

# Nanobodies as structural probes for the pathological aggregation of the Parkinson's disease associated protein $\alpha$ -synuclein

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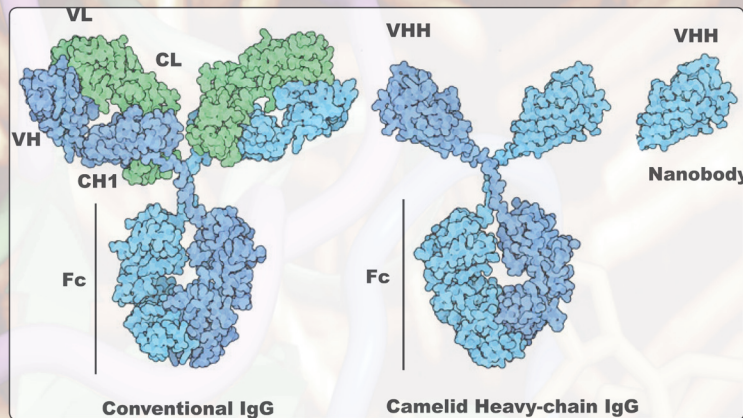
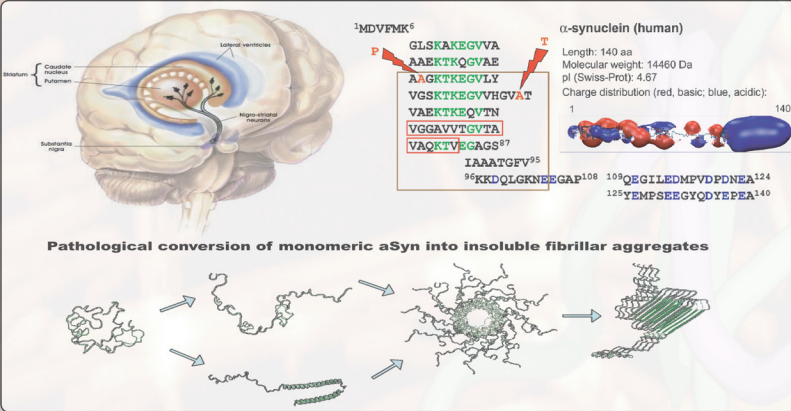
MRC Medical Research Council

## $\alpha$ -synuclein and Parkinson's Disease

$\alpha$ -synuclein ( $\alpha$ Syn) is a pre-synaptic protein of 140 residues and is believed to be a key player in the development of Parkinson's disease, a debilitating disorder caused by the loss of dopaminergic neurons of the Substantia nigra pars compacta of the brain. Although the amyloid form of  $\alpha$ Syn is a pathological hallmark of Parkinson's disease, the fibrils themselves do not seem to be the most toxic species. As in other amyloid diseases, smaller oligomeric species that are formed early on the  $\alpha$ -synuclein fibril-forming pathway, constitute the most toxic species that lead to cell death.

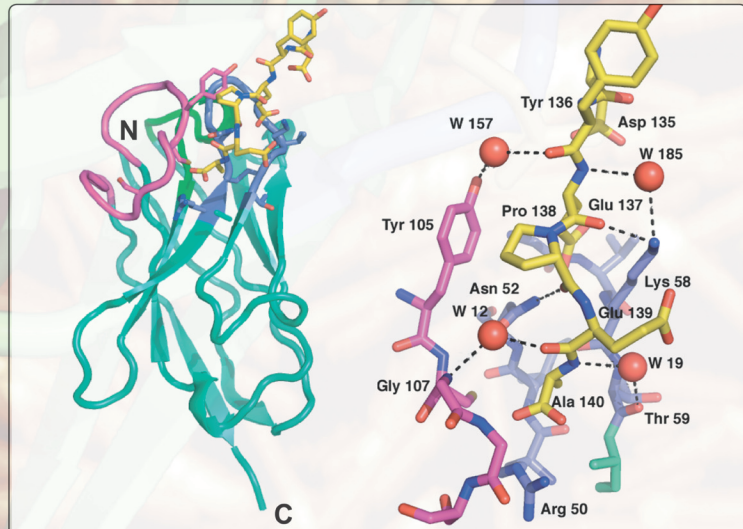
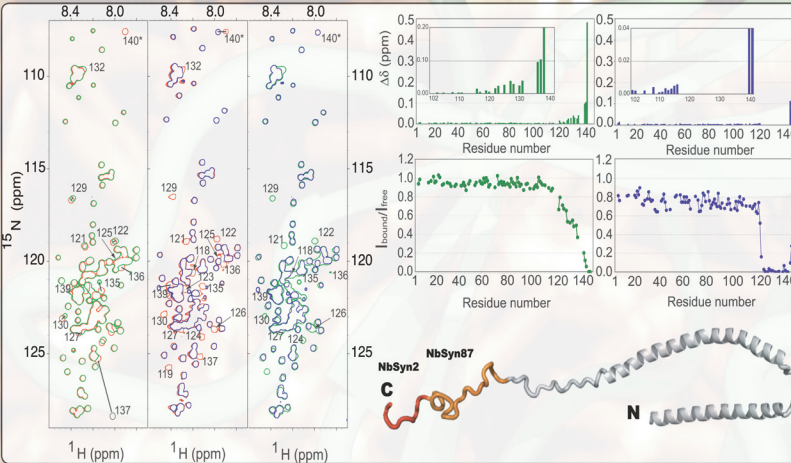
## Nanobodies

Nanobodies are the antigen-binding domains of camel heavy chain antibodies. Nanobodies are small (10 times smaller than a full length antibody), they have a simple single domain antigen recognition motif and have up to pico-molar affinities. They are also extremely stable, very resistant to aggregation, can be very easily produced recombinant at high levels and are amenable to high-throughput protein engineering and have superior properties in bio-distribution, targeting and clearance



## Epitope mapping by NMR spectroscopy

## Crystal structure of $\alpha$ Syn:Nanobody



## Probing fibril maturation by ITC

