

NEWSLETTER: INTERREG. PROJECT 'HERINNERINGEN'

Issue 3, 07.2019

RECENT PROGRESS:

1. Toxicity at maximum cell viability: Optimized *in vitro* exposure regimes assure absence of cytotoxicity during assessment of the impact of risk factors on human cortical neurons.;
2. Search for subtle changes: The differentiated cell lines are being exposed to the selected risk factors for genetic analysis;
3. Optimizing existing mouse models for Alzheimer's disease: These models are being exposed in order to define non-cytotoxic levels useful for further research

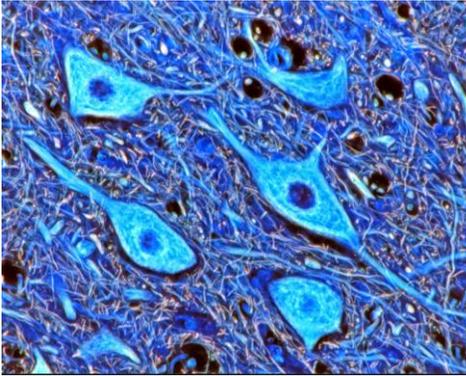


OPTIMIZATION OF *IN VITRO* EXPOSURE REGIMES TO ASSURE RISK FACTOR INDUCED ADVERSE EFFECTS IN THE ABSENCE OF TOXICITY

The selected human pluripotent stem cells were induced to differentiate into cortical neurons. Following quality control, the cells are being exposed according to the established exposure regimes. The samples will be subjected to differential genetic analysis to identify early processes that may be related to induction and early development of Alzheimer's disease.

While waiting for the results of these experiments, an extensive literature search has been performed to identify early processes leading to pathology. The knowledge is currently being structured according to the 'Adverse Outcome Pathway' concept a framework for the organization of available information linking the modulation of a molecular target [molecular initiating event (MIE)], via a sequence of essential biological key events (KEs), with an adverse outcome (AO). The focus is on potential molecular initiation events, key events leading to disease and the relation between these key events.

"Age is the most important risk factor for acquiring Alzheimer's, but which molecular and cellular processes support this susceptibility?"



'MEMORIES' IS HITTING THE ROAD

1. **29th Alzheimer Europe Conference, The Hague, Netherlands (23-25.10.2019): Making valuable connections.** The project is represented by a poster (PO.20.11) entitled: *Application of toxicologic approaches to develop a test for diagnosis of Alzheimer's disease before it strikes.*

2. **Project Symposium 2019, Leuven, Belgium (16.12.2019): The project organizes its second symposium entitled STOP Alzheimer's.** This symposiums targets industry, academia, caretakers and laymen. For further information visit <https://herinneringen.eu/nl>.

3. **12th FENS Forum of Neurosciences, Glasgow, UK (11-15.07.2020).** The project will contribute to the EURL-ECVAM initiated symposium



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entitled *Human oriented multidisciplinary approaches in Alzheimer's disease research.*

4. **11th World Congress on Alternatives and Animal Use in the Life Sciences., Maastricht, Netherlands (23-27.08.2020).** Memories has taken the initiative to propose a workshop for discussing *Biomarker-based in vitro tools targeting early Alzheimer's in a human relevant fashion.*

Project expertise

Icometrix (<https://icometrix.com>)

- Supporting prospective evaluation of selected biomarker signatures with Magnetic Resonance Imaging (MRI) for objective quantification of relevant brain structures in individual AD patients.

Stem Cell Institute Leuven, Katholieke Universiteit Leuven (<https://www.kuleuven.be/samenwerking/scil>)

- Providing the necessary iPSC expertise required for the identification and handling of relevant human iPSC lines, as well as production and quality control of iPSC-derived human neuron cell models for testing.

reMYND (<https://www.remynd.com>)

- Application of the genetic signatures to validate proprietary AD mouse models and to improve the assessment of *in-vivo* characteristics, pharmacokinetics, pharmacodynamics and the effects of experimental treatments.

ToxGenSolutions (www.toxgensolutions.eu)

- Valorisation of (epi-)genetic biomarker signatures as novel methods for diagnosis, novel tools for follow-up of disease progression or response to treatment in humans, and novel drug development.

Department of Biomedical Science, University of Antwerp (<https://www.uantwerpen.be/nl/faculteiten/faculteit-fbd/onderzoek/departementen-en-ond/dept-biomedische-wetenschappen>)

- Supporting evaluation of emerging biomarker signatures with well-characterized clinical samples (retrospective evaluation), and study cohorts (prospective evaluation).

Department of ToxicGenomics, University of Maastricht (<https://toxicogenomics-um.nl>)

- Providing the required expertise in (epi-)genetic approaches for the identification of early-AD specific peripheral biomarker signatures.