Research News -- MG Vaccine? New Targets? New Diagnostics?

MG Vaccine?

The MGFA reached out to Dr. Jon Lindstrom, whose work, along with co-investigators, has focused on the possibility of a vaccine for MG as reported recently in the *Journal of Immunology*.

1) What do you see as the significance of your results so far?

We have devised a way to specifically suppress the pathological autoantibody response to muscle nicotinic acetylcholine receptors (AChRs) in the animal model of MG. Experimental autoimmune myasthenia gravis (EAMG) is caused by immunizing rats with AChRs purified from the electric organ of Torpedo californica (an electric ray native to the Pacific Ocean). Vaccination of rats with the parts of human AChRs hidden from the immune system on the inside of muscle cells inhibits production of pathological autoantibodies directed at the parts of the AChR exposed on the outside of the muscle.

Vaccination prevents development of chronic EAMG and quickly and completely suppresses ongoing chronic EAMG. This suggests that this therapeutic vaccine would be effective on human MG. This therapy should be safe because immunization of normal rats with the therapeutic antigen does not cause EAMG. The therapy should be robust because the therapeutic antigen includes the cytoplasmic domains of all subunits of muscle AChR, so it does not depend on subtleties of immune responses to a single short peptide that might vary between individuals. The therapy should be long lasting because treated rats were resistant to re-induction of EAMG six months later by re-immunization with Torpedo AChR. Because the therapeutic vaccine is human AChR, it may work even more potently on humans than it does on rats.

What needs to be done before testing this therapy on human MG is to determine the best human-compatible adjuvant. We have been using a mild adjuvant used in animal studies (incomplete Freund's adjuvant). Alum based adjuvants usually used in human vaccines should work similarly. Ideally, we would like to test this formulation in EAMG to optimize dose and immunization schedule. Then we would like to test it on naturally occurring MG in cats to prove that it works on MG and further optimize dosing. This all depends on getting further grant support.

2) In the future, do you see this as a preventative vaccine or curative one, or both?

We see this as a curative vaccine that would suppress ongoing MG and prevent its recurrence. In principle, vaccination should prevent MG, but MG is rare so it would not be practical to preventatively vaccinate against it.

3) If someone you loved had MG, what would you say about the likelihood of a vaccine sometime soon?

We are anxious to see the vaccine available as soon as possible, but this may take several years. This will depend on getting support for further research, first in animals and then in humans, and on having the experiments work out as we think they will.

In other MG Research News …

New Targets?

Dr. Bryan Traynor, of the National Institutes of Health's Neuromuscular Diseases Research Section, and fellow researchers, have found three distinct disease associated loci for MG. One of these was CTLA4. The FDA has already approved two treatments targeting CTLA4, Abatacept for rheumatoid arthritis and Belatacept for renal transplant patients. The fact that these drugs have already been approved for use should help accelerate the time it will take for them for be investigated and potentially approved for use with MG patients. For more on the study visit: http://www.healthylivingmagazine.us/Articles/7246/ .

New Diagnostics?

A recent study has found a potentially valuable new test for MG. MG is hard to diagnose. Anti-body tests often produce false negatives. Many tests can only be done in specially equipped academic centers. Dr. Konrad Weber, University of Zurich, and colleagues explored whether ocular vestibular-evoked myogenic potentials (o-VEMP) could be used as a test for MG. Twenty-seven people with MG and a control group of 28 healthy people were part of the testing. As muscles fatigue in people with MG, there is a decreased response to stimulation. The o-VEMP test was created to test vestibular function in the ear, but Dr. Weber et al. adapted the test to find reduced functioning in the extra-ocular muscles of MG patients. There was a clear and steady decline in the response of MG patients as opposed to no decline among the controls. Although the study was successful, Dr. Weber cautioned that it was only a proof of concept study so far. Further testing will be done on patients who have not yet been diagnosed with MG. For more on the study visit the Medscape site at http://www.medscape.com/viewarticle/840409 -- free membership required.