Laudatio Jack W. Szostak

Your Royal Highness,
Your Excellencies,
Members of the Board of the Heineken Foundation and the Alfred Heineken Fondsen Foundation, in particular their Chair, Mrs. De Carvalho,
Ladies and gentlemen,

Dear professor Szostak,

The oldest of the Heineken Prizes, the one for Biochemistry and Biophysics, has often been awarded for a single outstanding discovery. This year, however, the prize will be awarded to Professor Jack Szostak for a range of highly original contributions to our understanding of the processes of life.

Born in 1952, Jack Szostak's career has been quite remarkable. He was only 19 years old when he started his PhD programme. He obtained his degree at Cornell University in 1977. He has been a professor at Harvard Medical School for most of his professional life, and now combines this position with an appointment as the Alex Rich Distinguished Investigator at Massachusetts General Hospital.

Many of his discoveries were initially controversial, but they often opened up new fields of research. Let me describe a few of his major findings.

In the early 1980s, Szostak and Rothstein discovered that the end of a linear double-stranded DNA triggers recombination in yeast in a manner similar to recombination events during meiosis (meiosis is the process of cell division that generates the germ cells in sexual reproduction). Szostak then made the unorthodox proposal that double strand breaks in fact could be the initiating event in normal meiotic recombination. This discovery had major practical implications for yeast genetics and biochemistry, as it became easy to transform yeast cells with DNA fragments of choice. This in turn allowed gene knockouts in yeast and, through the work of others, became the central technique in mouse genetics as well.

In 1982 Szostak collaborated with Elizabeth Blackburn, who received the Heineken Prize for Medicine in 2004. They found that the chromosome ends (called telomeres) of Tetrahymena could be attached to linearized yeast plasmids, which enabled the discovery of telomerase enzyme activity. These linear plasmids also provided the basis for the development of Yeast Artificial Chromosomes, which played a major role in the sequencing of the human genome.

In the mid-1980s Szostak became interested in the new field of catalytic RNA. Tom Cech, another Heineken Prize recipient (in 1988), had shown that an RNA molecule from Tetrahymena has unexpected enzymatic properties and was therefore called a "ribozyme". This had shattered the dogma that genetic information is carried by DNA and RNA and that enzymatic properties reside in proteins. It earned Tom Cech the Nobel Prize for Chemistry in 1989. Jack Szostak's early studies focused on the structure and function of ribozymes. He then began to search for new tools to test larger numbers of RNA sequences. He developed a powerful evolution and selection technique to identify novel functional RNA molecules from a large pool of completely random RNA sequences. This has allowed the Szostak lab to discover many RNAs with new catalytic properties. Another remarkable finding was that of DNA and RNA sequences with various new ligand binding activities.
This work was driven by Szostak's interest in the origin of life, in particular the idea of the "RNA world", which assumes that in early primitive forms of life both the genetic information and the enzymatic activities were RNA-based, rather than separated into DNA

and proteins as is now the case. Szostak's work has given strong support to the RNA-world hypothesis.

In the 1990s, Szostak extended the in vitro evolution/selection approach to peptides and proteins using a very clever trick whereby a newly translated protein remains attached to its own messenger RNA. This means that selection for a particular function can be applied to the protein, while the linked RNA allows amplification of the encoded genetic information. Again, this resulted in proteins with novel binding and catalytic properties. These in vitro selection or directed evolution methods are all based on a very large diversity of RNA or DNA sequences, for instance, and a powerful selection process for desired molecular properties. They emulate the process of Darwinian evolution and one might therefore say that what Charles Darwin was for the living world, Jack Szostak is for the laboratory. In him the Academy is honouring an outstanding and highly creative scientist who has made fundamental discoveries and developed important technologies in biology.

Dr Szostak, on behalf of the Jury I would like to congratulate you on your receipt of the H.P. Heineken Prize for Biochemistry and Biophysics, which I hope will be a major incentive for your future scientific research.

Prof. dr. Rob Kaptein,
Chair of the jury of the Dr. H.P. Heineken Prize for Biochemistry and Biophysics 2008