The current enthusiasm for agnostic genomewide association scans is being tempered by the realization that there may be many variants that do not achieve genomewide significance individually but if aggregated along common biological pathway would reveal meaningful associations. There has thus been a resurgence of interest in pathway modeling, the origins of which date back to the era of candidate gene studies. I will describe a Bayesian hierarchical modeling framework to analyze multiple genes, multiple environmental factors, and their interactions, incorporating the kinds of prior knowledge available in large databases like the Gene Ontology. For well-understood pathways with sufficient biomarker data, mechanistic modeling incorporating differential equation models for the underlying biological processes with statistical models of the random elements may be also possible. Examples of these approaches will be drawn from studies of colorectal cancer in relation to the folate metabolism pathway and of breast cancer in relation to ionizing radiation and DNA damage response pathways.