



# Advanced Non-animal Models in Biomedical Research: Neurodegenerative Diseases |

**Neurodegenerative diseases** are a common and growing cause of mortality and morbidity worldwide, particularly in the elderly. Research on human diseases relies extensively on animal models, however, effective **new therapies** for these serious diseases are still lacking. One reason for this is that animal models often poorly represent human physiology and pathology. In response, the European Commission's Joint Research Centre (JRC) has carried out an extensive review of advanced models being used for basic and applied research into neurodegenerative diseases. Researchers characterised and catalogued **568 models** to make them accessible for human relevant studies that avoid the use of animals.

## NEURODEGENERATIVE DISEASES

Neurodegenerative diseases such as Alzheimer and Parkinson are untreatable conditions leading to dementia. Alzheimer's disease affects **over 10 million people in Europe**. Animal models are extensively used in research although their scientific relevance is a matter of debate.

## LEGISLATIVE FRAMEWORK

**Directive 2010/63/EU** on the protection of animals used for scientific purposes sets out clear legal requirements for the implementation of the 'Three Rs' principles of **Replacement**, Reduction and Refinement of animal procedures. The final goal is that animal testing should be phased out and replaced by scientifically valid non-animal alternatives.

## LACK OF EFFECTIVE NEW THERAPIES

According to the latest statistics, in 2017 almost 7 million animals were used for basic, applied and translational research in the European Union.

However, **existing treatments** for neurodegenerative diseases **are very limited**, and only treat the symptoms. No new drug treatment for Alzheimer's disease has been approved since 2003 because of a

high rate of failure in drug development programs due mainly to lack of efficacy or unexplained toxicity.

This suggests that reliance on animal models is failing to identify novel therapies. In this context, the JRC's EU Reference laboratory for alternatives to animal testing (EURL ECVAM) carried out a study to provide an **extensive review of non-animal models** currently in use for basic and applied research in the area of neurodegenerative diseases.

## ADVANCED MODELS IN BIOMEDICAL RESEARCH

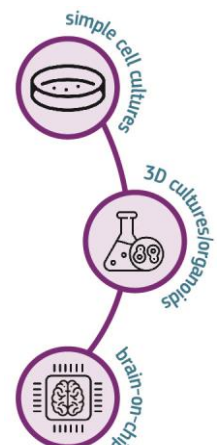
The abstracts of 13,000 scientific papers published between 2013 and 2018 were scanned for relevant human-based, non-animal models of neurodegenerative diseases. A total of **568 models** were identified from those papers as based on advanced technologies.

"Neurodegenerative diseases are one of the leading medical and societal challenges faced by EU society. It currently costs approximately €177 billions per year to care for people with dementia across Europe."

*World Alzheimer Report, 2016*



**568**  
models

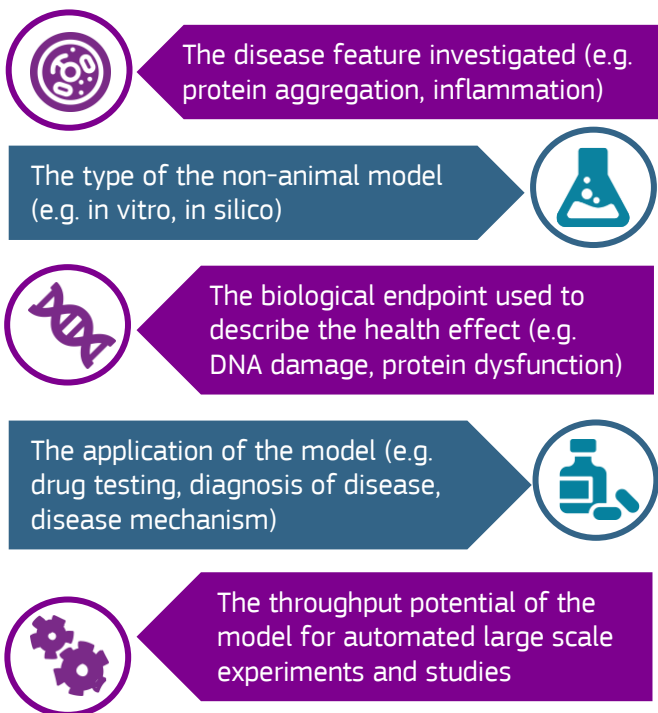


Joint  
Research  
Centre

This collection of models is freely available from the **JRC Data Catalogue**, while a **Technical Report** and a separately published **Executive Summary** will provide an in-depth meta-analysis of the approaches being used and elucidate the main findings.

## THE META-ANALYSIS OF THE MODELS

In this meta-analysis the selected models are characterised according to:



The collection shows that the largest part of the inventoried methods consists of induced pluripotent stem cells (iPSCs). However, **microfluidic/brain-on-a-chip' systems** show immense promise for the development of model systems that accurately mimic human neurodegenerative disorders.

## WHO IS THIS KNOWLEDGE FOR?

This collection represents an effective tool for **scientists** and **funding authorities** as well as all the various actors involved in the application of the **Directive**, such as Animal Welfare Bodies, Competent Authorities, National Committees and National Contact Points.

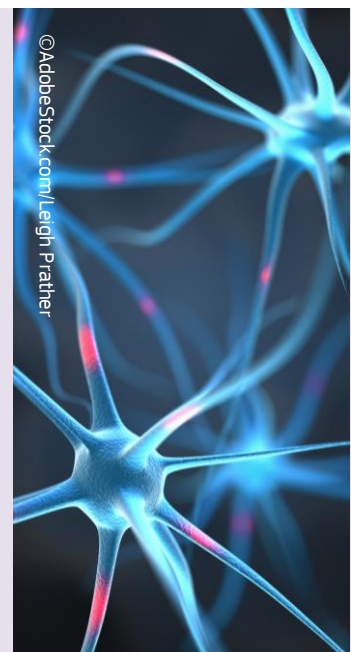
It has also the potential to be introduced in **education and training programmes** to inform new generation of researchers on effective non-animal models currently available and stimulate innovative approaches in biomedical research.

## Non-animal models for Alzheimer's Disease

Alzheimer's Disease (AD) is an incurable and debilitating condition that results in progressive degeneration and death of nerve cells.

**Induced pluripotent stem cells** offer a good model to study AD. Skin cells donated from patients affected by Alzheimer are reprogrammed into a pluripotent state capable to develop into any type of cell or tissue of the human body. Using differentiation factors, these pluripotent stem cells can generate one of the cell types of the brain called microglia. Microglia plays a key role in preserving the function of neural networks and responding to injury and disease. This model can be used to understand how microglia interact with other brain cells and influence the development of AD.

Unique tools for **proteomic analysis** of three-dimensional (3D) neurons and brain tissue from patients affected by Alzheimer are available today. The proteomics of 3D neurons from AD patients illustrate altered pathways similar to those found in ex vivo brains of AD patients. Dysfunctions present in 3D neurons from AD patients in vitro are comparable to the ones present in post-mortem AD brain tissue in vivo. This model can contribute to a more precise diagnosis of patients affected by AD.



©AdobeStock.com/Leigh Prather