Autophagic dysregulation in glaucomatous trabecular meshwork cells

Abstract Number: 5651

Author Block: Paloma B. Liton
1 Duke University, Durham, North Carolina, United States

Disclosure Block: Paloma B. Liton, None

Presentation Description: Primary open angle glaucoma (POAG) is a degenerative disease commonly associated with aging and elevated intraocular pressure (IOP). Higher resistance to aqueous humor (AH) outflow through the trabecular meshwork (TM) generates the elevated IOP in POAG; unfortunately the underlying molecular mechanisms responsible for elevated resistance are unknown. It is widely accepted, however, that differences between normal and POAG TM tissues are presumably a consequence of cellular dysfunction. Here, we investigated the autophagic function and response to chronic oxidative stress in TM cells isolated from glaucomatous and age-matched donor eyes. Glaucomatous TM cells showed elevated senescence-associated-beta-galactosidase (SA-β-Gal) and cellular lipofuscin, together with decreased steady-state levels of LC3B-II, decreased levels of pRPS6K-T389 and reduced proteolysis of long-live proteins. Moreover, the glaucomatous cultures failed to activate autophagy when exposed to hyperoxic conditions. These results strongly suggest mTOR-dependent dysregulation of the autophagic pathway in cells isolated from the glaucomatous TM. Such dysregulated autophagic capacity can have a detrimental impact in outflow pathway tissue, i.e. mechanotransduction, and thus represent an important factor contributing to the progression of the disease.