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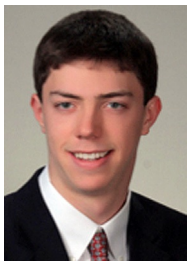
CHEMPHOTOCHEM
Cover Profile

Saposin B Binds the Lipofuscin Bisretinoid A2E and Prevents its Enzymatic and Photooxidation


Jay Tinklepaugh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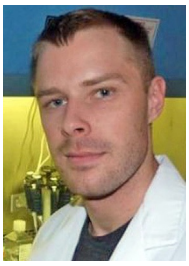
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The front cover artwork is provided by the group of Prof. Robert P. Doyle at Syracuse University (USA) and collaborators, Prof. Fadi Bou-Abdallah at SUNY Potsdam (USA) and Kelsey Moody at Ichor Therapeutics. The picture illustrates lipofuscin bisretinoid A2E blue-light-induced photooxidation and its protection by the lysosomal protein SapB. Binding of A2E by SapB protects A2E from both enzymatic degradation and photooxidation by blue light. Read the full text of the Communication at 10.1002/cptc.201700039.

What is the most significant result of this study?

The binding of lipofuscin bisretinoid A2E by the lysosomal protein SapB prevents A2E oxidation by enzymes or blue light. Such binding may also complicate attempts to produce an enzyme replacement therapy for A2E enzymatic degradation or photooxidation and/or play a role in the "transport" or movement of A2E inside the cell (and possibly out of the cell).

What prompted you to investigate this topic/problem?

A2E is a major fluorescent component of lipofuscin granules found in the lysosomes of RPE cells and is implicated in many diseases, including in age-related macular degeneration (AMD). The multi-substrate specificity of the human lysosomal protein SapB and its implications in drug toxicity and/or disease progression prompted us to investigate its interaction with A2E given the intralysosomal nature of A2E accumulation.

What new scientific questions/problems does this work raise?

SapB has been shown to "flush" bound ligand, such as coenzyme Q10 (CoQ10), in human urine. Since $(SapB\text{-}CoQ10)_{complex}$ has been observed in urine, it would be of interest to assay the urine of patients with AMD or SD (Stargardt disease) for the presence of the $(SapB\text{-}A2E)_{complex}$. Also, the possibility of A2E competition for activator suggests a need to assay for sulfatide build-up in patients with AMD or SD.

Acknowledgments

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