Neuroprotective effects of TGF-β1 in rat retinal β-amyloid-induced damage

G. Giurdanella[1], V. Fisichella [1], G.L. Romano[1], G.M. Leggio[1], C.B.M. Platania[1], M. Laudicina[1], S. Salomone[1], F. Caraci[2,3], C. Bucolo[1], F. Drago[1]

[1]Dept. of Biomedical and Biotechnological Sciences, School of Medicine, University of Catania, Catania, Italy
[2]Dept. of Drug Sciences, University of Catania, Catania, Italy
[3]IRCSS Associazione Oasi Maria S.S., Institute for Research on Mental Retardation and Brain Aging, Troina, Italy

Age-related macular degeneration (AMD) is the leading cause of irreversible central vision loss in elderly populations in developed countries. AMD is a neurodegenerative disease characterized by retinal beta-amyloid (Abeta) deposition. The etiology and pathogenesis of AMD are not completely understood and appropriate biological models may be helpful to identify new pharmacological targets. Here we tried to induce retinal damage by injecting Abeta oligomers in rats. Moreover, because Transforming-Growth-Factor-beta1 (TGF-beta1) has been shown to protect cortical neurons from Abeta-induced neurodegeneration (Caraci et al., 2008), we tested the hypothesis that TGF-beta1 may also protect retinal neurons, when challenged with Abeta oligomers. Human Abeta (1-42) oligomers were prepared according to the original protocol of Klein's group (Gong et al. 2003) and intravitreally injected (1microM) both in presence or in the absence of recombinant human TGF-beta1 (1ng/microl). After 48h, the animals were sacrificed and the eyes removed and dissected. The apoptotic markers BAX and Bcl-2 were assessed by Western Blot analyses in retina lysates. Treatment with Abeta oligomers induced a strong increase of BAX protein level (about 4-fold; $p<0.01$) and a significant reduction of Bcl-2 protein level (about 2-fold; $p<0.05$). Co-injection of TGF-beta1 triggered a significant reduction of BAX protein induced by Abeta. These data indicate that intravitreal injection of Abeta oligomers in rat induces molecular changes associated with apoptotic neuronal death in retina consistent with a potential pathogenetic role of Abeta oligomers in AMD. Finally, these findings suggest that TGF-beta1 can exert neuroprotective effects in retinal damage induced by Abeta oligomers.

References:
Caraci F., et al. (2008). Neurobiol Dis. 30, 234-42.
Gong Y., et al. (2003). PNAS. 100,10417-22.