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C. EUGENE BENNETT
DEPARTMENT OF CHEMISTRY

Spontaneous chemical modifications in long-lived proteins: what can alpha-crystallin in the lens tell us about lysosomal degradation in Alzheimer's disease?

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Mature fiber cells in the human eye lens, where protein turnover is essentially nonexistent, are an excellent model for studying the effects of time on long-lived proteins. We have demonstrated that many spontaneous chemical modifications, including nearly invisible changes such as isomerization and epimerization, occur abundantly within long-lived proteins including the alpha crystallins. Experiments relying on native mass spectrometry further demonstrate that these modifications significantly perturb crystallin assembly, and presumably function. Interestingly, outside of the lens, these same modifications are highly problematic in terms of lysosomal degradation. Incubation of substrates containing modified sites with lysosomal proteases reveals an inability to digest at the site of modification or even residues nearby. This disruption of protein degradation is expected to interfere with proteostasis and may be related to lysosomal storage observed in many age-related diseases. Methods for detecting these spontaneous age-related modifications, their chemical origins, and relationships to proteostasis will be discussed.

Date: Wed, Oct. 23, 2019
Time: 4:30-5:30 pm
Location: 208 Clark Hall

Students, meet the speaker over coffee and cookies in the Bennett Conference room at 3:30 pm