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Metabolomics of Metabolic Origins

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Abstract

For the emergence of life, the origin of metabolism stands as a central problem. How did early biomolecules arise to form an intertwined network of self-controlling metabolic reactions? In scenarios for a potential chemoautotrophic origin of life, the relevant conditions could involve volcanic discharges and ashes or gradients in volcanic hydrothermal vents. These conditions can also be mimicked in laboratory settings. The analytical procedures necessary to evaluate these systems are closely related to metabolomics approaches qualified to analyze living organisms. In both cases, the main challenge is to analyze diverse mixtures of molecules in terms of quality, quantity and also isotope compositions (when working with labeled precursors). Thus, metabolomics could also provide a powerful tool to study the metabolism of "ancient" organisms for example to identify signatures of pathways which could go back to the origin of metabolism. In our work settings, methods originally developed for the analysis of bacterial pathogens [1] [2] are now transferred to organisms considered to be "ancient" or to reaction mixtures mimicking "primordial chemistry". Analyzing extracts from these organisms or the cell-free reaction mixtures simulating origin-of-life scenarios provides a multitude of compounds. Even though many of them are still unknown, reaction mixtures mimicking conditions for the origin-of-life frequently show resemblances to extant metabolic pathways, like the formation of activated acetic acid [3], amino acids, α-hydroxacids [4], and fatty acids [5]. In turn, analysis of the "ancient" organisms is the basis for the quantitative description of hitherto unknown metabolic pathways and enzyme functions, like the dicarboxylate/4-hydroxybutyrate autotrophic carbon assimilation cycle [6] or a reverse citrate cycle involving the reverse reaction of citrate synthase [7]. In the workshop, we will present advances and examples of how methods of metabolomics have benefitted recent studies of metabolic origins.

Biography:

The Eisenreich group has a long-standing expertise in metabolic pathway analysis in a variety of organisms (more than 200 original papers dealing with metabolism). The studies ranged from the discovery of new biosynthetic pathways in methanogens to the elucidation of numerous biosynthetic pathways of natural products. The group also pioneered the technique of isotopologue profiling to elucidate the central metabolism of many pathogenic bacteria under medicinally relevant conditions. Under the guidance of Dr. Claudia Huber and Prof. Günter Wächtershäuser, the group is also working in the field of a potential chemoautotrophic origin of life.

Speaker Publications:

[1] Eisenreich W et al. (2006) 13C Isotopologue perturbation studies of Listeria monocytogenes carbon metabolism and its modulation by the virulence regulator PrfA. PNAS 103:2040-2045. [2] Häuslein I et al. (2016) Pathway analysis 13C-glycerol and other carbon tracers reveal a bipartite metabolism of Legionella pneumophila. Mol Microbiol 100:229-246. [3] Huber C, Wächtershäuser G (1997) Activated acetic acid by carbon fixation on (Fe, Ni) S under primordial conditions. Science 276:245-247.

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