015–2019

2015	Professor, Director Bernard Henrissat
2016	Professor Jens Nielsen
2017	Professor Emmanuelle Charpentier Professor Virginijus Siksnys
2018	Professor Gunnar von Heijne
2019	Professor Dame Carol Robinson

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