Joint Organic/Chemical Biology Seminar

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The Enzymatic Activity of Sirtuins: Beyond NAD+ -dependent Deacetylation

Tuesday
October 5, 2010
3:30 p.m.

Room 1315 Chemistry

Sirtuins are a class of enzymes known as nicotinamide adenine dinucleotide (NAD)-dependent deacetylases. Sirtuins regulate aging, transcription, and metabolism, and are important targets for treating cancer, Parkinson's disease, diabetes, and obesity. There are seven sirtuins in humans, SIRT1-7. Four of them (SIRT4-7) have very little or no deacetylase activity, which have caused many confusions and debates in the biological community. Our work demonstrated that SIRT5, a mitochondrial sirtuin with very weak deacetylase activity, catalyzes the hydrolysis of previously unknown acyl lysine modifications very efficiently. We further identified proteins that are modified by these novel acyl groups from mammalian mitochondria using mass spectrometry. This work demonstrated for the first time that sirtuins can prefer acyl groups other than acetyl. SirT5's novel activity suggests that other sirtuins with little or no deacetylase activity likely prefer other acyl groups too. This will greatly facilitate the study of these sirtuins and possibly lead to the discovery of more novel protein posttranslational modifications, some of which may be novel epigenetic modifications that regulate transcription.