Guest lecture

"Rationing methylation: effects on lipogenesis and gene expression when methyl donors are limiting"

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11 AM in the BMB seminar room

Amy Walker

Program in Molecular Medicine

University of Massachusetts Medical School

Abstract: Metabolic pathways provide the energy and building blocks our cells. However, certain metabolites can also act as signals, affecting cellular mechanisms controlling gene expression, signaling and growth. Using a metabolite to post-translationally modify a protein is a powerful way to modulate the protein's activity as cellular metabolic flux changes. We have investigated how changes in levels of the methyl donor, SAM (s-adenosylmethionine), are linked to changes in activating histone methylation patterns, as well as gene expression and survival during stress. Using C. elegans, we have found that animals with reduced function of sams-1, a SAM synthase, cannot mount transcriptional responses to a bacterial stress (Pseudomonas) or a toxin (R24). However, heat shock, which is activated by a distinct transcriptional mechanism, is less affected. Furthermore, we have found distinct functions for the H3K4 methyl transferases, set-2/SET1 and set-16/MLL in C. elegans stress responses. set-2/SET1 appears important for survival and stress response gene expression during Pseudomonas exposure. However, it is dispensable for toxin and heat stress responses. Strikingly, set-16/MLL is required for survival for all three of these treatments, highlighting its importance in regulating genes necessary for survival during stress. SAM levels decrease in multiple disease states from non-alcoholic and alcoholic fatty liver disease to cystic fibrosis. We hypothesize low SAM can limit transcriptional responses to stress, exacerbating tissue injury during disease.

Host: Professor Nils J. Færgeman, Department of Biochemistry and Molecular Biology, SDU.