Lanthanide-dependent metabolism is a nascent field of study with tremendous potential to define novel biochemical properties of enzymes and global changes to metabolic networks. Our studies have shown that lanthanides, from lanthanum (La^{3+}) to samarium (Sm^{3+}), can support methylotrophic growth of *Methylobacterium extorquens* AM1 in the absence of the methanol dehydrogenases, MxaFI and/or XoxF. By using a combination of system-level approaches, such as transcriptomics and metabolomics, as well as biochemical and phenotypic studies, we have unraveled key aspects of the network necessary to support lanthanide-dependent methylotrophy. Our major findings include (i) the identification and characterization of an additional, and non-XoxF like, alcohol oxidation system (named ExaF) that uses lanthanides for catalysis. Interestingly ExaF kinetic properties suggest that it is a more efficient ethanol dehydrogenase and formaldehyde dehydrogenase than methanol dehydrogenase. Phenotypic studies using mutant strains lacking the XoxF and ExaF systems corroborated its role in C_2 metabolism when lanthanum is present in the media. (ii) Using phenotypic and biochemical analysis, we have identified that *M. extorquens* can efficiently acquire lanthanides from the environment and that this process affect siderophore production, and (iii) Targeted metabolomics and RNA-sequencing analysis has allowed us to suggest changes in carbon distribution particularly for the production and consumption of organic acids such as formate, oxalate, and citrate.

Finally, as lanthanides are important components for the development of clean energy products and modern technologies, optimizing methylotrophic strains to develop biometallurgy-based technologies to recover lanthanides is a promising approach to mitigate the challenges of current extraction and recovery methods. Methylotrophic biometallurgy will allow us to (i) standardize extraction methods as current methods differ significantly depending on the ore source; (ii) reduce the production of acidic and radioactive byproducts during mining and recycling of lanthanides from commercial products.