biology and life sciences forum

MDPI

Abstract

Annexin A1 Regulates Retinal Gliosis in Diabetic Retinopathy †

Rafael André da Silva [1,*], Luiz Philipe de Souza Ferreira [2], Vinicius M. Paiva Roda [3], Daniel R. Bastos [4] and Cristiane D. Gil [1,2]

1 Biosciences Graduate Program, Institute of Biosciences, Letters and Exact Sciences, São Paulo State University (IBILCE/UNESP), São José do Rio Preto 15054-000, SP, Brazil; cristiane.gil@unifesp.br
2 Structural and Functional Biology Graduate Program, Paulista School of Medicine, Federal University of São Paulo (EPM-UNIFESP), São Paulo 04023-900, SP, Brazil; luiz.philipe@unifesp.br
3 Life Systems Biology Graduate Program, Institute of Biomedical Sciences, Universidade de São Paulo (USP), São Paulo 05508-000, SP, Brazil; vinicius.moraes95@usp.br
4 Department of Oncology, Universidade de São Paulo, São Paulo 01246-903, SP, Brazil; danielbastos.adm@gmail.com
* Correspondence: rafael.andre@unesp.br
† Presented at Cells, Cells and Nothing but Cells: Discoveries, Challenges and Directions, 6–8 March 2023; Available online: https://cells2023.sciforum.net/.

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-week-old STZ-diabetic or control animals) and GSE160306 (human retinas with different stages of DR). Retinas from 6-week-old STZ-diabetic mice showed raised transcripts of AnxA1 and GFAP compared to the 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 the control samples. The lack of AnxA1 caused increased glutamine synthetase expression (Müller cell marker) in the retinas from RD animals compared to the WT RD group. On the other hand, no alterations in the levels of caspase 3 and VEGF expression were showed in the AnxA1$^{-/-}$ groups. Despite both genotypes presenting with gliosis in the peripheral retinas, as shown by glial fibrillary acid protein (GFAP) immunostaining, the AnxA1$^{-/-}$ RD group exhibited decreased levels of GFAP compared to the RD WT group. In an 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; estreptozotocin; transcriptome

check for updates

Citation: da Silva, R.A.; de Souza Ferreira, L.P.; Paiva Roda, V.M.; Bastos, D.R.; Gil, C.D. Annexin A1 Regulates Retinal Gliosis in Diabetic Retinopathy. *Biol. Life Sci. Forum* **2023**, *21*, 12. https://doi.org/10.3390/blsf2023021012

Academic Editor: Alexander E. Kalyuzhny

Published: 20 March 2023

Copyright: © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

Author Contributions: Conceptualization R.A.d.S.; methodology: R.A.d.S. and C.D.G.; formal analysis and investigation: R.A.d.S. and C.D.G.; experimental procedures: R.A.d.S., L.P.d.S.F., V.M.P.R., D.R.B. and C.D.G.; funding acquisition: C.D.G.; resources: C.D.G.; supervision: C.D.G. All authors have read and agreed to the published version of the manuscript.

Funding: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), grant number 2022/02327-6. R.A.S., V.M.P.R and D.R.B was supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), finance code 001. L.P.S.F was supported by the FAPESP, grant number 2021/00270-4.

Institutional Review Board Statement: The experimental mouse model was conducted according to the Brazilian Law 11.794 of 8 October 2008, Decree 6899 of 15 July 2009, as well as with the rules issued by the National Council for Control of Animal Experimentation (CONCEA) and approved by the Ethics Committee on Animal Use of the Federal University of São Paulo (CEUA/UNIFESP) in the meeting of 08/09/2021 (protocol code 8518230821).

Informed Consent Statement: Not applicable.

Data Availability Statement: Data available on request due to restrictions.

Conflicts of Interest: The authors declare no conflict of interest.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.