

Professor uses evolution, informatics to uncover secrets of the genome

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Sudhir Kumar has sought to make his contributions broadly available to both the scholarly community and interested lay enthusiasts. He has assembled thousands of divergence times among organisms in the published literature into a resource known as TimeTree – a public knowledge-base for information on the evolutionary timescale of life. Photo by: Tom Story

What patterns exist in the evolutionary design of living things? What particular processes produced these patterns? And how might this information be used to untangle the complexities of health and disease, coded in human genes? These are among the central questions examined by Sudhir Kumar in his path-breaking research.

The evolutionary design of nature has given rise to the staggering [diversity of life](#) on Earth. But a full appreciation of the richness associated with the tree of life requires new techniques to harness large-scale data at the DNA level and bring order to its bewildering complexity.

"My research focuses on two broad areas," Kumar says. "We develop tools and methods that enable large-scale analyses of [DNA sequence data](#) and we conduct our own analysis to unlock various patterns."

Kumar, a professor of biology in the School of Life Sciences, within ASU's College of Liberal Arts and Sciences, directs the Center for Evolutionary Medicine and Informatics at the Biodesign Institute, where his group pursues four broad themes of research:

- personal genomics – involves analysis of [genetic mutations](#) and their propensity to cause disease
- disease origins – traces pathogen evolution to unravel dynamics of infections and assess [drug resistance](#)
- functional proteomics – aimed at discovering functionally important components of genomes
- discovery bioinformatics – involves computer modeling, analysis and simulation to discover patterns and test predictions

Kumar insists however that these categories are all closely intertwined. "I take a holistic approach, covering 4 billion years of evolution. This gamut of areas – from basic fundamental biology to applications of biology to improve human conditions – is what my research has been doing for the past 15 years," he says.

James Collins, Senior Sustainability Scientist, Global Institute of Sustainability and Virginia M. Ullman Professor of Natural History and the Environment, School of Life Sciences, stresses the importance of Kumar's contributions to ASU: "Every so often a university has an opportunity to stretch and hire someone who is really different in creative, interesting and important ways. In 1998, ASU's Biology Department had that opportunity and hired Sudhir Kumar. Since then his evolutionary bioinformatics research has proven time and again to be ahead of its time. He is an insightful thinker who uses an interdisciplinary approach to solving complex problems at the interface of evolutionary biology, genetics and computational thinking."

Collins adds that "professor Kumar is the sort of person who brings sustained, exceptional quality to his scholarship. Any university in the world would be thrilled to have him as a member of its faculty. At ASU we are very fortunate to count this gifted scholar as one of our own."

The powerful suite of methods developed by Kumar to observe evolution in action, from species divergence to the appearance of disease-related mutations in the [genome](#), have already yielded exciting revelations. In 1998 for example, Kumar and his collaborator Blair Hedges of Penn State used the largest evolutionary study of gene sequences to date to show that mammals emerged some 20 to 30 million years prior to the extinction of dinosaurs.

These and many other insights emerged, thanks to the revolutionary concept of molecular clocks used to accurately time species divergence and patterns of molecular evolution. The basic idea was first described in 1962 by Emile Zuckerkandl and Linus Pauling, who proposed that the rate of evolutionary change of any specific protein was roughly constant over time and over different lineages, allowing these protein changes to act as biological timekeepers. (Recently, the Kumar group has introduced RelTime, a tool designed to leverage the power of molecular

clocks to rapidly establish relative, rather than absolute times of species divergence – a significant innovation.)

The study of branching patterns of species, their rates of mutation and rates of change over time across a broad swath of life forms on Earth can also offer vital clues about which mutations are most likely to have implications for human health. By identifying regions of species genomes that tend to remain stable over evolutionary time, researchers like Kumar can zero in on gene mutations most likely to cause disease, separating them from benign alterations. The advent of rapid, low-cost gene sequencing has helped give rise to an entirely new discipline known as phylomedicine, in which Kumar is one today's leading pioneers.

Kumar has sought to make his contributions broadly available to both the scholarly community and interested lay enthusiasts. He has assembled thousands of divergence times among organisms in the published literature into a resource known as TimeTree – a public knowledge-base for information on the evolutionary timescale of life. This storehouse of evolutionary diversity also takes the form of a beautifully illustrated text, *The TimeTree of Life* and there is even an iPhone app available, allowing mobile users to easily enter any two organisms and rapidly learn their divergence times, accompanied by references to the relevant scientific studies.

Additionally, Kumar has created many sophisticated bioinformatics tools used to ferret out important mutations in the genome and assess their relevance. One of the most useful tools for researchers around the world is MEGA – Molecular Evolutionary Genetics Analysis – a software package that provides evolutionary analysis of gene sequences across individuals, populations and species, which Kumar developed along with colleagues Koichiro Tamura and Masatoshi Nei.

MEGA has been downloaded over 750,000 times, while a number of

Kumar's research studies of sequence data rank among the most highly cited in the biological and computer science literature, including his paper "A molecular timescale for vertebrate evolution," which appeared in the journal *Nature* in 1998 and ranks in the top 1 percent of all *Nature* papers in terms of citations.

According to professor James Elser, who nominated Kumar for this year's Regents' Professor award, "Sudhir Kumar is a visionary in merging the power of information technology with the digital world of DNA. His innovative work in developing the software MEGA for evolutionary studies, as well as other database and software infrastructure for biological analyses, is foundational for innumerable biologists. The impacts have been remarkable and are still accelerating globally. He is an enormous asset for the core life sciences strengths we have here at ASU." (Elser is the Regents' Professor & Parents Association Professor of ecology, evolution and environmental science and Distinguished Sustainability Scientist.)

Along with Kumar's diverse research interests comes a passion for educating young scientists through inquiry-based biology and informatics classes such as "Introduction to Comparative Genomics." He also mentors students at both undergraduate and graduate levels by providing hands-on experience in the laboratory, where real-world examples of evolutionary genomics concepts and relevant applications in biomedicine are taught.

Robert E. Page, Jr., vice provost and dean in the College of Liberal Arts and Sciences at ASU, summarizes the enthusiasm Kumar's research and teaching have generated across the university: "Sudhir is an extraordinary faculty member. Not only is he one of the most highly cited and productive evolutionary biologists, he is also an excellent teacher and citizen. Sudhir is one of our own homegrown superstars and ASU basks in the light of his accomplishments."

Sudhir Kumar is the recipient of numerous awards and accolades. He is a two-time finalist for the Arizona Governor's Celebration of Innovation, an ASU Faculty Exemplar and a winner of the Innovation Award in Functional Genomics. Kumar is an American Association for the Advancement of Science fellow, president of the Society for Molecular Biology and Evolution and current editor in chief of the MBE Society's journal.

Provided by Arizona State University

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