**MODULATION OF INFLAMMATORY VASCULITIS (IVS) AND ANTI-INFLAMMATORY TREATMENT BY THE GUT MICROBIOTA - A MOUSE HERPESVIRUS IVS MODEL**

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**Objective** - Inflammatory vascular syndromes (IVS) are rare but devastating arterial disorders. Previously, a *ser*ine *p*rotease *in*hibitor (serpin), Serp-1 protein, and Serp-1 reactive center loop (RCL) peptide S-7 (G305TTASSDTAITLIPR319) significantly improved outcomes in a lethal IVS model induced by mouse gamma herpesviral (MHV68) infection in interferon gamma receptor knockout mice (IFNγR-/-).

**Methods** - Here, we tested the hypothesis that the gut microbiome influences MHV68-induced vasculitis. IFNγR-/-mice (N=62) were split into control or 10-day antibiotic groups prior to infection with MHV68. Mice were treated with saline, fecal gavage, Serp-1 or RCL peptides S-7, or modified S-7 peptides MPS-8 and MPS-9. Genomic DNA extracts were Illumina sequenced for microbiome analysis by 16S rRNA.

**Results** - Microbiome suppression accelerated mortality and reduced survival from 60 to 20 days (P=0.036) in MHV68 IVS. Survival was reduced from 70% at 150 days to 20% at 30 days with Serp-1 treatment (P=0.003) and 0% at 30 days with S-7 treatment (P=0.0001). In contrast, modified MPS-8 and MPS-9 improved survival after microbiome suppression (P=0.001). Both Serp-1 and S-7 altered microbiome community structure (beta-diversity), while S-7 also altered community richness (alpha-diversity) versus saline controls. *Lactobacillales* were reduced and *Streptophyta* increased in saline-treated mice, while *Bacillales* were reduced and *Lactobacillales* increased in Serp-1-treated mice. In ongoing experiments, gut recolonization by fecal gavage improves survival compared to historical antibiotic-treated controls (100% versus 20% survival at 30 days, P=0.0068).

**Conclusion** - Microbiome richness, structure, or sub-population composition, may play a crucial role in modulating lethal vasculitic syndromes and treatment response.