2016 King Faisal International Prize for Science and Medicine

The King Faisal Foundation in Riyadh, Saudi Arabia, has awarded the 2016 King Faisal International Prize (KFIP) for Science in the field of biology to Vamsi Krishna Mootha from USA, and Stephen Philip Jackson from the UK. Mootha has used the mitochondrion as a model to identify the link between pivotal molecular factors involved in mitochondrial dysfunction and major human diseases such as diabetes and other metabolic disorders. Jackson is recognized for his outstanding contribution in defining the link between the basic mechanism of genomic DNA instability and its relationship to cancer. The Prize for Medicine has been awarded to Joris Andre Veltman and Han Grrit Brunner (both from the Netherlands) in recognition of their prominent role in moving into clinical practice a novel method of analysing DNA, referred to as next-generation sequencing (NAS). The Prize consists of a certificate, hand-written in Diwani calligraphy, summarizing the laureate's work; a commemorative 24 carat, 200 g gold medal, uniquely cast for each Prize and a cash endowment of Saudi Riyal 750,000 (about US$ 200,000). The winners will receive their awards in a ceremony in Riyadh under the auspices of the King of Saudi Arabia.

Mootha was born in Kakinada, India and his family moved to USA when he was an infant. He comes from a family of doctors. His father is a doctor, as are his two brothers, his sister, and all of their spouses. In 1993, Mootha received his B S in Mathematical and Computational Science from Stanford University. He too joined the family's medical fold, but with his tastes sharpened for laboratory research. He received an MD (1998) from Harvard University Medical School. It was as a first-year medical student at Harvard that he found his passion: mitochondria, the microscopic 'power plants' inside cells that convert food into energy. Following an internship and residency in Internal Medicine at Brigham and Women's Hospital, he pursued postdoctoral training in genomics at the Whitehead Institute.

Mootha is an Investigator of the Howard Hughes Medical Institute and a Professor of Systems Biology and of Medicine at Harvard Medical School. His laboratory is based in the Department of Molecular Biology and Center for Human Genetic Research at Massachusetts General Hospital. Mootha is currently not clinically active, but leads a research team dedicated to fundamental mitochondrial biology and disease. His research group consists of clinicians, computer scientists and biologists, who work collaboratively to elucidate the network properties of mitochondria, and how these properties go awry in human disease[1]. His work has led to the discovery of over a dozen Mendelian mitochondrial disease genes, that mitochondrial dysfunction is associated with the common form of type-2 diabetes mellitus, and the molecular identity of the mitochondrial calcium uniporter[2]. His team has also developed generic, computational tools that have been widely used in biomedical research. Mootha's laboratory is using a combination of microscopy, mass spectrometry and computation to identify all the component machinery of the mitochondria. His group has clocked about 1100 proteins so far. They have mapped the evolutionary history of each of these proteins and are using this information to identify protein functions and disease genes. They are also using chemical genomics to find disease biomarkers and identify therapeutic strategies. Mootha has received a number of honours, including the MacArthur Foundation Fellowship (2004), the Judson Daland Prize of the American Philosophical Society (2008), the Keilin Medal of the Biochemical Society (2014), Padma Shri from the Government of India (2014), and election to the United States National Academy of Sciences (2014).

Jackson was born in 1962 in the UK. He received his B S in Biochemistry from University of Leeds in 1983, and was awarded the Ph D in 1987, for his work on the yeast RNA splicing carried out at Imperial College London and Edinburgh University. Jackson is now the Frederick James Quick Professor of Biology and a Fellow of St John's College, Cambridge. He is a Senior Group Leader and Head of Cancer Research UK Laboratories at the Gurdon Institute, and an Associate faculty member at the Wellcome Trust Sanger Institute. Jackson's work focuses on the DNA-damage response (DDR), which optimizes cell survival and genome integrity by detecting DNA damage, signalling its presence and mediating its repair[3]. As DDR defects are associated with neurodegenerative diseases, immune deficiencies, premature ageing, infertility and cancer, this research might suggest new ways to alleviate such conditions. These works have established a link between the basic mechanism of genomic DNA instability and its relationship to cancer. His group has used super-resolution microscopy to visualize the spatial and temporal distribution of DDR proteins[4] (see ref. 5). Specifically, Jackson has unravelled the salient components of the pathway involved in DNA repair. He is also credited with an innovative approach to bring his findings into tangible therapeutic products to treat cancer. It is hoped that, together with the work of others, such research will indicate how defects in the DNA damage response can lead to diseases such as cancer, neurodegenerative diseases and premature aging, and how such diseases might be better diagnosed and treated. Jackson has received several prizes, including the Eppendorf European Young Investigator of the Year (1995), the Tenovus Medal (1997), the Biochemical Society Colworth Medal (1997) and the Anthony Dipple Carcinogenesis Young Investigator Award (2002). More recently, in recognition of his achievements, he has received the Biochemical Society GlaxoSmithKline Award (2008), and the BBSRC Innovator of the Year Award (2009) in recognition of his 'outstanding contributions to understanding DNA repair and DNA damage response signalling pathways'. He has also received the Royal Society Buchanan Medal (2011), and the Gagna A. & Ch. Van Heck prize (2015) for 'his cardinal contributions related to cellular events that detect, signal the presence of and repair DNA damages'. He is an elected member of several professional societies and organizations, including the European Molecular Biology Organization (1997), the Academy of Medical Sciences (2001) and the Fellowship of the Royal Society (2008).

The Prize for Medicine has been awarded to Joris Andre Veltman and Han Grrit Brunner in the field of 'clinical application of next-generation genetics'. As mentioned earlier, they were selected in recognition of their prominent role in

moving into clinical practice a novel method of analysing DNA, i.e. NGS. This has greatly improved the way of identifying genes that cause disease in patients and families suspected of having an inherited disorder. They have also initiated strong international collaboration in both research and diagnostics. New mutations have long been known to cause genetic disease, but their true contribution to the disease burden can only now be determined using family-based whole-genome or whole-exome sequencing approaches. One of the goals in genetic research aims at identifying genes in biochemical and physiological processes to reveal genetic causes of rare and common diseases. Previous obstacles such as costly genotyping or sequencing have been reduced with the chip-based genomewide association studies, now culminating into the NGS methodologies or next-generation genetics. The scope of next-generation DNA sequencing is transitioning from research to diagnostics (and beyond), but the conditions for routine clinical application have not been clearly defined. Technological limitations for fast and affordable sequencing of a patient's DNA are rapidly diminishing. At the same time, more and more is known about the role of DNA variation in disease susceptibility, disease development and response to treatment. Consequently, more and more pediatricians, cardiologists and other medical specialists would like to apply NGS-based diagnostics[6].

Veltman was born in 1971. He is a Professor of Translational Genomics at the Radboud University Medical Center, Nijmegen, and at the Maastricht University Medical Center, Maastricht. Veltman has been fascinated by the possibilities of genomics technologies to explain the causes of human diseases ever since these technologies became available. For this purpose he has built a multidisciplinary research group with expertise in genome technology, molecular biology, computational science and clinical genetics. His group was the first to identify a disease gene using genomic microarrays and the first to implement these microarrays for diagnostic genome profiling in intellectual disability. In the last 10 years his group has been using intellectual disability as a model disease to learn the basic concept of genotype–phenotype correlations. To study the impact of all forms of genomic variation on human disease, Veltman established the NGS technology and was the first to identify dominant disease gene mutations using whole-exome sequencing and recently provided strong experimental evidence for a *de novo* paradigm in intellectual disability[7]. Veltman is also actively involved in the implementation of NGS approaches in routine clinical diagnosis. His ultimate goal is to advance medical sciences by integrating his knowledge on the impact of genome variation in routine clinical decision-making[8].

Brunner was born in 1956. He is a Professor of Medical Genetics and Head of the Department of Human Genetics at the Radboud University, Nijmegen Medical Centre, and Head of the Department of Clinical Genetics of the Maastricht University Medical Center, Maastricht. Brunner dealt with hereditary diseases in the context of human behaviour and brain development, muscle dysfunction (examples: myotonic dystrophy, the subject of his dissertation) and skeletal dysfunction, malformations and gonads. He has been a member of the teams that found the genes of several human malformation syndromes. His current interests are in the genetic basis of human brain development, mental retardation and microdeletion syndromes[9]. Brunner has served on the board of the Dutch Human Genetics Society. He is currently a member of the Scientific Programme Committee of the International Congress of Human Genetics, and chairman of the Scientific Programme Committee for the European Society of Human Genetics. He is a member of the editorial board of the *Journal of Medical Genetics*, *Clinical Genetics*, and *Molecular Syndromology*. So far, a total of 65 scholars from 13 countries have been awarded the King Faisal International Prize for Medicine.

The Prizes are named after the third king of Saudi Arabia, to recognize dedicated men and women whose contributions make a positive difference, including to scientists and scholars whose research results in significant advances in specific areas that benefit humanity. Each year, the King Faisal Foundation awards KFIP for Service to Islam, Islamic Studies, Arabic Literature, Medicine, and Science. The Prize for Science rotates among the fields of physics, mathematics, chemistry and biology[10]. Within three decades, KFIP is ranked among the most prestigious awards. To date, there are 17 KFIP laureates who also received Nobel Prizes (mostly after the KFIP). A total of 54 scholars from 12 countries have been awarded the KFIP for Science. Mudumbai Seshachalu Narasimhan is the only Indian to have won in this category (for mathematics)[11]. The other major science prizes instituted by the Middle Eastern region are the UNESCO Sultan Qaboos Prize for Environmental Preservation[12], and the recently launched Mustafa Prize for Science by Iran[13].

The Science Prize for the year 2017 will be awarded in the field of physics. The topic for the Medicine Prize is 'biologic therapeutics in autoimmune diseases'. The deadline for all nominations is Sunday, 1 May 2016. Details are available at http://www.kff.com/ and http://www.kfip.org/

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Sameen Ahmed Khan, Department of Mathematics and Sciences, College of Arts and Applied Sciences, Dhofar University, Salalah, Sultanate of Oman.
e-mail: rohelakhan@yahoo.com