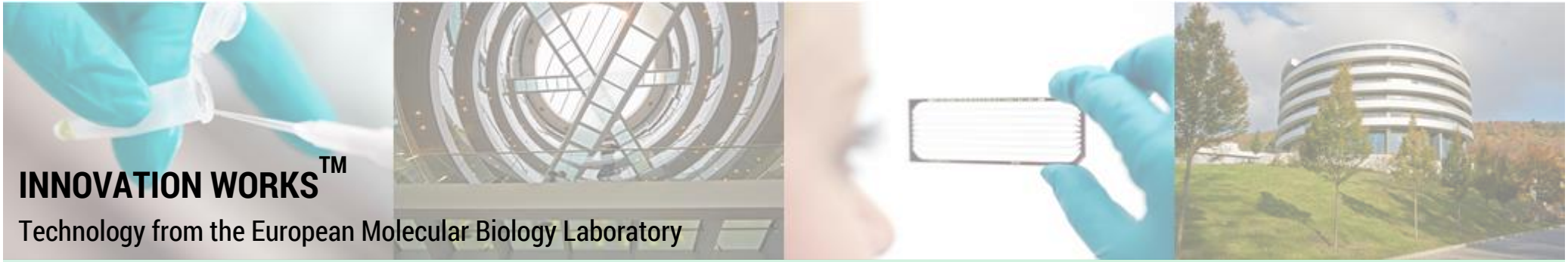

INNOVATION WORKS™

Technology from the European Molecular Biology Laboratory

Serpin A1 as Target and Companion Diagnostic for Parkinson's Disease Dementia (PDD)

EMBLEM Ref. 682

Challenge

- there is a clear lack of treatment options for Parkinson's Disease Dementia
- early treatment and diagnosis is critically for patient outcomes

Commercial Opportunity

- Differential glycosylation of SerpinA1 as target / companion diagnostic towards clinical use
- first-in-class potential
- collaboration and/or license, including access to well-documented, standardized collection of patient material

Technology

- two studies with different methods conducted by the inventors showed that differences in the sialylation of serpinA1 isoforms discriminate between PD and PDD patients
- SerpinA1 and/or glycosyltransferases as possible targets for PDD
- CIEF-Immunoassay of serpinA1 would allow for diagnosis in a standardized, fast and high-throughput manner as companion diagnostic or for patient identification and stratification

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Key Inventors

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Intellectual Property

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EMBLEM
TECHNOLOGY TRANSFER

Serpin A1 as Target and Companion Diagnostic for Parkinson's Disease Dementia (PDD)

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Up to 80% of PD patients can develop Parkinson's Disease Dementia (PDD). Currently diagnosis comprises a number of neuropsychological tests which are time consuming, costly and - more importantly - they only identify individuals after significant pathophysiology is already established. However, early treatment of cognitive deficits is critical for patient outcomes and significantly reduces the economic burden of the disease.
To date, treatment options are limited and early identification of individuals at risk is still hampered by the lack of an early, presymptomatic, diagnostic and predictive marker to reliably identify individuals most likely to benefit from pharmacological treatment of cognitive deficits and to stratify presymptomatic patients.

Serpins are a broadly distributed family of protease inhibitors. Some of them have been shown to be druggable targets, especially in connection with coagulation / cardiovascular disorders, and a number of marketed drugs targeting serpins are available to date.
Structural changes due to aberrant modification are a likely mechanistic link to PDD pathology. Serpins contain an exposed mobile reactive loop that is presented to the target proteinase.

This marked molecular flexibility renders the Serpins susceptible to mutations or aberrations, resulting in undesired intermolecular linkage and polymer formation. The effects of such aggregation are cumulative, leading to loss of cellular function. This process is found in genetic mutations of Serpins that result in liver damage and dementia (Familial encephalopathy with neuroserpin inclusion bodies (FENIB)), respectively.

The inventors showed in two different studies - one on 93 individuals sampled from three centres and one on 102 individuals sampled from two centres - that differences in the sialylation of serpinA1 isoforms distinguish between PD and PDD patient groups.
The capillary isoelectric focussing immunoassay (CIEF-immunoassay) developed in the second study, allows for the analysis of serpinA1 isoforms in CSF samples in a high-throughput, reliable and standardized manner.

These findings highlight the importance of serpinA1 in PDD as it might provide a novel target for developing treatments, act as a companion diagnostic for presymptomatic PDD treatment and could be established as the first predictive diagnostic marker for PDD.

References

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