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## SÉMINAIRE

# Tracing the evolution of central metabolism: from the last universal common ancestor to the diversity of contemporary pathways

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In the three domains of life (Bacteria, Archaea, Eukaryotes), a wide diversity of metabolisms provides energy and chemical material supply with a major impact on all ecosystems. This diversity emerged from an ancestral metabolic network that has been reshaped for billions of years by several evolutionary events, including innovations, horizontal gene transfers, and tinkering, which remain largely understudied. I will describe recent results on the evolutionary history of two fundamental metabolisms.

The first is the pathway for biosynthesis of Iron-Sulfur (Fe-S) clusters, essential cofactors in the three domains of life. By combining accurate annotation of protein families with phylogenomic analyses, I reconstructed a comprehensive scenario for the origin and evolution of Fe-S cluster synthesis<sup>1</sup>. My results challenge the widely held view that this process emerged in response to Earth oxygenation. I discovered indeed two additional "minimal" machineries largely distributed in both Bacteria and Archaea, that I inferred to date back to the last universal common ancestor, well before the Great Oxidation Event.

The second metabolism is methanogenesis, a pathway specific to Archaea and of great societal impact<sup>2</sup>. I carried out an exhaustive investigation of hundreds of enzymes involved in this process, with a particular focus on the hydrogenase/oxidoreductase complexes involved in energy conservation and cofactor regeneration. My results indicate an extreme modularity and intricate evolutionary history that shaped the current distribution of these key enzymes in methanogens and other microorganisms. I also highlighted the surprising existence of an ancestral oxidoreductase complex, forcing a rethink of the energetic metabolism of LUCA, relative to that of ancestors of Bacteria and Archaea.

Building on this work, I will present my long-term project which aims at understanding the constraints that apply on the evolution of central metabolic pathways across the Tree of Life, paving the way to the discovery of fundamentally new enzymatic activities and with implications on more applied studies in biotechnology and synthetic biology.

<sup>1</sup>Garcia, P. S., D'Angelo, F., de Choudens, S., Dussouchaud, M., Bouveret, E., Gribaldo, S., & Barras, F. (2022). An early origin of iron-sulfur cluster biosynthesis machineries before Earth oxygenation. **Nature Ecology and Evolution**.

<sup>2</sup>Garcia, P. S., Gribaldo, S., & Borrel, G. (2022). Diversity and evolution of methane-related pathways in archaea. **Annual Review of Microbiology**.