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***Title: Turning off the Immune response in Rheumatoid Arthritis sufferers: investigating anti-collagen II (AC II) antibodies***

Rheumatoid Arthritis (RA) in an autoimmune disease affecting the joints, lungs and blood vessels. The social and economic burdens of RA are massive: it affects ~1% of adults worldwide, reducing survival by an average of 10 years, and costs up to $100,000 per patient annually. Furthermore, ~40% of the RA population remains undiagnosed, with intermittent or mild symptoms in the earliest disease stages. Previous studies have shown that the HLA-class II genes underlie the major genetic susceptibility, with the development of autoimmunity marked by the appearance of autoantibodies directed against self-proteins or “antigens”, including joint proteins. Type II collagen is a protein only found in joint cartilage that the immune system responds to in RA. Previous studies show that about 50% of RA patients are making anti-collagen II antibodies at disease onset. Other autoantibodies - present in 70% of patients at onset - are called anti-citrullinated peptide antibody (ACPA) and rheumatoid factor (RF). Clinical subtypes of RA are now identified by the presence (seropositive) or absence (seronegative) of ACPA and RF autoantibodies. Seropositivity is associated with carriage of *HLA-DRB1* RA-susceptibility genes and a more severe outcome.

Professor Thomas and her team are developing treatments to target and turn off the immune response to specific self-antigens, such as citrullinated peptides or collagen II. It is anticipated that such targeted treatments will have fewer side effects than existing treatments, and could be eventually used in at-risk individuals as prevention i.e. to reduce the risk of a future immune response. In this project students will test anti-collagen II antibodies in patients with RA and at-risk relatives, and determine whether they are produced at higher levels in patients carrying *HLA-DRB1* RA-susceptibility genes. The genetic testing has been done already in the patients and relatives. Students will also compare the levels of anti-collagen II in mice before and after immunization with collagen II to induce a model of RA.

The principles underpinning this antigen targeted approach in RA are applicable to other autoimmune diseases such as type 1 diabetes and celiac disease, which are also associated with HLA-DRB1 genes and tissue-specific antigens.