439226 Universally Essential Cofactors in Prokaryotes

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The prediction of growth phenotypes with genome-scale metabolic models (GEMs) is heavily dependent on the composition of microbial cells as reflected in the biomass objective functions (BOFs). Different strategies for composing BOFs have been adopted, especially with regards to the pool of small molecules that is added to the building blocks of the major macromolecules. This has hindered several applications of GEMs, especially comparative studies. Indeed, when using biologically plausible BOFs borrowed from GEMs of closely related species, we observed a considerable impact on essentiality predictions. Towards addressing this problem, we integrated 71 BOFs of manually curated prokaryotic GEMs with 33 gene essentiality datasets, curated enzyme-cofactor association data and a vast array of literature publications. The study revealed universally essential cofactors in prokaryotic metabolism. This set of universally essential cofactors was validated with improved gene essentiality predictions and the identification of a missing biosynthetic pathway for *Mycobacterium tuberculosis* in iNJ661v, the most recent GEM for this species. We hope that this set of organic cofactors will facilitate reconstruction and analysis of a wide range of prokaryotic GEMs.

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