Fundamental Research

The molecular and cellular bases of neurodegenerative diseases are still poorly understood. In order to develop better therapies, scientists at DZNE investigate how nerve cells are damaged and which targets are most relevant for the development of new medicines. Most neurodegenerative diseases share the deposition of misfolded proteins. We therefore believe that unifying cellular mechanisms are characteristic for these diseases.

Fundamental research at DZNE comprises various themes, including:

**Ageing and age-related cognitive impairment**
Age remains the main risk factor for neurodegenerative diseases such as Alzheimer’s and Parkinson’s disease. However, the biological links between ageing and neurodegeneration are
largely unknown.

The synapse and its dysfunction in disease
There is a growing consensus that early disturbances in synaptic activity and structure – i.e. glitches in the connections between nerve cells – are an early and possibly entirely reversible phase of neurodegenerative diseases. Therefore much attention is focused on mechanisms of synaptic dysfunction. We approach the problem by studying physiological signalling and its alterations in rodent models and by researching into genetic and epigenetic regulators of synaptic plasticity.

Inflammatory responses and their possible role in neurodegeneration
The role of inflammation in the progression of neurodegenerative diseases is a subject of extensive debate. Research projects include studies on the interaction of neurons and non-neuronal cells. Neurodegenerative diseases might be accompanied by inflammatory processes which activate the immune system. We also investigate the mechanisms of this immune response.

Protein dysfunction and axo-dendritic injury
Prior to neuronal demise, neurodegeneration is associated with protein missorting or altered protein processing. Typically changes in protein sorting and degradation affect transport processes within the nerve cells and synaptic activity. We try to understand mechanisms
leading to protein alterations. Our goal is to find ways of preventing damage to axo-dendritic networks.

**Disease mechanisms in diseases models**

DZNE scientists work with a variety of disease models to study disease mechanisms such as protein misfolding, aggregation and missorting. We also try to understand neuroprotective mechanisms which may serve as promising therapeutic targets.

**Stem cells and regenerative medicine**

DZNE scientists carry out research on adult neurogenesis and use induced pluripotent stem (iPS) cells as cellular models of neurodegenerative diseases. We explore mechanisms of plasticity, restoration, and compensation from extrinsic and intrinsic sources, a research field known as regenerative medicine. Within this line of research we intend to apply insights from developmental neurobiology to the identification of novel treatment and prevention strategies.

**Epigenetics and genome-environment interactions**

While genetic factors play an important role in the aetiology of neurodegenerative disorders there is accumulating evidence that the presence of a healthy vs. diseased state critically depends on the interaction between genes and environment. Thus, we try to elucidate the mechanisms by which the combination of genetic and
environmental risk factors contributes to the pathogenesis of neurodegenerative diseases.