Parkinson vaccine is promising

A very promising therapy for Parkinson's disease has now under investigation in human patients. The Austrian company AFFiRiS launched a two year long clinical trial of a vaccine designed to stop Parkinson's disease progression. So what's the rationale for such approach?

Parkinson's disease is the second most common neurodegenerative disorder among the elderly. Current treatments only alleviate some of the symptoms for a few years, but they become ineffective in the long run and do not stop the disease. Therefore it is of outmost importance to develop therapeutic strategies that characterize a beneficial change, specifically, slowing or even halting the disease process. As a result, the clinical symptoms are expected to stop worsening, improve or disappear.

Lewy bodies (LBs) are hallmark lesions in the brains of patients with Parkinson's disease (PD),the studies shown that alpha-synuclein is one of the major components of LBs(as a driver of synucleopathies such as Parkinson's disease).which led to the development of a novel class of drug candidates characterized by the potential for disease modification.
First member of this new class, the AFFITOPE (which is Syn-lowering vaccine).

The idea underpinning the Parkinson's vaccine is simple. by prime the immune system to restore natural tolerance against α-synuclein in Parkinson disease.

Active and passive aSyn targeting immunotherapies were found to modify disease in mice overexpressing human aSyn and recapitulating various aspects of synucleopathies.

This vaccine (PD01A) is a peptide-carrier conjugate vaccine. Antibodies elicited by PD01A react with aSyn and spare beta-synuclein, a family member not involved in pathology but able to compensate physiological aSyn functions.

Preclinical studies involving the subcutaneous administration of PD01 demonstrated the induction of a humoral immune response fulfilling the prespecified criteria: reactivity towards aSyn, but not bSyn. Experiments done in transgenic mouse models of synucleopathies showed that immunization with PD01 reduces the level of cerebral aSyn and ameliorates aSyn-triggered neuropathologic alterations such as neuronal cell loss and dendritic Density in two independent mouse models of synucleinopathies.

This approach holds the promise of a change towards concrete therapeutic measures with the potential to positively influence or even stop the course of the disease through disease modification.

Demonstration of a disease-modifying activity will presumably require:

- identification of patients in early stages(before the occurrence of too extensive, and thus irreversible neurodegeneration) of their disease with a high specificity
- The availability of biomarkers and clinical end points informing on a change, such as slowing/halting, of the disease process.
- high diagnostic specificity that does not refer to severity but, instead, combines disease-specific symptoms with biological markers of the disease; combining a measure of the episodic memory as a specific symptom with biological disease parameters such as CSF levels of Ab and Tau/phospho-Tau or hippocampal atrophy.

In conclusion; AFFiRiS´ vaccination program aims to reduce cerebral levels of α-synuclein which will result in reducing neurodegeneration caused by α-synuclein aggregates. The vaccine is still in the very early stages of testing, but that the idea is novel and the approach is promising. Safety, tolerability, and clinical efficacy will need to be demonstrated before the vaccine can move to the next phase of clinical testing.

AFFiRiS has started the project "Parkinson" in 2007 and clinical trials with the first vaccine, PD01A, started in 2012. PD01A is the first agent directed against α-synuclein and worldwide the first α-synuclein-targeting vaccine to be tested in humans. PD01A is complemented by PD03A, a vaccine whose clinical evaluation in a phase-I-study will start in mid-2014.

6/8/2014

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