

# Antibody Blocking Research

*Dr. Genain has discovered the rogue antibody molecules that attack the core of a MS patient. Genes that make these are being cloned and harnessed in the laboratory, where the antibodies are being modified and rendered harmless.*

## Results/Current Status

Dr. Genain and his team have discovered the first of these antibodies and shown they cause irreparable damage to brain cells, the myelin and the neurons. The team has strong evidence that disability (paralysis, blindness, sensory problems, bladder problems, and cognitive difficulties, etc.) that builds up over the years in MS patients (primary and secondary progressive MS) is linked to antibodies much more so than the transient impairments that comes with attacks in earlier phases of MS. Antibodies are produced by “factory” cells, called plasmocytes. The “go” signal to antibody factories is given by B cells. To address this problem, a cancer drug called Rituxan, which destroys B cells, is now being tried in nationwide trials of relapsing remitting and primary progressive MS (Discussed in following section).

## Proposed Future Research (**Blue** -partially funded/**Red**- not currently funded)

- 1. Discover new antibodies by a unique high throughput molecular approach to capture all antibody genes in the patient.** Screen them in animal and cell culture systems; render these antibodies harmless by molecular engineering, and use these modified [human] antibodies to eliminate the harmful antibodies from the myelin and the brain.
- 2. Refine treatments that will kill only the culprit B cells and not the ones that are needed for our natural defenses.**
- 3. Get rid of the existing factory cells that make the destructive antibodies.**  
Various means consisting of conjugating (eg, linking, tagging, binding, attaching chemically or by molecular cloning) the target for the antibodies (identified in 1.) to a molecule that will either kill the cells that are to be destroyed, or send them a signal to self-destruct (apoptosis: a natural mechanism we all use everyday to “recycle” old cells that have done their

job in our bodies). Another possible approach is an extracorporeal version, (photo-excision, irradiation) – i.e. pump the blood through a device where the harmful cells are trapped and selectively destroyed, then the blood is re-injected. These approaches are already used in human diseases like malignancies and cardiomyopathies. They are called various names such as selective photolysis and cell apheresis.

### **Expected Results (1-3 years with appropriate funding)**

- 1) Stop the progression of MS in patients in all stages of MS
- 2) Selective antibody blocking
- 3) Eradicate the “bad commanders” for antibody factories

### **Current and Proposed Funding**

NMSS and NIH are currently funding \$250,000/year. In order to accelerate research \$1M/year will provide the following:

#### **Staff**

Hire 2 MD or PhD level post docs and 4 technicians.

#### **Equipment:**

- 1) Thermocyclers and single cell (B cell/plasmocyte) sorter
- 2) Bacteriophage Molecular Cloning station
- 3) Logistical contracts - with mass spectrometry, proteomics and recombinant protein and glycolipid production specialized services
- 4) Protein Arrays Spotter and Reader - procured with software to analyze proteomics results and computerizing models of the structure of protein antigens and glycolipids with their respective interactions.
- 5) High pressure optimization-capable chromatography system, (\$200,000).

FACS (Fluorescence activated cell sorter): \$180,000.