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Professors
Sir Shankar Balasubramanian | Sir David Klenerman

The Novo Nordisk Prize 2024

Nomination of Sir David Klenerman and Sir Shankar Balasubramanian

The Novo Nordisk Foundation is awarding the 2024 Novo Nordisk Prize to Professor Sir Shankar Balasubramanian and Professor Sir David Klenerman for their groundbreaking contribution to high-speed, robust and affordable DNA sequencing, revolutionising the life sciences and clinical medicine.

DNA sequencing is the bedrock of modern biology and medicine and has revealed the blueprint of life. However, individual humans have 3 billion bases of DNA in the genome, creating a challenge to sequence the genome of an individual both rapidly and at low cost. Balasubramanian and Klenerman realised that DNA could be sequenced in a massively parallel manner by monitoring an enormous number of DNA synthesis reactions simultaneously, enabling an individual human to be rapidly sequenced. The approach they co-invented is now known as next-generation sequencing (NGS) because it significantly improved the speed and cost over the existing DNA sequencing technology.

Balasubramanian and Klenerman both graduated from the University of Cambridge, where they also earned their PhD degrees at the Yusuf Hamied Department of Chemistry; Klenerman, in 1985, with a thesis entitled Infrared chemiluminescence using a SISAM spectrometer and Balasubramanian, in 1992, with a thesis entitled Studies on the reaction mechanism of chorismate synthase. They both went on to the United States as postdoctoral fellows and returned to the University of Cambridge to become faculty members at the Yusuf Hamied Department of Chemistry.

Professor Sir Shankar Balasubramanian is a nucleic acids chemist, the Herchel Smith Professor of Medicinal Chemistry at the Yusuf Hamied Department of Chemistry and Senior Group Leader at Cancer Research UK Cambridge Institute at the University of Cambridge. His major accomplishments include: 1) co-inventing NGS technology; 2) characterising DNA G-quadruplexes in human cells and their role in regulating gene expression; and 3) inventing methods for sequencing epigenetic DNA bases. Professor Sir David Klenerman is a biophysical chemist and Professor of Biophysical Chemistry at the Yusuf Hamied Department of Chemistry at the University of Cambridge and the UK Dementia Research Centre at Cambridge. His major accomplishments are: 1) co-inventing NGS technology; 2) developing and applying single-molecule fluorescence to biology and biomedicine; 3) developing and applying nanopipette-based scanning ion-conductance microscopy; and 4) imaging the early events of T-cell triggering to determine the molecular mechanism.

In the late 1990s, Sir Balasubramanian and Sir Klenerman started to collaborate on fundamental studies that led to the development of NGS and the formation of Solexa. They brought together their unique backgrounds and knowledge of nucleic acid chemistry, polymerase mechanism of action and biophysical techniques, initially to advance the science, but this rapidly led to their major conceptual advance that this could lead to dramatically effective, rapid and inexpensive nucleic acid sequencing. The original experiment they aimed to perform was to observe the motion of a polymerase at the single-molecule level as it synthesised DNA on an immobilised surface. However, they realised that the same experimental set-up could be modified to create a next-generation DNA sequencing method that had the potential to improve sequencing speeds by a factor of a million. Based on this, Sir Balasubramanian and Sir Klenerman founded the company Solexa in 1998 to develop this technology.

Five key areas needed to be developed and integrated for the NGS revolution: 1) reversible terminator chemistry and an engineered DNA polymerase; 2) development of the surface and associated imaging of direct fluorescent incorporation reactions; 3) massive parallelisation of sequence reactions; 4) advances in instrumentation and software; and 5) surface-based DNA amplification, which the company licensed. Overall, this pioneering technology was truly interdisciplinary and innovative, leveraging the chemistry and biophysical expertise of Sir Balasubramanian and Sir Klenerman.

In summary, the Committee on the Novo Nordisk Prize finds that Professor Sir Shankar Balasubramanian and Professor Sir David Klenerman are worthy recipients of the 2024 Novo Nordisk Prize based on their systematic, transformative, clinically important and highly original contributions to high-speed, robust and affordable DNA sequencing, revolutionising the life sciences and clinical medicine.

Cover photo and page 3:
Millennium Technology Prize

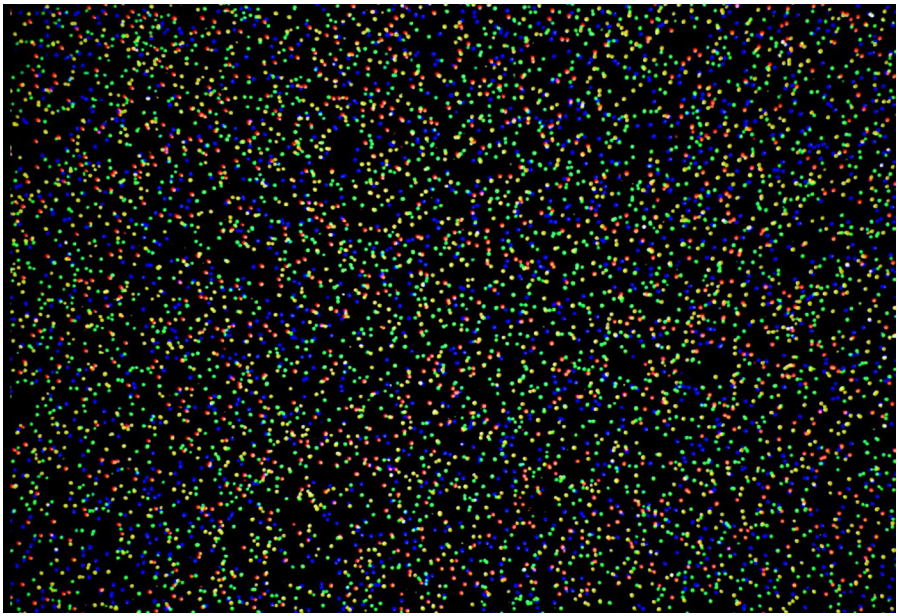
Photos page 8, 11, 14 & 15:
Nathan Pitt ©University of Cambridge

About Sir David Klenerman

1979	MA, Natural Sciences, University of Cambridge
1982	PhD, University of Cambridge
1985–1985	Postdoctoral fellow, Stanford University
1987–1994	Research Scientist at BP Research
1994–2007	Lecturer and Reader, University of Cambridge
2007	Professor of Biophysical Chemistry, University of Cambridge
2012	Fellow of the Royal Society
2015	Fellow of the Academy of Medical Science
2016	Royal Society Glaxo Wellcome Professor of Molecular Medicine
2018	Group leader, UK Dementia Research Institute, Cambridge

About Sir Shankar Balasubramanian

1988	BA (Hons) Natural Sciences, University of Cambridge
1991	PhD, University of Cambridge
1991–1993	SERC/NATO Research Fellow, Pennsylvania State University
1994–1998	Royal Society University Research Fellow
1998–2008	Lecturer, Reader and then Professor of Chemistry, University of Cambridge
2008–	Herchel Smith Professor of Medicinal Chemistry, University of Cambridge
2010–	Senior Group Leader, Cancer Research UK, Cambridge Institute
2011	Fellow of the Academy of Medical Science
2012	Fellow of the Royal Society
2023	Foreign Member of the National Academy of Sciences (USA)



Illuminating the code of life: the colourful revolution of next-generation sequencing

In a moment of serendipity, two then unknown chemists conversing in a pub laid the groundwork for a genomics revolution, dramatically reducing sequencing time and costs. Their innovation not only paves the way for personalised healthcare but also deepens understanding of human diversity and disease, showcasing the profound impact of curiosity-driven research in the scientific world.

This story delves into the quest to understand the essence of life, the uniqueness of each individual and the reasons behind people's susceptibility to both rare and very common diseases. It highlights how this knowledge empowers us to discover, diagnose and ultimately cure these conditions. The narrative unfolds around two chemists and their two postdoctoral fellows who, while conversing over a pint of beer at a local pub, stumbled on a groundbreaking idea.

"We were merely experimenting, to be honest. However, it is worth mentioning that we were in Cambridge, a place with a rich history of interest in DNA, thanks to predecessors like Watson and Crick and, of course, Fred Sanger. Their stories are well known and frequently discussed in Cambridge, making it impossible to ignore, regardless of one's interests," explains Sir Shankar Balasubramanian, Herchel Smith Professor of Medicinal Chemistry, Yusuf Hamied Department of Chemistry at the University of Cambridge.

We were merely experimenting, to be honest. However, it is worth mentioning that we were in Cambridge, a place with a rich history of interest in DNA."

Sir Shankar Balasubramanian

The Human Genome Project, conducted not far away at the Wellcome Sanger Institute, also played a significant role.

"In many ways, our journey is a synthesis of all this history. The Human Genome Project aimed to sequence a single genome over 13 years. However, since people are inherently diverse, understanding the genetic basis for our differences requires sequencing numerous human genomes. During our discussions, we realised that our method could be adapted to read the DNA code much faster," says Sir David Klenerman, Royal Society GSK Research Professor, Yusuf Hamied Department of Chemistry at the University of Cambridge.

Ability to see single molecules

In 1994, when Sir David Klenerman and Sir Shankar Balasubramanian joined the University of Cambridge, neither was contemplating DNA sequencing, nor did they know each other.

"We were different types of scientists: Sir David was a physical chemist, and I was an organic chemist-biochemist. We joined the department around the same time," recalls Sir Shankar Balasubramanian.

Sir Shankar Balasubramanian, with his background in organic chemistry, completed his PhD and then worked at Pennsylvania State University in the United States before joining Cambridge's Yusuf Hamied Department of Chemistry. Sir David Klenerman, after being doing postdoctoral studies at Stanford University, returned to the United Kingdom to work at BP Research for seven years.

"We were both young academics in search of interesting problems to tackle. In my field, there was a burgeoning revolution in the ability to see and analyse single molecules, which enabled us to observe biology in action," clarifies Sir David Klenerman.

Met over a cup of tea

Sir Shankar Balasubramanian was also exploring the dynamics of DNA polymerase – a cellular copy machine for DNA, reading the original genetic blueprint to ensure that every new cell receives an exact copy of the genetic material.

"We had submitted a manuscript, and a reviewer requested an experiment that required time-resolved laser fluorescence detection, which was not available in my lab. I was trying to find someone who could assist with that experiment. Then my former supervisor, Chris Abell, who knew both of us, suggested that I talk to Sir David Klenerman. He was known for his expertise in lasers, making him the perfect person for the task," explains Sir Shankar Balasubramanian.

This is how Sir Shankar Balasubramanian and Sir David Klenerman met – over a cup of tea. They addressed the reviewer's question, and their article was subsequently accepted, marking their first co-authored publication.

"That experience helped us get to know each other better and understand our interests and areas of specialisation. During these conversations, we developed the idea to combine Sir David's expertise in single-molecule fluorescence spectroscopy, a groundbreaking approach at the time, with my research interests," says Sir Shankar Balasubramanian.

Very specific and fundamental

The two new partners decided to embark on a joint project, although it presented challenges.

"Because we were newcomers, our research groups were small and our fields were not well established. We were seeking something intriguing to pursue. Thus, we embarked on a basic project," explains Sir David Klenerman.

Their idea involved building a single-molecule fluorescence microscope to observe the dynamics of DNA polymerase. By linking fluorophores – chemical compounds that emit light upon light excitation – they aimed to monitor the enzyme as it bound to its DNA substrate, extended the DNA and synthesised new DNA strands.

"Our first joint grant application was funded, providing the necessary resources. We still keep that grant application as a memento. It is fascinating to look back at it, especially since sequencing was not mentioned. Our goal was to observe the process and learn from it, a very specific and fundamental objective," he adds.

From years to days

However, the experiment did not proceed as smoothly as they had hoped. To commiserate and brainstorm solutions, they visited the Panton Arms pub with their two postdoctoral fellows, Mark Osborne and Colin Barnes. The Wellcome Sanger Institute, playing a pivotal role in the Human Genome Project nearby, was determining the 3 billion bases of the human genome for the first time.

"The Human Genome Project underscored the need for a more rapid and cost-effective sequencing method. There was significant interest in this field, making it the right place and time for us, working on fundamental science that happened to be highly applicable to an important problem," says Sir Shankar Balasubramanian.

During their discussions at the Panton Arms, the researchers realised that their work could be adapted to meet this need.

"The Human Genome Project sequenced one genome in 13 years, but our new idea could potentially reduce the time required to sequence a human genome by a factor of 100,000 – from years to days. I joked with the landlord that I would make him very famous one day. 'If you do, free beers for life,' he responded."

Series of colours changing

Reading genomic DNA is akin to reading ordinary books but is in some ways much simpler, since it comprises only four letters: adenine, cytosine, guanine and thymine – A, C, G and T. In addition, the two strands of DNA helices that form our genomes are chemically linked, pairing A with T and C with G.

"To read the sequence, we anchored one end of a DNA strand and began building its complementary strand. Our idea, based on our fluorescence colour-coding experiments, was to colour code each of the four building blocks in green, blue, red and magenta. This would enable us to read the code as the strand extended by observing the emitted colours," explains Sir David Klenerman.

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Sir David Klenerman

The researchers spaced single DNA molecules far enough apart on a surface to differentiate them, enabling them to observe the colours emitted as the corresponding DNA strands were synthesised.

"By recording these colour changes, we could determine the sequence of the DNA molecule on the surface. We planned to remove the bases at all spots and then remove the fluorophore and repeat the sequencing cycle, recording the colour of the dye incorporated at each spot. This process would be repeated multiple times."

Tearing the book apart

In hindsight, brilliant ideas often seem simple and obvious. The true genius and simplicity of the new sequencing method lay in its parallelisation. Instead of sequencing a single molecule at a time, researchers would sequence millions simultaneously. This approach was crucial for navigating through the 3 billion letters of the human genome. This task was roughly equivalent to reading the entire Lord of the Rings series, including The Hobbit prequel, 1000 times.

"While traditional sequencing approaches would typically only read small sections of a book, our approach was to read very short fragments from millions of different positions within the book, and then piece together the content afterwards," explains Sir Shankar Balasubramanian.

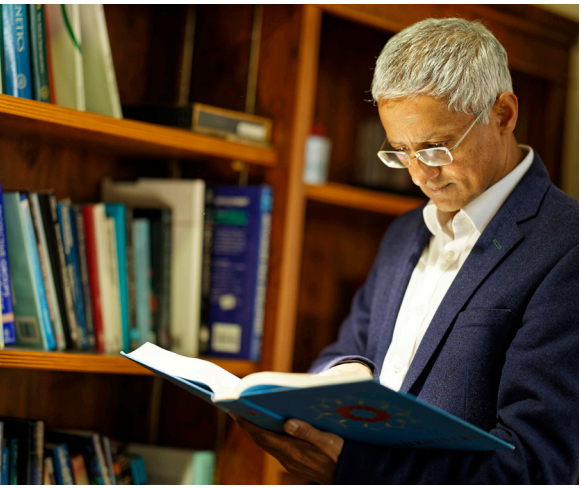
Sir Balasubramanian and Sir Klenerman would fragment the DNA into millions of tiny pieces and then attempt to reassemble it. Each piece contained a number of "words". By identifying the overlapping words between pieces, they could determine how the pieces connected, gradually reassembling the entire genomic "book". This process was akin to solving a giant puzzle, with each piece representing a small part of the story. By matching these parts, they could recreate the complete genome.

"We would extract genomic DNA, fragment it and attach the millions of fragments to a surface, sequencing the millions of pieces simultaneously. The Human Genome Project provided what we now call a reference sequence, which offers insight into the structure of a genome. By sequencing DNA fragments, we could use a computer to determine where each sequence originated from and realign it to the reference human genome, thereby constructing a new genome," elaborates Sir David Klenerman.

We can do this

In November 1997, Sir Shankar Balasubramanian and Sir David Klenerman met with venture capitalists from the bioscience investment firm Abingworth, armed with just a few slides detailing their ambitious ideas and calculations. They proposed that their concept, if realised, could increase the rate and reduce the cost of gene sequencing by 10,000 to 100,000 times. This proposal was sufficient to convince the investors to support the Cambridge chemists.

"In 1998, we founded the start-up company Solexa. We chose the name Solexa because sol



signifies light, and it was a contraction of solo, as in single molecules of DNA," explains Sir Shankar Balasubramanian.

Like any technology, the Solexa sequencing technique required extensive review and innovation. Initial investment was several hundred thousand, then stepped up to a couple of million to expand into Solexa's own premises, they established Solexa's first physical laboratory and began recruiting experts. The key challenges of synthesising the blocked nucleotides, mutating the polymerase, arraying the DNA on a surface and optimising the surface chemistry were all overcome by a talented team of researchers at Solexa.

However, to solve the remaining challenge of simplifying the imaging method and obtaining larger signals, Solexa licensed a patent for surface amplification developed by Pascal Mayer and colleagues at Manteia Predictive Medicines: the last component needed to get the sequencing technology fully functional.

"Instead of studying a single molecule of DNA, we finally ended up amplifying every DNA molecule into thousands of copies of DNA sequences at the same location. This amplification resulted in spots of blue, green, red and yellow that were easier to detect, simplifying the method. Consequently, we obtained millions of coloured spots on a chip the size of a human hair, each corresponding to a fragment of DNA," says Sir David Klenerman.

A genome per hour

The Solexa team designed chips, surfaces, enzymes, nucleotides, fluorescent labels, optics and engineering components to construct the first next-generation sequencing machine – dubbed 1G because it could sequence a billion bases of DNA in a single experimental run, matching the global

sequencing capacity around the time when Sir Shankar Balasubramanian and Sir David Klenerman initiated their project.

"People often ask whether there was a single moment of inspiration. However, it was not as straightforward as two guys walking into a pub and emerging with a sequencing system. It was more about establishing a series of connections, since several conceptual challenges needed to be addressed. We tackled each area separately and then considered how to integrate them. It was through this iterative thinking that we reached a point where we felt confident: 'We can do this,'" recalls Sir Shankar Balasubramanian.

In 2006, the team showcased the Solexa sequencing of the PhiX174 bacteriophage, a virus that infects bacteria. In November 2008, the sequencing of the first African genome was published in *Nature*, alongside the first Asian genome and the first cancer genome, demonstrating Solexa's capability for rapid and accurate genomic sequencing.

"The most recent sequencing systems can now sequence several trillion bases per run – a further 1,000 to 10,000-fold improvement on the first Solexa instrument. Thus, these instruments can sequence the equivalent of a genome in roughly about an hour. The Human Genome Project took about 13 years and cost several billion US dollars. Today, sequencing a genome costs less than 1,000 US dollars."

We are all different

Even though it was still considered fantasy or at least theoretical at the time, Solexa sequencing – today known as next-generation sequencing – attracted significant investment interest because of its potential to drastically reduce the cost and time required for DNA sequencing.

"We are, of course, all different. Understanding the genetic basis for what makes us all unique, including disease-related aspects, would require sequencing many human genomes. This required a method that was much faster and more affordable than the methods available at that time," explains Sir David Klenerman.

Potential applications included personalised medicine, in which genetic information could guide individualised treatment plans. In November 2006, United States–based Illumina made a USD 650 million offer to buy Solexa, making the project one of the greatest commercialisation success stories to emerge from the University of Cambridge.

"We had meetings discussing the possibilities if one could sequence the human genome. But the applications and the impact have gone well beyond what we speculated about at those meetings, including early diagnosis of cancer and prenatal screening. If you improve anything by a factor of a million, predicting how the technology will be used can be difficult."

Decoding cancer

If you consider human DNA as a complex instruction manual, errors can lead to cancer. Next-generation sequencing acts as a sophisticated tool, detecting these errors with

precision. Thus, this technology has already transformed how cancer is understood, offering insight into its genetic basis and paving the way for targeted treatments.

"Initiatives like the International Cancer Genome Consortium and Genomics England represent monumental efforts in mapping the cancer genome, aiding in identifying key mutations responsible for various cancers."

For instance, the discovery of a mutation in the BRAF gene in about half of melanoma cases has revolutionised treatment options.

"Today, doctors prescribe a drug that targets the protein encoded by BRAF. This results in a very good response for tumours, especially melanomas that have this mutation. This is an example of using information from your genome and the tumour's genome to prescribe a drug that will be more effective for that specific case."

This knowledge can significantly improve patient outcomes. This level of precision in treatment underscores the value of understanding the genetic landscape of tumours. Today, whole-genome sequencing of many types of cancer and certain complex patterns of mutations are helping clinicians to make treatment decisions.

"I predict that we will see significant advancements over the next two decades. But clinicians are already using data in this way. It turns out that cancer cells release some of their DNA content into the bloodstream. So, by drawing blood and isolating this DNA, which

"Initiatives like the International Cancer Genome Consortium and Genomics England represent monumental efforts in mapping the cancer genome, aiding in identifying key mutations responsible for various cancers."

Sir Shankar Balasubramanian

is floating around without associated cells, early detection of cancer becomes one of the most promising ways to ensure better survival outcomes and help patients."

Unlocking answers for rare genetic diseases

Diagnosing rare genetic diseases is akin to finding a needle in a haystack. Next-generation sequencing has offered a new, powerful solution, dramatically improving the ability to diagnose these conditions and treat the people who have them swiftly and accurately.

"Unfortunately, young children are sometimes born with developmental issues. When they visit the doctor, the doctor may struggle to diagnose the problem or devise a treatment plan. The new sequencing techniques have facilitated the rapid diagnosis of conditions such as Menkes disease among young children. By comparing the DNA of the child with that of their parents, clinicians were able to pinpoint the mutation within days," says Sir Shankar Balasubramanian.

This rapid diagnostic process exemplifies how next-generation sequencing is changing the landscape for treating rare diseases. By significantly reducing the time to diagnosis, next-generation sequencing enables more rapid and targeted therapeutic interventions, making a profound difference in patient outcomes.

"This rapid process is particularly important in neonatal intensive care. Thus, next-generation sequencing is already revolutionising the approach to rare genetic diseases, offering hope for more effective diagnosis and treatment strategies. Its integration into healthcare systems marks a significant advancement in personalised medicine."

Navigating the pandemic

The COVID-19 pandemic underscored the universal threat posed by infectious diseases. Again, next-generation sequencing was instrumental in deciphering the genetic code of the virus, enabling the tracking of its spread and the evolution of new variants worldwide.

"An international effort led to the sequencing of more than 1 million SARS-CoV-2 genomes. This global initiative was crucial for understanding the dynamics of the pandemic and guiding public health strategies worldwide," explains Sir David Klenerman.

And the application of next-generation sequencing goes beyond tracking; it is about understanding why certain individuals are more severely affected by SARS-CoV-2 and informing the development of future vaccines. This wealth of genetic information is key to combatting not just COVID-19 but future infectious threats as well.

"The extensive sequencing of SARS-CoV-2 showcases the critical role of next-generation sequencing in pandemic response and preparedness. It highlights the importance of global collaboration in addressing public health crises and the potential of genomics in shaping future healthcare strategies."

Afterlife

The impact of next-generation sequencing, envisioned by Sir David Klenerman and Sir Shankar Balasubramanian, now extends beyond their initial dreams. It has transformed forensic science, enhancing the accuracy of criminal investigations. Moreover, it promises to advance agricultural biotechnology by

facilitating the development of crops more resilient to climate change and pests and aids in environmental monitoring and biodiversity identification.

"Obviously, as the company has matured, you can start to play different roles. I actually stayed involved as a scientific adviser and consultant for another 10 years after Illumina acquired Solexa. Have we been struggling to find anything worthwhile to work on since then? So, on a personal level, people always talk to me about sequencing, but I want to talk about all the other stuff we have been excited about over the past 10–15 years," explains Sir Shankar Balasubramanian.

Throughout his career, Sir Shankar Balasubramanian has focused on DNA research: first, understanding the primary sequence of DNA, which led to the development of sequencing technology.

"Second, I have delved into the world of epigenetics, inventing methods for sequencing chemical modifications on DNA, such as methylation and hydroxymethylation. This work saw the birth in 2012 of the forerunner of Biomodal Limited, advancing our ability to read these epigenetic marks with precision. Lastly, I have explored the secondary structure of DNA, specifically the four-stranded G quadruplex structures."

Key pathological features

These complex DNA structures have been controversial because, for years, their existence and significance in living cells have been debated. Critics questioned their biological relevance and role.

"Recent breakthroughs over the past decade confirm their real presence in human cells and their crucial role in regulating gene expression and affecting cell identity, particularly in cancer. These structures reveal the complex and fascinating nature of DNA. I have been wrestling with this problem for 25 years and will take it with me to the afterlife if I have not cracked it."

Beyond sequencing, Sir David Klenerman's interests have broadened to include the study of protein misfolding diseases, such as Alzheimer's and Parkinson's, through innovative single-molecule fluorescence techniques. These efforts aim to better understand the molecular mechanisms of

these diseases and to develop diagnostic and therapeutic strategies.

"Transitioning to Alzheimer's and Parkinson's research, we applied similar principles of high-resolution molecular analysis, but this time focusing on proteins rather than nucleic acids. We used single-molecule fluorescence techniques to study the misfolding and aggregation of proteins, which are key pathological features in both diseases. In this way, we hope to uncover the mechanisms leading to these neurodegenerative diseases," says Sir David Klenerman.

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Sir David

We were not trying to do anything useful

What literally started with an idea drawn on a piece of paper in the Panton Arms in 1997 has today brought about several revolutions. For Balasubramanian and Klenerman, this is a great testament to how empowering basic science is and how, if implemented well, it can have a major impact.

"Scientists working together can solve major problems in society. I think this should still be very evident right now, with the COVID-19 pandemic only a few years behind us. We all need to think about where science can go, but it is equally important to realise that the idea came from basic science. So, the message is: if you want the next breakthrough technology, please fund basic science."

How to optimally foster innovation is a big topic of debate around the world. According to Sir Shankar Balasubramanian and Sir David Klenerman, there is no single correct answer to this. However, they are concerned about the popular trend of encouraging people in universities to engage more and more in applied or translational research.

"My view is that this is not the first thing I would do with resources. Our story did start with basic science. The grants that funded the basic work had no application in mind. We were not even trying to do anything useful. It was just curiosity that drove us. It is often about observations but also the context in which the observation was made, steering things in a certain direction. This can result in unexpected and sometimes momentous outcomes," explains Sir Shankar Balasubramanian.

Do take risks

Sir Shankar Balasubramanian is concerned that if organisations force university researchers to pursue only "useful" research, projects have to be so well defined that they will be short term and incremental.

"This is unlikely to be transformative. So, I emphasise highlighting the absolute importance of funding basic science very strongly if you want true innovations to emerge. Without strong support for basic science, your innovation pipeline will quickly dry up."

Equally important is who you decide to fund. The Solexa journey started when Sir Shankar Balasubramanian and Sir David Klenerman were relatively junior and more prepared to take risks than they are now.

"I would say, especially to the young researchers out there: do take risks, and try to identify and tackle big questions that you feel could make a significant impact if you can. Opportunities like that are rare, but if you see them in what you are doing, I strongly encourage you to go for it and give it a try. The worst thing that can happen is that you may fail. And then you try again," concludes Sir David Klenerman.

The 2024 Novo Nordisk Prize is being awarded at a prize ceremony in Bagsværd, Denmark on 19 April to Professors Sir David Klenerman and Sir Shankar Balasubramanian from the Yusuf Hamied Department of Chemistry at the University of Cambridge.

The Novo Nordisk Prize
- Advances in medical sciences

The Novo Nordisk Prize recognises an active scientist for her/his excellent research, inspirational leadership and mentoring, leading to a major discovery or breakthrough in biomedical science. The prize is intended to reward and further support biomedical research in Europe.

The Prize of DKK 5 million (EUR 672,000) consists of a research grant of DKK 4.5 million (EUR 605,000) and a personal award of DKK 0.5 million (EUR 67,000). An additional DKK 0.5 million will be awarded for hosting an international symposium within the Prize recipient's field(s) of research. In addition, in celebration of the award, the recipient gives a lecture lasting about 1 hour at his or her workplace, sponsored by the Foundation.

Nomination call
Nominations are invited from the scientific community worldwide defined as academics and scientists working in companies. The public call is published on the Foundation's website in the spring. The nomination and review processes are confidential.

Selection process
At the meetings the Committee considers the nominees' research contributions and medical impact of their discoveries based on the submitted nominations. The short-listed candidates are then selected for further evaluation including a comprehensive bibliometric analysis and international peer review.

The peer reviews, bibliometric report and the nominees' scientific leadership impact serve as basis for the Committee deliberations and decision of awarding the Prize.

The award event usually takes place in the spring at the Novo Nordisk Foundation Prize Celebration.

History of the Prize
The prize, originally DKK 50,000, was first awarded on 16 February 1963. The prize was called the Novo Prize from 1963 until 1989, when it was renamed the Novo Nordisk Prize. Until 2020 the Prize was given for a Danish contribution. From 2021 the prize is awarded for a European contribution.

Committee on the Novo Nordisk Prize

- → **Professor Jørgen Frøkiær, chair**
  Aarhus University Hospital,
  Aarhus University
- → **Professor Harriet Wallberg**
  Karolinska Institutet
- → **Professor Molly Stevens**
  University of Oxford
- → **Professor Hans-Gustaf Ljunggren**
  Karolinska Insitutet
- → **Professor May-Britt Moser**
  Norwegian University of Science and Technology
- → **Professor Lars Fugger**
  John Radcliffe Hospital,
  University of Oxford
- → **Professor Liselotte Højgaard**
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