



Press release

Mapping of a rare brain disorder in babies leads to award of The Brain Prize 2020

They have mapped Rett syndrome, a rare neurological disorder that primarily affects girls during their early childhood. Their research also gives a unique insight into the epigenetics and overturns previous understanding, indicating that neurological developmental disorders are not necessarily irreversible. For this, two neuroscientists are now receiving the world's most prestigious prize for brain research – the Lundbeck Foundation Brain Prize.

When a girl with Rett syndrome is born she looks like all other healthy babies. During her first years, she develops as she should, puts on weight and shows no signs that her genes are hiding an ugly disease. However, when she reaches the age of one or two, her development stagnates. She gradually loses the skills she has acquired, develops characteristics similar to autism and begins to make involuntary movements with her hands. Her condition eventually stabilises, and she can slowly begin to develop, but she will remain developmentally disabled for the rest of her life.

Today, thanks to the two internationally renowned neuroscientists **Huda Zoghbi** and **Adrian Bird**, we are familiar with and understand this unusual neurological disorder, Rett. Furthermore, their ground-breaking research has brought us closer to a treatment. For this, the two professors are receiving the world's most prestigious prize for brain research, The Lundbeck Foundation Brain Prize, worth DKK 10 million.

Professor Richard Morris, Chair of the prize's Selection Committee, explains the reasoning behind the award:

'The Brain Prize 2020 is awarded to Professor Huda Zoghbi and Sir Adrian Bird for their fundamental and pioneering work on Rett syndrome. Their work established the importance of epigenetic regulation in both brain development and the maintenance of normal adult brain function. It also points to novel opportunities for treatment of this and other neurodevelopmental disorders.'

Jan Egebjerg, Director of Research at the Lundbeck Foundation, which is celebrating 10 years of The Brain Prize, stresses the significance of this new breakthrough in the field of brain research:

'The brain is incredibly complex and, therefore, a great many of its basic mechanisms – for instance, when it comes to disease – are still uncharted territory. Brain disorders are a huge burden – to the individual and society alike. So, it's vital that we give a boost to brain research. Above all, this means giving research more money. But it's also important that we honour the researchers who often dedicate their entire careers to uncovering new territory and to delivering the greatest advances in brain research. These are some of the aims of The Brain Prize,' he says.

This year's prizewinners

About Professor Huda Zoghbi

Huda Zoghbi is a Lebanese-born American professor of genetics at Baylor College of Medicine and Texas Children's Hospital in Houston. Among other things, she identified the gene that causes Rett syndrome.

Read full biography here: <https://www.lundbeckfonden.com/en/person/dr-huda-zoghbi/>

About Sir Adrian Bird

Sir Adrian Bird is a professor of genetics at Edinburgh University, where he has spent most of his career. He is described as a pioneer of epigenetics, and he designed, among other things, the first mouse model of Rett syndrome.

Read full biography here: <https://www.lundbeckfonden.com/en/person/sir-adrian-bird/>

About Rett syndrome

Rett syndrome is a rare, congenital neurological developmental disorder that primarily affects girls, since the male fetuses typically perish during pregnancy. In the rare cases in which boys survive, they are usually more seriously affected by the disorder than girls.

The syndrome was first described by Austrian doctor Andreas Rett in 1966, and almost simultaneously Swedish Dr. Bengt Hagberg discovered the disease in his patients, and with his scientific publication on the discovery, he named the syndrome after Rett. But the syndrome was not widely known until 1983 when the scientific journal *Annals of Neurology* published an article on the disorder. Shortly after this, Huda Zoghbi diagnosed her first Rett patient, a five-year-old girl, at Texas Children's Hospital.

Rett syndrome is caused by a mutation in the MECP2 gene. The disorder results, to varying degrees, in mental and physical disability. During the first years of their lives, the children seem to develop normally, although they are often described as 'easy and quiet'. However, once they reach the age of one to two, their development stagnates. Among other things, they begin to show signs of autism and to make involuntary movements with their hands. The condition eventually stabilises and the child can then slowly begin to develop but will remain developmentally disabled for the rest of its life.

Patients also often have trouble breathing and sleeping and may suffer from epilepsy and scoliosis. Around 50% of sufferers are unable to walk.

Rett syndrome is an extremely rare disorder. Only two or three girls a year are born with the syndrome in Denmark, and Danish experts know of 118 girls or women, and three boys or men, living with the syndrome today.

In Denmark, everyone with Rett syndrome is treated at the Centre for Rett Syndrome at the Department of Paediatrics and Adolescent Medicine, Juliane Marie Centre, Rigshospitalet.

About epigenetics

When the human genome, the complete set of DNA, was mapped in 2001, it was expected that a number of feared diseases would be easier to diagnose, and maybe even to treat. If only we could identify the 'correct' DNA, it would be easy to identify the pathogenic, genetic mutations. Unfortunately, as it turned out, this was not so simple.

Scientists have since discovered that DNA expression in the individual cell is modified by mechanisms, such as methylation, which do not involve changes to the actual DNA code but rather 'turn on and off' codes on the two-metre long strand of DNA. These are known as epigenetic

changes – originating from the Greek word for ‘over and above’. The changes may, for instance, be linked to environmental impacts or the stage of development of the individual cell. They shape DNA expression by controlling which parts of the DNA should be active in a given cell at a given time. This is vital for the cell to retain its normal function – from cell generation to cell generation.

MECP2, which was identified by Sir Adrian Bird in 1992, works by recognising modified segments and, thus, linking these epigenetic changes to the general mechanisms for gene expression. It gives a molecular explanation of how epigenetic modifications can alter gene expression. Thus, mutations in the MECP2 gene can lead to changes in a wide range of genes that are regulated by epigenetic modifications.

About The Brain Prize

The world’s largest prize for brain research is Danish. It is called The Brain Prize and is awarded once a year to one or more researchers who have made an unprecedented contribution to international brain research. This includes research into health and diseases of all aspects of the brain, and in all disciplines – from basic neuroscience to applied clinical research.

The organisation behind prize is the Lundbeck Foundation: Denmark’s largest private funder of brain research. It is the Foundation’s ambition to enhance Denmark’s global position in the field of brain research, and this was the reason for establishing the prize in 2010. The prize is accompanied by a monetary award of DKK 10 million.

The Brain Prize is a tribute to individuals from all corners of the world who devote their brains to helping ours. However, its aim is also to raise awareness of a research field as infinite as the universe itself, yet no less fundamentally important to explore – because the brain’s complexity is matched only by its potential.

In order to be considered for the prize, you must be nominated by other researchers. The prize’s Selection Committee – a panel consisting of nine of the world’s leading neuroscientists – then reviews all nominations and picks the researcher, or researchers, to receive the year’s prize.

The Brain Prize has its tenth anniversary in 2020, and His Royal Highness Crown Prince Frederik will present the winners with the prize on 13 September at a grand celebration at the Royal Danish Playhouse, Copenhagen.

One of the objectives of the prize is to strengthen the Danish brain research environment through collaboration with the prizewinners so that, in time, Denmark will join the ranks of the most talented brain research nations in the world and improve its ability to diagnose and treat the increasing number of patients with brain disorders. The Lundbeck Foundation therefore encourages prizewinners to help inspire Danish brain researchers after the award of the prize – for example, by giving lectures and participating in conferences and other outreach activities in Denmark.

For further details please contact:

Jan Egebjerg, Director of Research at the Lundbeck Foundation, tel. +45 2119 3713

Pernille Thorborg Jasper, Media Relations Manager at the Lundbeck Foundation, tel. +45 2118 9132