CROM3TOP, or Cross-species Multimodal Modular Model of Tolerance to Pathogens, is a highly generalized and powerful Bayesian probabilistic framework. It can feed on (possibly temporal) high-dimensional multi-omics data across various host and pathogen species, to develop a rich ontology that defines a probabilistic model which can differentiate between two or more phenotypes of interest, like the state of tolerance or sensitivity to pathogens. At its core, CROM3TOP is a dynamic Bayesian network whose conditional independence structure is designed by scraping multiple online curated repositories of biological networks. We use them to define directed relationships between various biomolecules at multiple omic levels, like transcription factors, genes, enzymes, signaling molecules, other proteins, various metabolites, and even the microbiome, so as to capture a more integrated model of emergence of phenotypes. Moreover, CROM3TOP describes a pan-species model, which means that various host species are interrelated, which results in an exciting experiment-analysis scenario wherein we can learn about a species of interest by conducting experiments on another host species. This is achieved by using transfer learning, via the space of metabolites which are assumed common across species and act as a “bridge” over which to transfer the parameter distributions. The transfer learning is further helped by using hierarchical Bayesian priors that bring about parameter tying across species. Additionally, since most host-pathogen responses proceed in modules, it is possible to induce a modular structure within the model by introducing a latent space of hidden nodes that anchor these modules, and carry out structure learning before generating the final Bayesian network structure. Because we work in the Bayesianist paradigm, it is possible to generate comparatively rich models with even more smaller-sized datasets. Although the model size can be huge, and with thousands of parameters, the conditional dependency structure allows for quick and parallelizable learning at every node of the Bayesian network. Some powerful advantages of this probabilistic model is the plethora of inference queries which can be made to it, from finding out most probable omic values corresponding to given phenotypes, to finding important features that induce phenotypic changes, which can help design more targeted drug therapies.