With increasing health care costs and inefficiency in many treatment strategies, the health care system is bound to transform in the coming years. A key driver for this change is the generation of big data, development of detailed mathematical models and an increased participation of patients in their own health. The use of mathematical models to study biological systems, i.e. analyze large datasets and simulate system behavior, is referred to as systems biology, or when applied to study medicine, systems medicine. This approach enables integrative analysis of different types of data, including different data types, and can hereby provide new insight into complex biological systems that cannot be obtained by any other mean. Here I will discuss the challenges of using systems medicine for advancing the development of personalized and precision medicine, and it will be illustrated how the concept of genome-scale metabolic models can be used for integrative analysis of big data with the objective of identifying novel biomarkers that are foundational for personalized and precision medicine.