

UCSD Bioinformatics Researcher Studies Tumor Genome Architectures With Career Award

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Postdoctoral researcher Benjamin Raphael is one of only eleven scientists nationwide honored by the Burroughs Wellcome Fund (BWF) for work at the intersection of computer science, mathematics, and biology. The mathematician and computer scientist from the University of California, San Diego's Jacobs School of Engineering will receive \$500,000 over five years from BWF to support his research in the area of high-resolution analysis of tumor genome architectures. Raphael works in the Computer Science and Engineering (CSE) department's Bioinformatics Laboratory, led by CSE professor Pavel Pevzner.

One of five different BWF award programs, the Career Award at the Scientific Interface (CASI) is awarded by the North Carolina-based fund to support physical or computational scientists conducting biological research. Awards to this year's winners totaled \$5.4 million, and the fund has invested roughly \$13 million in the program since its inception in 2002. The awards are typically designed to bridge advanced postdoctoral training and the early years of faculty service. "This award is extremely important to me because it comes at a critical time in my career," said Raphael, who co-organized a conference on regulatory genomics at UCSD earlier this year, co-sponsored by the California Institute for Telecommunications and Information Technology [Cal-(IT)²].

In a sense, Raphael says, he has come full circle. The Virginia-bred researcher majored in mathematics and biology as an undergraduate at MIT. Raphael then came to UCSD to earn his doctorate in mathematics. "Towards the end of my Ph.D. studies," he said, "I wanted to do something more applied, and bioinformatics was an exciting area." Raphael was awarded an Alfred P. Sloan Fellowship in 2002 because, he says, "the Foundation recognized the need for quantitative Ph.D.'s to work in biology."

The 30-year-old researcher works at the cutting-edge of genomic science - and health. His work began with an analysis of regulatory sites in the mouse genome that others in Pevzner's lab were analyzing for their evolutionary implications, including genome rearrangements that account for the different paths humans and rodents have taken since splitting off from a common ancestor roughly 87 million years ago. These rearrangements "happen in cancer naturally," Raphael notes, adding that "by studying the rearrangements we can identify genes that are important for tumor growth, development and malignancy, and these may serve as diagnostics of tumor stages."

Raphael's work in cancer genomics began in late 2002, when Colin Collins and Stas Volik, experimental biologists at the University of California, San Francisco (UCSF) Cancer Center, sought out Pevzner's group to do computational analysis of genome rearrangements implicated in breast cancer. "You can view the breast cancer genome as an extremely fast-evolving human genome," says Pevzner. "Now that the human genome has been sequenced, we can do the same for specific cancer cells, not just any cell in the body."

"We are up to five tumor genomes that we study, including the genomes for prostate cancer, brain tumors, and so on," Raphael adds. "We are looking at rearrangements that are common to certain cell types, and the work is accelerating because the public is putting pressure on science agencies to fund cancer research."

Raphael and Pevzner hope to team with the UCSF Cancer Center on a Tumor Genome Project. "The idea is that there is all this sequencing capacity left over from decoding the human, mouse, rat, chicken and other genomes," said Raphael. "Public funding agencies will now be under pressure to support sequencing efforts that are important medically. Sequencing tumor genomes helps us to understand better how tumors behave and progress."

Pevzner and Raphael have also held discussions about the Tumor Genome Project with UCSD Cancer Center director Dennis Carson, and Richard Kolodner, a member of UCSD's Ludwig Institute for Cancer Research. Both lent their support to BWF's awards committee on Raphael's behalf.

"Cancer in a sense is a breakdown of DNA repair, and the rearrangements that we see are unrepaired mistakes in the process of DNA replication," adds Raphael. "There are whole classes of genetic diseases that are inherited and passed down from a parent. Mutations in our DNA can be single-letter changes like those that occur in cystic fibrosis, or they can involve multiple chromosomal rearrangements such as those associated with solid tumors."

Raphael was planning to apply for a faculty position this year, but says the BWF award will afford him an easier transition. "I now have a little more freedom to do research and stay here at least one more year," he explains. "I plan to apply for a faculty appointment in 2006." His future destination is unclear: "Depending on the university, bioinformatics work is happening in the computer science department, math department, biology department, or in an interdisciplinary center." Raphael says that he favors teaching in a quantitative department but wants to maintain close ties with biological researchers.

"I think this award shows UCSD is a great environment for doing work at the intersection of biological sciences, quantitative mathematics and computer science," says Raphael. "It is an award for UCSD, not just for me."

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