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innovating vaccines

A peptide conjugate vaccine against Alzheimer's disease

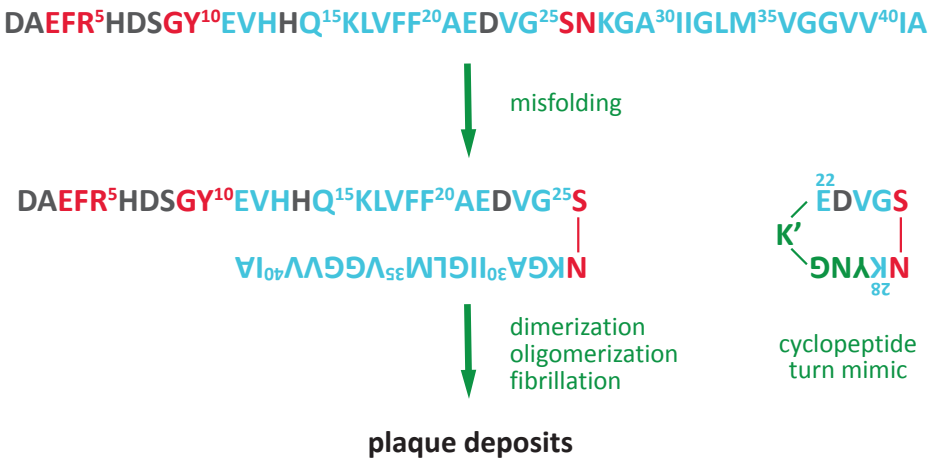

Figure 1. Schematic misfolding of human amyloid β around S26 and N27. Residues in red are solvent accessible; residues in blue (and to a lesser extent in gray) are shielded from the solvent. Based on Olofsson et al. [3]. The peptide cyclo-[Aβ (22–28)-YNGK'] is a mimic for misfolded Aβ. YNGK' is a turn-stabilizing sequence and K' is a side-chain-modified lysyl residue for selective conjugation to a protein carrier.

Intravacc has developed an amyloid β-derived cyclopeptide conjugate vaccine against Alzheimer's disease (AD). When administered to mice, the vaccine induces a good level of antibodies against the homologous peptide, as detected by immunoassay. The antibodies also bind to misfolded toxic amyloid β oligomers and fibrils, as well as amyloid plaques in mouse and human brain tissue [1]. In mice, the vaccine induces a modest - but significant - protection against a direct infusion of toxic amyloid β oligomers into the brain [2].

Benefits

- The vaccine induces antibodies with specificity for misfolded Aβ.
- Antibodies induced will not interfere with a physiologically relevant function of Aβ.
- The vaccine might be administered before the onset of AD symptoms.
- The vaccine and its application are covered by a patent [4].

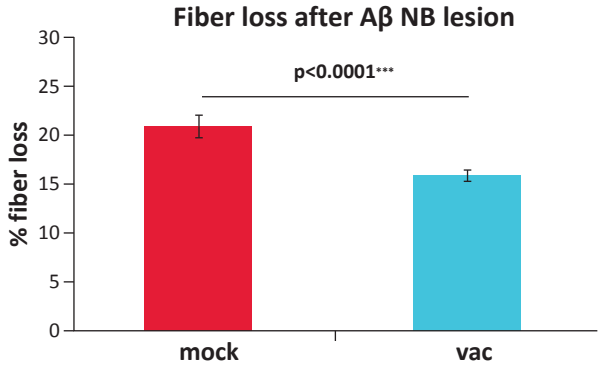

Figure 2. Compared to mock mice, immunized mice showed significantly reduced fiber loss in the cortex after a challenge with toxic oligomeric Aβ as measured by immunostaining [2].

Background

Soluble oligomeric (misfolded) species of amyloid-β (Aβ) are the main mediators of toxicity in Alzheimer's disease (AD). These oligomers form aggregates of insoluble fibrils that precipitate as extracellular and perivascular plaques in the brain. Active immunization against Aβ is a promising disease modifying strategy. However, eliciting an immune response against Aβ in general may interfere with its biological function and was shown to cause unwanted side-effects. Therefore, we have developed a novel vaccine, based on conformational neo-epitopes that are exposed in the misfolded oligomeric Aβ, inducing a specific antibody response.

References

1. Hoogerhout *et al. PLoS ONE* (2011).
2. Mulder *et al. J. Alzheimer's Dis.* (2016).
3. Olofsson *et al. J. Biol. Chem.* (2006).
4. Hoogerhout and Van den Dobbelsteen. EP20080159385 20080701, WO2010002251 (A1), US2011182928 (A1), AU2009266552 (B2)

Intravacc

Intravacc is a renowned, not-for-profit R&D organization. With our unique capabilities and infrastructure, we are able to optimize vaccines, vaccine processes and vaccine technologies. Our aim is to increase equality in access to vaccines throughout the world in order to contribute to public health. We achieve this by transferring our knowledge and technologies to public and private partners worldwide and collaborative R&D. A team of 150 professionals is at your disposal at Utrecht Science Park Bilthoven in The Netherlands.

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