**BETA 2 GLYCOPROTEIN I PEPTIDE PROTECTS FROM CARDIAC ISCHEMIA REPERFUSION INJURY IN MICE**

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*Objective*: The aim of this study was to investigate the role of Beta 2 Glycoprotein I Peptide (Β2GPI) and its Domain V in cardiac ischemia and reperfusion injury (IRI) using wild-type and B2GPI deficient mice.

*Background*: Reperfusion after a period of ischemia results in reperfusion injury (IRI), which involves activation of the inflammatory cascade. In cardiac IRI, natural antibodies (NAb) play a prominent role through binding to altered neoepitopes. Beta 2 Glycoprotein I (β2GPI) is an abundant circulating plasma protein that binds to neoepitopes on damaged cells, including anionic phospholipids through its highly conserved Domain V. Domain I of β2GPI binds circulating NAbs and may provide a link between the innate immune system, natural antibody binding and cardiac IRI.

*Methods and results*: An *in vivo* mouse coronary artery IRI model was inducted. Compared with control, treatment with Domain V prior to IRI prevented binding of endogenous β2GPI and resulted in smaller myocardial infarction size in both WT and β2GPI deficient mice. Domain V treatment in WT mice also resulted in less neutrophil infiltration, less apoptosis and improved ejection fraction at 24 h. Beta 2 deficient mice had the same infarct size as WT mice. As a result, further investigations were performed in Rag-1 -/- mice. Rag-1 -/- antibody deficient mice reconstituted with IgM NAbs confirmed that Domain V prevented IgM NAb induced cardiac IRI. Domain V remained equally effective when delivered at the time of reperfusion, which has therapeutic clinical relevance.

*Conclusions*: Based upon this study, Domain V may function as a universal inhibitor of NAb binding in the setting of cardiac IRI, which offers promise as a new therapeutic strategy in the treatment of cardiac IRI.