P-1.118

Biophysical Insights into the Interactions of S100 Family Proteins with Artificial Lipid Bilayers

Rimgaile Tamulyte [1], Darius Šulskis [2], Marija Jankunec [1]

[1] Institute of Biochemistry, Life Sciences Center, Vilnius University, Vilnius, Lithuania

[2]Institute of Biotechnology, Life Sciences Center, Vilnius University, Vilnius, Lithuania

Neuronal cell death induced by cell membrane damage is one of the major hallmarks of neurodegenerative diseases. Neuroinflammation precedes neuronal loss; however, whether and how inflammation-related proteins contribute to the loss of membrane integrity remains unknown. We employed a range of biophysical tools, including high-speed atomic force microscopy, fluorescence spectroscopy, and electrochemical impedance spectroscopy, to ascertain whether the pro-inflammatory proteins S100A8, S100A9, and the heterocomplex they form induce alterations in biomimetic lipid membranes upon interaction. We found that the apo-forms of the aforementioned proteins interact with anionic lipid membranes composed of phosphatidylserine (PS), causing membrane disruption through a detergent-like mechanism. In the case of S100A9, additional phase-specific interactions were observed, leading to the disassembly of gel-like lipid domains. These disruptive effects were markedly attenuated in the presence of Ca2+ ions, suggesting that S100-mediated membrane destabilization is favored under intracellular-like conditions characterized by low calcium levels and high PS content. Overall, our results provide a mechanistic basis for understanding the molecular interactions between S100 proteins and the plasma membrane, highlighting them as potential contributors to the onset of neurodegenerative diseases.