AB047. Membrane binding of S100A10 protein and AHNAK peptide involved in cell membrane repair

Xiaolin Yan[1], Marie-France Lebel-Beaucage[2], Samuel Tremblay[1], Gary Shaw[3], Dror Warschawski[4], Élodie Boisselier[1]

[1]Department of Ophthalmology, Faculty of Medicine, Saint-Sacrement Hospital, Laval University, Quebec City, QC, Canada; [2]Department of Ophthalmology, Faculty of Medicine, Saint-Sacrement Hospital, Université du Québec à Trois-Rivières, Trois-Rivières, QC, Canada; [3]Department of Chemistry, Faculty of Biomolecular NMR, University of Western Ontario, London, ON, Canada; [4]Department of Chemistry, Faculty of Sciences, Université du Québec à Montréal, Montreal, QC, Canada

Correspondence to: Élodie Boisselier, PhD. Hôptal du Saint-Sacrement-Centre universitaire ophtalmologie, 1050 chemin Sainte-Foy, Québec, QC G1S 4L8, Canada. Email: elodie.boisselier.1@ulaval.ca.

Background: The S100A10 protein might be an early biomarker of diabetes development leading to diabetic retinopathy. The protein complex S100A10/annexin A2 allows the recruitment of the C-terminal of AHNAK protein (AHNAK C-ter peptide) to the membrane in presence of calcium, before forming a platform which can initiate membrane repair. However, no molecular data are currently available on membrane binding of the different proteins involved in this complex. We aim to study the membrane binding of S100A10, AHNAK C-ter peptide and their complex to better understand their roles in cell membrane repair process.

Methods: Firstly, S100A10 will be overexpressed and purified by affinity chromatography and AHNAK C-ter peptide will be synthesized. Langmuir monolayers membrane model will then be used to characterize the interactions between these proteins and different phospholipids found in membranes. The secondary structure, orientation and membrane organization of these proteins will be studied by Polarization Modulation Infrared Reflection-Absorption Spectroscopy. Their lateral localization will be determined through the influence of these proteins on the physical state of lipids by fluorescence microscopy.

Results: The optimization of the overexpression, purification and cleavage of the GST tag procedure to obtain pure S100A10 was completed. Protein identification by mass spectrometry and circular dichroism stability pre-studies were performed. In parallel, AHNAK C-ter peptide was studied by Langmuir monolayer model and the results indicate this peptide prefers lipids with negatively charged polar heads and unsaturated acyl chains. Preliminary solid-state NMR results confirm this phenomenon at 37 ℃.

Conclusions: Our research will complete current knowledge on membrane binding of S100A10 and AHNAK C-ter peptide. We could also identify the conditions leading to modifications of these membrane bindings, and possibly to the loss of protein function. Thus, this project helps to better determine their roles in membrane repair, as well as in other physiological mechanisms in which these proteins are involved.

Keywords: S100A10; AHNAK; diabetic retinopathy; membrane repair

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