The Rocky Mountain MS Center at Anschutz is a unique partnership between the Rocky Mountain MS Center, the University of Colorado and the University of Colorado Hospital.
# My background

**B.S. from Colorado State University**
- Major: Animal Science
- Minor: Physiology

**Ph.D. from University of Colorado**
- Major: Immunology
  - Anti-viral responses
  - The role of B cells in allergy

**Post-doctoral studies at Array BioPharma**
- Drug discovery from target identification to Phase I
- Multiple inflammatory and autoimmune diseases

**Assistant professor at the University of Colorado in the department of Neurology and Research for the Rocky Mountain MS Center**

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# Research in multiple sclerosis: accelerating a cure

**Our goal:** To cure your disease

**How will we accomplish this?**
- We need to be able to study you, and your specimens (blood and spinal fluid) to better understand the disease.
- Once we know more about the disease, we can use targeted therapies to better treat you

**MS is a disease that has been around for a long time. So, why haven’t we achieved this yet?**
**Major events in the history of multiple sclerosis**

1868: MS described by Jean-Martin Charcot

1935: A laboratory model of multiple sclerosis developed by Thomas Rivers, ultimately suggesting an autoimmune basis for the disease. Virus based

1948: Multiple antibodies discovered in the spinal fluid by Elvin Kabat and others, provided a diagnostic test suggestive of MS and linking MS to immune system problems

1970-1990: Major discoveries made pertaining to the immune system

1993: Beta-interferon 1b (Betaseron) approved as the first drug to alter the course of MS.

MS has classically been defined as a virus triggered autoimmune disease, and thus you have been treated accordingly

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**Characteristics of classical autoimmune diseases**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Antibodies recognize a dominant self-antigen</th>
<th>Antibodies recognize cell surface proteins or soluble proteins</th>
<th>Each immune cell only recognize one antigen</th>
<th>Damage occurs in peripheral organs/tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid Arthritis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Lupus</td>
<td>Yes</td>
<td>Yes/No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Myasthenia Gravis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>No</td>
<td>No?</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Is MS a classical autoimmune disease? You decide.
Why have we been mislead for so long?

Since we cannot cut you up and take out your brains to study them, much of the research in MS has been done with laboratory models.

Classical Autoimmune diseases generally have good laboratory models that mimic human disease, and disease in peripheral organs makes them easier to study.

Researchers have tried for a LONG time to design better models that mimic human disease, and although the current models have elements that mimic MS, they just are not good enough.
## Therapies in laboratory models of MS

Generally speaking,

- Therapies that work well in laboratory models have not worked well in MS patients and therapies that have not worked well in these models have shown efficacy in MS patients.

### Why is this important?

- The FDA likes to see evidence that your therapy will have a good chance of working in humans.
- They want to see evidence that it worked in a laboratory model.

## MS is a unique disease

We have learned the most about the biology of the disease from success and failures of therapies in clinical trials.

### What we do know is....

- MS is an immune mediated disease
- B cells likely play an important role

### What we don’t know is....

- What causes MS?
- Does the immune system directly attack the nervous system or does it tell the cells in the nervous system to attack itself?
- What are the B cells doing? The data from the clinical trials suggests that antibodies by themselves my not be the culprit.
How are we going to design better therapies for you?

We must answer what we don’t know.

What causes MS?

* We are working with collaborators on this

Does the immune system directly attack the nervous system or does it tell the cells in the nervous system to attack itself?

* We are going to work on this ourselves in the laboratory, and in collaboration with other researchers

What are the B cells doing? The data from the clinical trials suggests that antibodies by themselves may not be the culprit.

* We are going to work on this ourselves in the laboratory, and in collaboration with other researchers

The immune system is complex

Organs of the Immune System

- Tonsils and adenoids
- Lymph nodes
- Lymphatic vessels
- Thymus
- Lymph nodes
- Spleen
- Peyer’s patches
- Appendix
- Lymph nodes
- Lymphatic vessels
- Bone marrow

Artwork by Jeannine Roller, ©2004
There are many different cell types within the immune system.

Immune cells talk to each other, but also to cells outside of the immune system.
What is a B cell?

B cells were first discovered in birds

- Thymus
  - T = Thymus
- Bursa of Fabricius
  - B = Bursa
**B cells make antibodies**

We now believe that B cells are one of the major cell types involved in MS.

Part of your diagnosis includes the presence of antibodies in your spinal fluid.

![Diagram of B cells](image)

Secreted antibodies can activate B cells and other immune cells to fight off pathogens (Good! 😊) or to attack self (Bad! ☹️).

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**B cells do more than just make antibodies**

![Diagram of B cell interactions](image)

B cells can interact with other immune cells through receptor/ligand interactions and MHC Class II.

Soluble factors can be secreted by B cells and influence other immune cells.

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**B Cells**

**Other Immune Cells**

BCR, Receptor/ligand interactions, MHC Class II,
What do B cells have to do with the brain?

Techniques to study the interactions between B cells and cells of the nervous system?

Activated B cells are incubated with brain slices
Then we determine how healthy the cells in the brain are using microscopy.

How are we going to answer the questions that are key to designing better therapies for you?

- By studying the function of B cells from MS patients
- By studying how B cells communicate with the cells of the nervous system
- By designing a better model that is dependent upon B cells
Is there a way to prevent disease?

Vaccines

Most of us think of vaccines in the sense of being immunized for a pathogen so that when we encounter it again, our immune system immediately attacks it, and we never get sick.

The vaccine strategy in MS is the opposite.

We want to “tolerize” cells to the antigens, so that when they encounter it, they don’t respond.
### Considerations for a tolerizing MS vaccine

<table>
<thead>
<tr>
<th>Antigen(s)</th>
<th>Adjuvant</th>
<th>Route of Administration</th>
<th>Components of vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myelin components</td>
<td>Alum</td>
<td>Intramuscular or subcutaneous</td>
<td>Whole protein</td>
</tr>
<tr>
<td>Other?</td>
<td>Cytokines (IL-4, IL-10)</td>
<td>Intranasal</td>
<td>Portions of the protein (peptides)</td>
</tr>
<tr>
<td>None</td>
<td>Oral</td>
<td>DNA encoding antigen</td>
<td></td>
</tr>
</tbody>
</table>

### How can you help us help you?

- Merrily supply us with your samples if we ask you and you don’t mind
- Sign up for clinical research trials—we want to help you not ruin your life (Please consult your physician first)
- Be proactive about your disease—Education, Education, Education!
## How can we cure MS?

The only way to get a cure is to......

- Stop your immune system from attacking the CNS and repair the damage that has already been done
- Develop a tolerizing vaccine

We must work on this together.

Help us help you!

## Acknowledgements

Rocky Mountain MS Center

- Karen Wenzel and staff
- Dr. Vollmer, and all of the doctors at the RMMSC