# Human Neural Organoid Paradigm for the Study of Accelerated and Normal Age-Related Degeneration and Drug Screening

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FIELD OF ACTIVITY
Drug Discovery, Ageing, Neuroscience

KEY WORDS
Neural organoids, induced pluripotent stem cells (iPSCs), accelerated ageing, neurodegeneration, Cockayne syndrome, Alzheimer's disease, drug screening, cellular senescence

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**PATHOLOGY OVERVIEW**

Age-related neurodegenerative diseases such as Alzheimer's and Parkinson's disease remain major unmet medical needs. Modelling these complex disorders has been limited by the inability of animal models and conventional 2D cultures to reproduce the human brain's cellular diversity, architecture, and ageing dynamics.

**CLINICAL NEEDS**

There is a growing need for human-relevant systems that capture both neurodevelopmental and neurodegenerative processes to accelerate drug discovery, identify biomarkers, and evaluate interventions targeting ageing mechanisms. A unique opportunity lies in developing human models in which degenerative processes are dramatically accelerated.

**TECHNOLOGY DESCRIPTION**

A human neural organoid paradigm derived from induced pluripotent stem cells (iPSCs) obtained from:

- Healthy donors (age-matched controls)
- UV-sensitive syndrome (UVSS) patients (resistant to accelerated neurodegeneration and ageing)
- Cockayne syndrome (CS-I and CS-II) patients (accelerated neurodegeneration and ageing)

This unique four-model ensemble **reproduces distinct aspects of normal and accelerated ageing, including prenatal neurogenesis defects, neuronal loss, and cellular senescence.**

**Key innovations:**

- Recapitulates both neurodevelopmental and neurodegenerative phenotypes in 3D brain-like structures.
- Identifies DNA-repair–independent ageing pathways linked to neurodegeneration.
- Enables comparison between UVSS and CS organoids to filter non-ageing-related mechanisms.
- Provides a human-based screening platform for compounds that protect against or reverse

neurodegenerative defects.

## TARGET PRODUCT PROFILE

**Purpose**: Human neural organoid platform for modelling ageing and neurodegeneration, and for preclinical drug screening.
**Model inputs:** iPSCs from defined genetic backgrounds (healthy, UVSS, CS).
**Applications:** Mechanistic studies, target validation, compound screening, ageing biomarker identification.
**Format:** 3D neural organoid cultures amenable to high-content imaging and omics analysis.
**Setting:** Academic and industrial neuroscience and pharma R&D labs.

## MARKET OUTLOOK

The global neurodegenerative disease therapeutics market exceeds $45 billion (2024) and continues to expand with ageing populations. Demand for predictive, human-based preclinical models is rapidly increasing. Neural organoids offer a next-generation alternative to animal models, enabling early-stage drug testing and mechanistic validation.

## PUBLICATIONS

Crochemore C, Chica C, Garagnani P, et al. Epigenomic signature of accelerated ageing in progeroid Cockayne syndrome. *Aging Cell*. 2023;22(10):e13959. doi:10.1111/acel.13959

Crochemore C, Cimmaruta C, Fernández-Molina C, Ricchetti M. Reactive Species in Progeroid Syndromes and Aging-Related Processes. *Antioxid Redox Signal*. 2022;37(1-3):208-228. doi:10.1089/ars.2020.8242

Crochemore, Fernández-Molina C, Montagne B, Salles A., 2019, CSB promoter downregulation via histone H3 hypoacetylation is an early determinant of replicative senescence. Nature Comms 10: 5576 (*mechanistic links between CS and regular ageing*)

## PATENTS

Patent application pending for neural organoid models of accelerated and normal ageing.