Title: Neuro-inflammatory Process in Glaucomatous Retinal Ganglion Cell (RGC) Pathology

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Glaucoma is a degenerative optic neuropathy that can if left untreated lead to blindness. Glaucomatous neurodegeneration has been considered the result of either mechanical or vascular changes in the optic nerve head (ONH). The immune system is also somehow involved although the exact mechanism is still unclear. Our lab together with others has shown an association between oral health and primary open-angle glaucoma (POAG). We have also reported that peripheral inflammation caused by lipopolysaccharide (LPS) exacerbates glaucomatous neurodegeneration in mouse models of glaucoma through microglial activation and the innate immune system (via Toll-like Receptors (TLRs)). We now have additional preliminary data that LPS from periodontal pathogen *Porphyromonas gingivalis* (*P. gingivalis)* exacerbates glaucomatous neurodegeneration in mice and that the effect is likely not mediated by infiltrating macrophages or T-cells. In addition, we have evidence that periodontal bacteria can be detected in the retina and optic nerve (ON) of non-glaucomatous mice (see preliminary data below). LPS is of course known to affect vascular permeability. We are currently exploring the hypothesis that oral bacterial pathogens (as in other diseases) affect the vascular system and through that the immune system to enhance glaucomatous neurodegeneration *in susceptible individuals*. Although an effect on the immune system is likely not unique to oral bacteria (i.e. bacteria in the gut and respiratory track may have similar effects), pathogenic oral bacteria that cause periodontitis are known to cause systemic vascular dysregulation. Periodontal disease is well known to affect vascular reactivity and cause endothelial cell dysfunction both of which have been suggested to play a role in glaucomatous neurodegeneration. It is actually worth noting that ON head hemorrhages which are highly suggestive of vascular dysregulation are one of the strongest risk factors for development and progression of glaucoma (both in the presence and absence of elevated intraocular pressure (IOP).