

Diagnostic value of skin RT-QuIC in Parkinson's disease: a two-laboratory study

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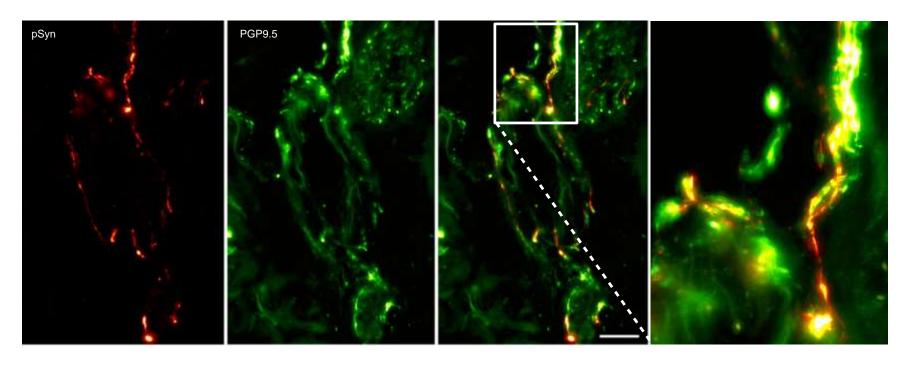








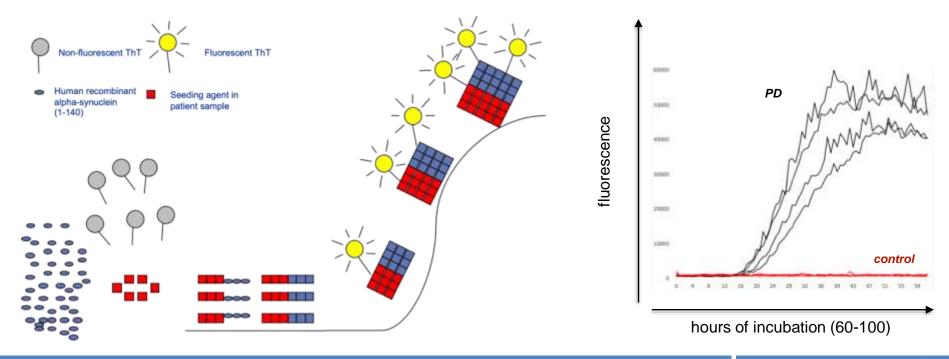
α-synuclein pathology present in dermal nerves



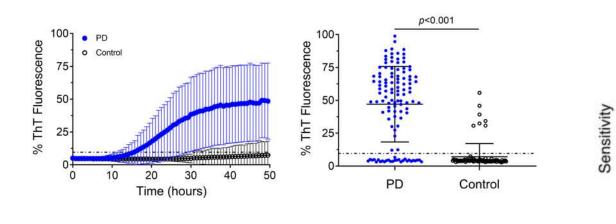
Skin biopsy of a patient with REM-sleep behaviour disorder (RBD) - **prodromal** synucleinopathy

α-syn seeding assays transform the diagnostics field

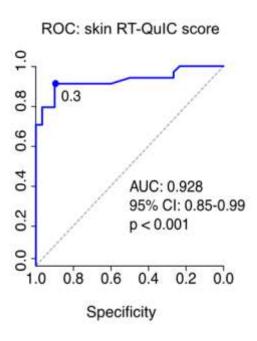
α-syn showing prion-like behaviour *in vitro* in real-time quaking induced conversion (RT-QuIC) / protein misfolding cyclic amplification (PMCA)



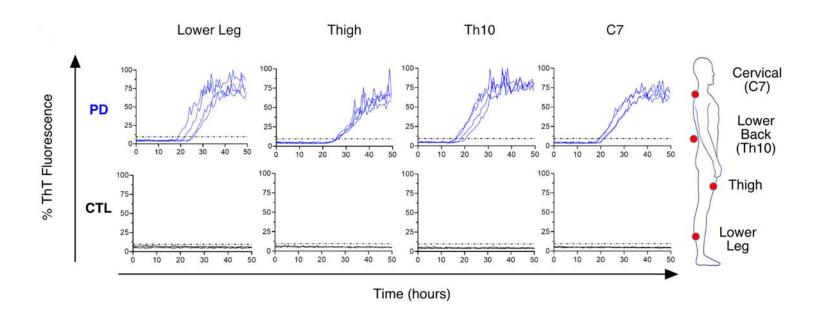
α-syn seeding in PD skin is (at least) as efficient as CSF



- 2 laboratory comparison study
- To include results of multiple biopsy sites and compare results of both assays -> composite skin RT-QuIC score



α-syn pathology widespread in the skin and highly reproducible

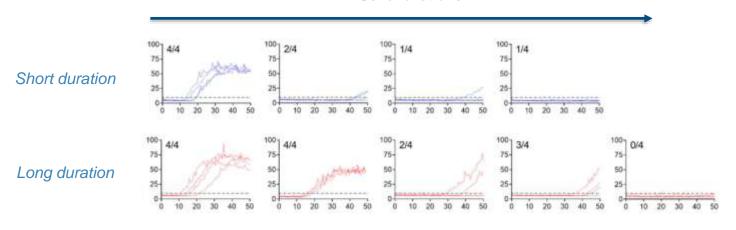


Quantification superior to IHC

Based either on number of positive replicates (crossing a certain threshold), maximum fluorescence or speed of aggregation (e.g. lag phase)

More precise quantification - end point dilutions to determine the seeding dose (SD₅₀)

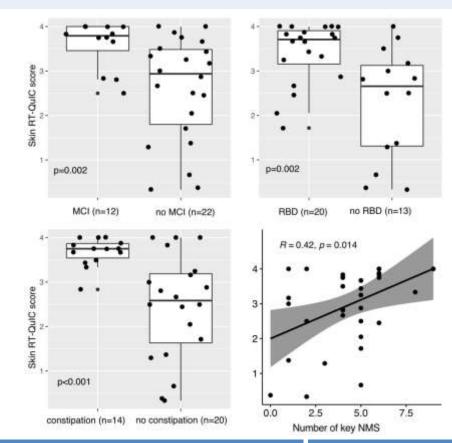
Serial dilutions



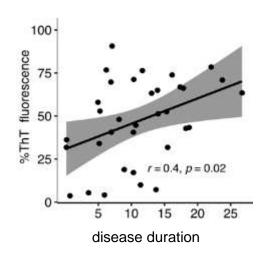
Shu Chen

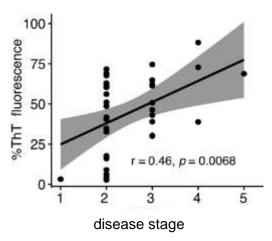
Extent of peripheral α-syn pathology correlates with phenotype

- Mild cognitive impairment, RBD and constipation correlate with α-synuclein seeding
- "Malignant phenotype"?



There is some correlation with disease duration/stage





Limitations:

- low number of PD patients (n=34)
- mostly stage 2-3
- the shorter the disease duration
 the more unreliable is the
 reference (clinical) diagnosis

Acknowledgements

Neurology

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My team



Antonia Kohl technician



Jonas Rößle medical student



Daniela Schmitt medical student



Celine Panzer medical student











Most important collaborators

Shu G. Chen, Western Case, Cleveland Wuerzburg ENT department: Stephan Hackenberg, Kristen Rak RBD group: W. Oertel (Marburg), E. Schäffer (Kiel), M. Sommerauer (Köln)

Best wishes from Würzburg!

