



BASIC//DISCOVERY

MODELING the SYSTEMS of LIFE

Rajanikanth Vadigepalli, PhD, professor of pathology, anatomy and cell biology, is a chemical engineer and systems biologist who views the body as a series of systems nested within systems, interacting in dynamic ways. He and his colleagues use high-powered computers to create complex models of how tissues and organs function, which they compare to observations of in vitro and in vivo lab models. The iterative process enables them to find minute, molecular level effects with outsized significance.

One of Dr. Vadigepalli's primary research focuses is the liver. He and his collaborators

analyze the organ at molecular, cellular and tissue levels to learn how complex, cause-effect relationships trigger liver cells' normal regenerative activity (a surgically reduced liver usually regrows in months)—and, conversely, what happens when exposure to excess alcohol or fats overcome cells' regenerative capacity and the whole liver begins to fail. Their work is changing some long-held assumptions. For example, alcoholic liver failure has long been viewed as a process where the organ tolerates alcohol for a period and then suddenly decompensates at one catastrophic

inflection point. However, Dr. Vadigepalli has found that alcoholic liver failure is actually a progressive process: damage accumulates over time as individual cells become more sensitive to injury with each passing insult; eventually, a tipping point is reached when too many individual cells lose function and the larger system—the liver—fails.

By helping to explain how systems actually work, Dr. Vadigepalli is opening new paths for diagnosing, treating and preventing an array of serious diseases and for bringing regenerative medicine ever closer to reality. ■

