ABSTRACT

Thesis: Role of Group A Streptococcus (GAS) M6 Class 1 Epitope in Antiphospholipid Syndrome

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Antiphospholipid Syndrome (APS) is an autoimmune disorder characterized by thrombosis, recurrent fetal loss, and the presence of pathogenic levels of antiphospholipid antibodies (aPL). APS has been shown to develop as a result of an overly-stimulated immune system. This commonly results from infection but the exact etiology remains unknown. Rheumatic Fever (RF)/Rheumatic Heart Disease (RHD) are an autoimmune consecution of higher lethality than APS. RF/RHD shares multiple secondary disease manifestations, alluding to a common pathogenesis and significant levels of streptococcal antibodies have been found in APS patients. Group A Streptococcus is a bacterial strain belonging to the Streptococcus *pyogenes* family. It has an established role in the autoimmunity observed in RF/RHD. The M protein of GAS in particular, demonstrates structural homology to vital host structures thereby facilitating molecular mimicry. It has not previously been shown whether GAS M protein is sufficient to induce APS. The aim of this study was to determine whether injection of the M6 protein epitope, 10F5, is sufficient to induce the production of antiphospholipid antibodies. **Methods** Lewis Rats

were divided into groups, Experimental (EX, n=6), Experimental Control (EC, n=6), and Negative Control (NC, n=4). Animals were bled at time point 0, weeks 4, 6, and 8. Additionally, EX and EC groups received injections of peptide with adjuvant and water with adjuvant respectively at day 1 and 4 weeks post initial injection. The NC group was not injected. ELISA was performed on the serum collected at each time point and the concentration of aPL quantified. **Results** There was a significant difference in the serum concentration of aPL between the NC and the EX groups ($p < 0.00003$). From T2-T4 there was a72% decrease in serum aPL in the NC group, a 12% increase in the EC group and a 16% increase in the EX group. **Conclusion** Injection of Class 1 Epitope is sufficient to produce antiphospholipid antibodies and therefore induce the marker for Antiphospholipid Syndrome in Lewis Rats. However, further studies are needed in order to establish a clearer connection between the aPL produced and induction of the actual disease.