

TITLE OF PROJECT

Regulatory T lymphocytes and antibody production in arthritis: a role for the enzyme sphingosine kinase



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Project Description

We have recently shown that the enzyme sphingosine kinase (SK) plays a major role in the development of collagen-induced arthritis (CIA). CIA is a multi-faceted disease which involves the production of anti-collagen antibodies, effector T cells and complement activation. Our preliminary data suggests that there is a significant difference in the type and amount of antibody production against collagen in SK-1 knockout mice with CIA. In addition, literature clearly suggests that dysfunctional 'regulatory T lymphocytes' (Tregs) contribute to arthritis development. At the same time, SK-1 is known to regulate the movement and activity of other T lymphocytes family members throughout the body. The effect of SK-1 on Tregs is yet to be determined.

The current application investigates whether particular subsets of white blood cells (regulatory T lymphocytes, as well as B lymphocytes) are involved in mediating this chronic debilitating disease which attacks the joints.

Summary

This project will use the animal model of collagen-induced arthritis which closely mimics rheumatoid arthritis of humans. During the development of this disease, the student will monitor the development of anti-collagen antibodies as well as the movement and activation of regulatory T lymphocytes. Lymphocyte subsets will be isolated from blood as well as spleen and draining lymph nodes using cutting edge cell sorting techniques, as well as new cytokine and antibody detection kits. The functional capabilities of these cells will be tested in vitro to determine and compare, for example, which sub-classes of antibodies are produced. **We believe that by understanding the mechanisms in CIA development potential therapeutic targets can be generated.**

References

1. Allende et al. Mice deficient in sphingosine kinase 1 are rendered lymphopenic by FTY720. *J.Biol.Chem.* 2004;279:52487-52492.
2. Campbell et al. Collagen-induced arthritis in C57BL/6 (H-2b)mice: new insights into an important disease model of rheumatoid arthritis. *Eur. J. Immunol.* 2000;30:1568-1575.
3. Kelchtermans H et al., Defective CD4+CD25+ regulatory T cell functioning in CIA: an important factor in pathogenesis, counter-regulated by endogenous IFN γ . *Arthritis Res Ther*