

Abstract

Annexin A1 regulates retinal gliosis in diabetic retinopathy[†]

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Abstract: In diabetic retinopathy (DR), Müller cell gliosis contributes to retinal degeneration and inflammation. In this context, we highlight annexin A1 (AnxA1), an anti-inflammatory protein able to regulate neurodegeneration and angiogenesis, however, its mechanisms of action were poorly explored in DR. This study evaluates the function of AnxA1 in streptozotocin (STZ)-induced DR in wild-type (WT) and knockout (AnxA1^{-/-}) mice after 12 weeks. In addition, *in silico* analysis was performed with GSE111465 (whole retinas from 6-weeks-old STZ-diabetic or control animals) and GSE160306 (human retina with different stages of DR). Retina from 6-weeks-old STZ-diabetic mice showed raised transcripts of *AnxA1* and *GFAP* compared to controls. After 12 weeks, RD was associated with increased levels of AnxA1, formyl peptide receptor 2 (Fpr2) in the WT retina, as well as cleaved caspase 3 and vascular endothelial growth factor (VEGF) compared to control samples. Lack of AnxA1 caused increased glutamine synthetase expression (Müller cell marker) in retinas from RD animals compared to WT RD group. On the other hand, no alterations in the levels of caspase 3 and VEGF expression were showed in AnxA1^{-/-} groups. Despite both genotypes presented gliosis in peripheral retina, as shown by glial fibrillary acid protein (GFAP) immunostaining, AnxA1^{-/-} RD group exhibited decreased levels of GFAP compared to RD WT group. In silico study with human retinas, the severity of DR is associated with higher levels of AnxA1 mRNA expression. Additionally, a positive correlation between AnxA1 and GFAP mRNA levels was detected. These results allow us to conclude that AnxA1 participates in the progression of RD and that this protein can regulate the expression of GFAP.

Keywords: Annexin A1, Gliosis, Müller cells, diabetes, diabetic retinopathy, streptozotocin, transcriptome.

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by the Ethics Committee on Animal Use of the Federal University of São Paulo (CEUA/UNIFESP) 2
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