ABSTRACT: Genome annotations provide a detailed description of the metabolic activities an organism can carry out. A metabolic network can be reconstructed from genomic data and serves as a framework to build computational metabolic models. These models can make phenotypic predictions about the behavior of an organism given different genetic or environmental perturbations. Comparisons between model predictions and experimental data can then be used to identify missing components and interactions in biochemical networks. These comparisons provide a mechanism to improve our understanding of biological networks and genomes and in turn lead to improved models. Once accurate models are developed they can be used to design strains in silico for improved phenotypes. The development and analysis of metabolic models for Escherichia coli K-12 and Salmonella typhimurium LT2 will be presented and examples of their applications in network design and discovery will be discussed.