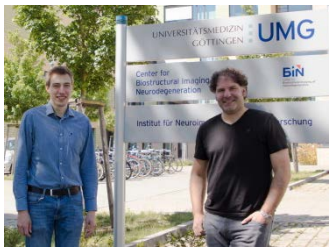
Press Release

No. 085e, 17. July 2020

New biosensor detects cell-to-cell transmission of the Parkinson-associated protein α-Synuclein

Scientists of the Cluster of Excellence Multiscale Bioimaging develop a new biosensor capable of detecting the transmission of human α-synuclein, a key protein associated to Parkinson's disease. Published in Nature Communications.

(mbexc/umg) Human alpha-synuclein (hαSyn) is a physiological protein that is primarily found in nerve cells, and is involved in the development of various neurodegenerative diseases, such as Parkinson's disease, Lewy-Body dementia and multisystem atrophy. In the course of these devastating diseases, hαSyn can form larger insoluble aggregates or middle size oligomers, which lead to the death of the affected nerve cells in the brain. Recent studies also show that these toxic aggregates are transmitted from one nerve cell to the next nerve cell by a mechanism similar to that of prion diseases. However, there is a controversial debate in basic research about how this process takes place exactly.



From left to right: Christoph Gerdes and Felipe Opazo at the entrance of the Center for Biostructural Imaging of Neurodegeneration (BIN) of the UMG. Foto: O. Díaz, BIN.

The lab of Dr. Opazo develops new probes from alpaca antibodies (nanobodies) to be used as tools in neurosciences and super-resolution microscopy. The Alpacas Pepe, Atahualpa, James and Castano (l-r), NanoTag Biotechnology GmbH. Foto: Dr. F. Opazo, BIN.

Scientists at the Göttingen Center for Biostructural Imaging of Neurodegeneration (BIN) of the University Medical Center Göttingen have now succeeded in developing a biosensor that can be used to visualize the transmission of the hαSyn protein between neurons. In the recently published study, the teams of Dr. Felipe Opazo (BIN) and Prof. Dr. Silvio O. Rizzoli, Institute of Neuro- and Sensory Physiology (UMG) describe the development of the biosensor "Fluorescent Reporter for Human αSyn", in short FluoReSyn.

The results presented here prove that the new FluoReSyn biosensor can become a valuable tool for investigating the transmission of human alpha-synuclein, and has great potential for clinical research and diagnostics. For the first time, the new biosensor allows the reliable observation in cultured nerve cells and in animal models of how the hαSyn protein transmits its message from cell to cell. The new biosensor therefore is a suitable tool to decipher the molecular mechanisms of hαSyn-associated neurodegenerative diseases. The study was funded by the Göttingen Cluster of Excellence Multiscale Bioimaging: from molecular machines to networks of excitable cells (MBExC) and published in the renowned journal "Nature Communications".

Original publication:*Gerdes C, Waal N, Offner T, Fornasiero EF, Wender N, Verbarg H, Manzini I, Trenkwalder C, Mollenhauer B, Strohaeker T, Zweckstetter M, Becker S, Rizzoli SO, Basmanav FB, Opazo F (2020) A nanobody-based*

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Editor University Medical Center Göttingen, Georg-August-University, Executive Committee

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fluorescent reporter reveals human α-synuclein in the cell cytosol. NAT COMMUN, 11: 2729 (2020). DOI: 10.1038/s41467-020-16575-0

Prerequisite for the development of preventive and therapeutic strategies for synuclein-associated, neurodegenerative diseases is a fundamental understanding of the molecular mechanisms that lead to the development and spread of these diseases. The development of the FluoReSyn biomarker represents a major step forward in the study of these mechanisms.

“The presented results prove that FluoReSyn is a very useful tool to study the transmission mechanism of hαSyn. After appropriate optimization, our biosensor may even be able to serve as a diagnostic marker for αSyn-associated neurodegenerative diseases”, says Dr. Felipe Opazo, senior author of the publication.

New Biosensor FluoReSyn

The methods used to date for detection of hαSyn transmission are based either on genetic manipulation of the protein or pre-labelling using fluorescent markers. These methods are criticised because they may alter the physiological structure of hαSyn, and can thus lead to an impairment of the natural function and localisation of this protein.

The team of Dr. Opazo used anibodies derived from alpacas, also known as “nanobodies” due to their miniatured size. These nanobodies can be engeniered to carry a fluorescent molecule and they have the unique ability to be used as reporters in living cells. Whith this technology, the present study characterized the FluoReSyn biosensor, which is able to reveal the entrance of external hαSyn proteins (transmission), and enables to detect hαSyn in a dose-dependent manner. Using cells, that stably express FluoReSyn, the scientists interestingly succeeded in detecting the entrance of a transmittable form of hαSyn from cerebrospinal fluid of Parkinson patients.

*The **Göttingen Cluster of Excellence Multiscale Bioimaging: From Molecular Machines to Networks of Excitable Cells (MBExC)** is funded since January 2019 in the framework of the Excellence Strategy of the German Federal and State Governments. Applying a unique and multiscale approach, MBExC investigates the disease-relevant functional units of electrically active cells of heart and brain, from the molecular to the organ level. The MBExC unites numerous partners from the university and extra-university institutions in Göttingen. The overall goal: to understand the relationship between heart and brain diseases, to link basic and clinical*

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research, and thus to develop new therapeutic and diagnostic approaches with social implications.

FURTHER INFORMATIONEN
Lab of Dr. Felipe Opazo: https://opazolab.de
Lab of Prof. Rizzoli: http://www.rizzoli-lab.de
About BIN: https://www.cfbin.uni-goettingen.de
About MBExC: https://mbexc.de

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