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Abstract Supplement

W.9. Novel Candidates for Genetic Control of Collagen Induced Arthritis are Involved in Transcriptional Regulation of B-Cell Proliferation

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Introduction: Rheumatoid Arthritis (RA) is the most common autoimmune disease, caused by a complex interplay of genetic and environmental factors. This project aims to investigate the role of proteins encoded by four genes in a 2 Mega base-pair fragment on mouse chromosome 5 (*Eae39r*), identified in genetic studies of Collagen Induced Arthritis (CIA), an experimental model for RA.

Methods: CIA is induced in mice by immunization with collagen type II. The whole genomes of the parental mouse strains have been sequenced by NGS. Congenic and control mice have been characterized by flow cytometry, *in vitro* lymphocyte activation assays and transcript level studies. Breeding of lymphocyte-specific knock-out mice and pathway studies are currently underway.

Results: Our recent CIA experiments in *Eae39r* congenic, sub-congenic and control mice have shown that a sub-locus is controlling the severity of arthritis, in addition to antibody titers. Differential expression of the genes located in this sub-locus has been observed in spleens and specifically B cells of naïve *Eae39r* congenic and control mice that can be attributed to various regulatory variations identified by NGS. *In vitro* activation experiments have shown increased B cell proliferation in response to anti-IgM antibody stimulation in congenic mice as compared to littermate controls, along with down-regulation of these genes upon stimulation.

Conclusion: The genes located in the *Eae39r* fragment are identified to have a role in lymphocyte proliferation and arthritis development. We expect that one or more of these proteins are important for disease mechanisms in RA and can be developed as potential drug targets.