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Supporting Patients through Education & Research

Scientific Summary & Progress Report - Autoantigen specificity in Juvenile Idiopathic Arthritis – Dr Sarah Tansley

Background **-** This project has established that a dense fine speckled/homogeneous antinuclear antibody (ANA) pattern on immunofluorescence in patients with JIA is associated with an increased risk of uveitis. The ANA pattern suggests an antigenic target associated with DNA/chromatin.

Determine the specificity of ANA **-** As based on our previous work Hep-2 cells are known to contain the JIA antigen(s) of interest, I have obtained Hep-2 cells for culture. The cells have been successfully grown and an adequate stock for future work stored in liquid nitrogen at the University of Bath.

The immunofluorescence pattern described above suggests a nuclear location of the antigen. I have optimized the procedure for obtaining a nuclear enriched extract of Hep2 cells that can be used as an antigen source. I have used the Hep2 cell nuclear extract in western blotting experiments with JIA patient sera but have thus far been unable to detect the JIA antigen using a standard blotting technique. Possible reasons for this include, that the antigen has a very low molecular weight, the antigen has a conformational epitope, is rapidly degraded or the antigen is not a protein but RNA or DNA.

Future directions **-** Planned experiments include further optimization of the blotting procedure to detect low molecular weight proteins and RNA immunoprecipitation to detect an RNA antigen. If these prove unsuccessful alternative approaches may include protein microarray analysis.

Other work **-** In addition to the above project I have prepared a paper on anti-HMGCR autoantibodies in patients with juvenile dermatomyositis (JDM) and this has been submitted for publication to Arthritis and Rheumatology. I have also prepared a paper for submission describing the autoantibody associated clinical phenotype of patients with JDM in the UK JDM cohort (379 patients).

Impact **-** The work on JIA was presented as an oral abstract at the British Society of Rheumatology annual conference April 2016. The work on anti-HMGCR in JDM was presented as a poster presentation at the same conference:

Sarah L Tansley, Juliet Dunphy, Amelia A C Jobling, Roberto Carrasco, , Angela Midgley, Michael Beresford, Andrew D Dick, Lucy R Wedderburn, Wendy Thomson, CAPS, Athimalaipet Ramanan & Neil J McHugh. *A dense fine speckle pattern on immunofluorescence is strongly associated with the development of uveitis in children with juvenile idiopathic arthritis.*

Sarah L Tansley, Zoe E Betteridge, Stefania Simou, Clarissa Pilkington, Mark Wood, Kishore Warrier, Lucy R Wedderburn & Neil J McHugh on behalf of the JDRG. *A diagnostic and treatment challenge: The prevalence and clinical associations of anti-HMGCR autoantibodies in a large UK juvenile-onset myositis cohort.*

The prevalence and clinical associations of anti-HMGCR autoantibodies in a large UK juvenile-onset myositis cohort has been submitted as a paper publication.

Obtaining control samples has required collaboration with other centres including UCL, the University of Liverpool and the University of Bristol. We have also collaborated with Inova. Such collaborations help to raise our national and international profile as a centre for specialised autoantibody testing in rheumatological diseases.

Future impact: Identification of an autoantigenic target in JIA will impact on patient investigation and diagnosis particularly with regard to uveitis risk. It may impact on policy in terms of uveitis screening recommendations/guidelines and have cost savings to the NHS and other organisations by better targeting for ophthalmological screening and preventing unnecessary appointments.