

TOPICS

“The re-emergence of antigen specific tolerance as a potential therapy for MS”- Prof. Lawrence Steinman (Stanford University, EEUU).

Ideal therapy for inflammatory disease in the nervous system would preserve normal immune function, while suppressing only the pathologic immune responses that damage tissue and allowing for repair. In principle, antigen specific therapy would eradicate unwanted adaptive immune responses-antibody and T cell mediated-while preserving the integrity of other adaptive responses to infectious agents and retaining the ability to fight malignancy. However, at this time, for multiple sclerosis we do not have compelling evidence that would support any particular dominant immune response to any specific antigen or even a limited group of antigens. In fact, there are adaptive immune responses to a wide swathe of proteins and lipids found on neurons and myelin in MS. Unless controlling a few of the known immune responses is sufficient, antigen specific therapy in MS may not have enough of an impact to modulate clinical outcome. However, in other neuroinflammatory conditions like neuromyelitis optica, the adaptive immune response is highly focused. Trials of antigen specific therapy for neuroinflammatory disease might first be tested in diseases with a more limited adaptive immune response like neuromyelitis optica. The likelihood of a significant success for this therapeutic strategy might then ensue.

“Antigen-specific Treg-cell-expanding nanomedicines for the treatment of autoimmune disease” - Dr. Pere Santamaria (IDIBAPS- Hospital Clínic de Barcelona and Alberta University, Canada).

Our work focuses on advancing nanomedicines for the treatment of autoimmune diseases, in which our own immune system attacks and destroys specific cell types and tissues. The antigenic complexity of these pathogenic immune responses (many different proteins are being targeted in these autoimmune responses) is a barrier to the design of strategies that can selectively purge the immune system of self-reactive lymphocyte cell clones without impairing systemic immunity (i.e. the ability of our immune system to counter infections).

We have discovered that treatment with nanoparticles (NPs) coated with mono-specific, disease-relevant peptide-major histocompatibility complexes (pMHCs, the molecules that are responsible for stimulating the type of white blood cells that cause autoimmune diseases) can blunt several different autoimmune responses in different animal models. We have established that pMHC-NP therapy functions by triggering the conversion (and subsequent expansion) of pathogenic (disease-promoting) T lymphocytes into disease-suppressing progeny, in a very specific manner. These disease-suppressing self-reactive T-cells go on to suppress the activation and recruitment of all the other antigenic specificities that contribute to disease progression. This expansion is dramatic, correlates with therapeutic efficacy, including duration of disease reversal, and can be monitored by analysis of peripheral blood, thereby functioning as a biomarker of therapeutic efficacy. pMHC-based nanomedicines thus represent a new class of drugs potentially useful for treating a broad spectrum of autoimmune conditions in a disease-specific manner

“Clinical application of tolerogenic dendritic cells in autoimmune diseases” - Dr. Daniel Bénitez (IDIBAPS-Hospital Clínic de Barcelona).

Development of novel immunotherapies is of utmost importance to treat a group patients affected of autoimmune or immune-based diseases with no standard treatments. Dendritic Cells (DCs) have been investigated in clinical trials, principally with the goal of stimulating immune responses against cancer or infectious diseases. Very few clinical studies have taken advantage of their specific immunosuppressive potential. Tolerogenic DCs may represent a new therapeutic strategy for human immune-based diseases, such as Crohn’s disease, where the perturbations of the finely tuned balance between the immune system and the microflora result in disease. We have established a GMP protocol to generate autologous tolerogenic DCs able to be applied in clinical trials. A Phase IB clinical trial in Crohn’s disease patients was conducted at our institution. The administration of tolerogenic DCs in patients is safe and well tolerated. Interestingly, the same protocol and experimental approach including myelin protein derived peptides will be investigated in Multiple Sclerosis and Neuromyelitis Optica (MS/NMO) patients with the aim to induce antigen-specific T cells tolerance to prevent or ameliorate the inflammatory reaction.

“Antigen-specific tolerization as a treatment for multiple sclerosis and other autoimmune diseases”- Prof. Roland Martin (Zurich University, Switzerland).

Autoimmune diseases are characterized by aberrant immune responses against specific protein components of our body’s tissues. As an example, it is believed that myelin proteins are targets in multiple sclerosis (MS), while components of beta islet cells in the pancreas are targeted in patients suffering from type I diabetes. Silencing these misguided immune responses in an antigen-specific way and re-establishing immune tolerance offer hope to correct the autoimmune process at its roots and with minimal side effects. Our group has been studying cellular immune mechanisms in MS for a long time and recently examined a promising approach that had been explored in animal models for several autoimmune diseases and for over three decades. This tolerization approach employs autologous cells coupled with autoantigenic peptides. After adaptation of the procedure to human cells, we conducted a phase I clinical trial in MS, which showed that the procedure is safe and well tolerated. We currently prepare for a larger scale phase II clinical trial, which we plan to start late in 2015.

“A patient-centered model based on science”. Dr. Virginia de las Heras (medical department of neuroscience at Novartis).

Novartis (NVS) is a Swiss group based in Basel devoted to health care. Its strategy, mission, vision and values are based on a scientific developmental model orientated to and centered on people who have diseases and their needs. NVS has been focusing on a business model based on science in the last years. That has enabled NVS to develop more efficient research, achieve more safety and efficacy in their drugs, tackle orphan diseases and develop new molecules more quickly. NVS has moved from the classical model “1 disease-1 molecule” to the new one “1 molecule-several diseases”.

NVS has been working on Neurociences for more than 50 years, bringing different treatments to several diseases, among them Alzheimer's disease and multiple sclerosis (MS). Regarding the latter, NVS achieved the first modified oral treatment for MS: Fingolimod. Fingolimod has an innovative mode of action and affects both the periphery and central nervous system. Its launch into the market has had a huge impact on both health care professionals and patients.

Last but not least, NVS recently reached an agreement with Banner in order to develop new treatments for Alzheimer's disease.