Images clockwise from bottom left:
Drug molecule, iStock; genetic map, Martin Krzywinski/Science Source; HIV virus, NIAID/Seth Pincus/Elizabeth Fischer/Austin Athman/Science Source; mosquito, Mark Giles/Science Source; male papilio aristodemus, free domain.
New Research Centers Blur Scientific Boundaries

One day last May, Ron Levy sat in his temporary office in the Bio-Life Building speaking with Nan-Jie Deng, one of his assistant research professors. They were discussing Deng’s research, which involves using free energy molecular dynamics simulations to design inhibitors against HIV viral proteins.

Levy, Laura H. Carnell Professor of Biophysics and Computational Biology, directs the Center for Biophysics & Computational Biology—one of seven new research centers or institutes that, over the past year, have doubled the number of CST research entities, creating a collaborative critical mass of internationally renowned researchers.

Underscoring that cooperative thrust, later that day Deng reported on his progress at a joint seminar involving Levy’s center and the Institute for Computational Molecular Science headed by Dean Michael Klein. Finally, Levy, who was lured away from Rutgers University and whose lab is on the top floor of the Science Education and Research Center (SERC), spoke with Bill Flynn, a graduate student. The topic: Flynn’s efforts to use deep sequencing data to determine patterns of correlated mutations in HIV proteins.

Explaining why he came, Levy says, “I’ve known Michael Klein for years, and knew that great things were happening here in computational science. It’s really exciting.”

USING COMPUTING POWER AND ADVANCED FACILITIES

CST has hired more than 60 faculty members since 2007 and, over the past two years, a handful of senior faculty who are leaders in their fields. Why did such a distinguished group uproot well-established research labs to come to CST? SERC was part of the allure. “To attract scientists from around the world, you need to have great facilities to launch an initiative of the magnitude we are contemplating,” says Sudhir Kumar, Laura H. Carnell Professor of Genomic Medicine and founding director of the Institute for Genomics and Evolutionary Medicine (iGEM).

Given these new researchers’ need to mine and analyze huge data sets, another draw was the ultrafast, powerful capabilities of Temple’s High-Performance Computing Cluster and its related virtual server, TUscloud—the kind of computing power that opens new scientific frontiers.

“From basic questions on evolution to critically important questions on human health, much of modern life-science research involves the development and application of advanced computing technologies,” says Jody Hey, who arrived a year ago from Rutgers
Kumar was also attracted by the chance to work with CST colleagues and researchers from the College of Public Health, School of Medicine and Fox Chase Cancer Center. “Genomics is part of many exciting research endeavors in these disciplines,” says Kumar. “It’s a tool to measure the kind of differences we have from one another and also the diversity in the blueprint of life. With this unique angle, we can connect various entities at Temple.”

This collaborative urge triggered a domino effect of additional high-level hires. After arriving from Rutgers last fall, Hey suggested recruiting Kumar from Arizona State University, where he appeared to be set for life after being named a Regents’ Professor just three years earlier. Both Hey and Kumar have been recent presidents of the Society for Molecular Biology and Evolution.

In turn, Kumar approached S. Blair Hedges, a longtime collaborator from Pennsylvania State University. Along with Kumar and another former Arizona State professor now at Temple, Ananias Escalante, Hedges is Laura H. Carnell Professor of Biodiversity and a founding member of iGEM and director of his own Center for Biodiversity.

University to direct the Center for Computational Genetics and Genomics (CCGG).

Hey’s primary research includes developing new ways to use genome sequence data to study the divergence of populations, from fruit flies to apes to humans, and in particular the evolutionary history of human populations in Africa. “If we have DNA sequences of the genomes from many populations from around the world and we want to understand how those populations spread and are diverse from each other, there’s a very large amount of data that we need to be able to fit into a complex evolutionary model,” says Hey. “That requires tremendous computing power.”

**INTERDISCIPLINARY COLLABORATION**

Another attraction for new faculty is the chance to collaborate with talented researchers within the college and beyond. “People are attracted by the fact that at its highest levels—from president to provost and the dean—Temple has a science- and tech-supportive administration,” says Levy. “Great research stems from being around great people.”

John Perdew, who came to Temple from Tulane University and is one of the world’s most cited physicists, agrees: “I now have more potential collaborators. Our proximity in SERC brings together computational researchers from many different areas in physics, chemistry and biology, as well as top researchers from the Philadelphia region.”

Kumar was also attracted by the chance to work with CST colleagues and researchers from the College of Public Health, School of Medicine and Fox Chase Cancer Center. “Genomics is part of many exciting research endeavors in these disciplines,” says Kumar. “It’s a tool to measure the kind of differences we have from one another and also the diversity in the blueprint of life. With this unique angle, we can connect various entities at Temple.”

This collaborative urge triggered a domino effect of additional high-level hires. After arriving from Rutgers last fall, Hey suggested recruiting Kumar from Arizona State University, where he appeared to be set for life after being named a Regents’ Professor just three years earlier. Both Hey and Kumar have been recent presidents of the Society for Molecular Biology and Evolution.

In turn, Kumar approached S. Blair Hedges, a longtime collaborator from Pennsylvania State University. Along with Kumar and another former Arizona State professor now at Temple, Ananias Escalante, Hedges is Laura H. Carnell Professor of Biodiversity and a founding member of iGEM and director of his own Center for Biodiversity.

**BETTER PHARMACEUTICALS**

Funded by the National Institutes of Health and National Science Foundation, Levy’s Center for Biophysics & Computational Biology (CB2) focuses on leading-edge computational research that explores the intersection of biology, chemistry and biophysics.
“We work on problems in biology from a chemistry background to design better pharmaceuticals that improve health,” says Levy. “The targets of most drugs are large protein molecules, but it is not obvious, from either experimental data or looking at the molecules’ structures, how to best design pharmaceuticals.”

Enter structure-based design utilizing model simulations, a field whose long-considered promise has begun to be fulfilled in the past five years with the development of more powerful and accurate simulation methods. These techniques are now capable of creating a framework and making a connection between tremendous amounts of available experimental and structural data. CB2 researchers use such methodologies, Levy says, “to target new drugs that take out of action important proteins that are essential for the functioning of the AIDS virus.”

Levy’s lab also uses molecular simulations to assure that drugs bind as tightly as possible to their targets so that they can be taken in the smallest doses and minimize side effects. Finally, his group uses sequence-based and statistical techniques to investigate how viruses mutate in order to develop resistance to drugs.

“Resistance often doesn’t happen because of one mutation but because of a complex pattern of mutations,” he says. “It’s an ingenious process that you have to outwit because the mutations change the protein you have targeted just enough so that the drug isn’t effective anymore, but not so much that the protein isn’t still effective.”

GENETIC COMPONENTS OF DISEASE

Genome analysis, which requires sophisticated computational methodologies, is at the heart of Kumar’s iGEM. He notes that many diseases, including brain and breast cancers, have genetic components. Given the millions of genetic differences that exist between human beings, researchers want to know which of these differences are potentially harmful, and when and how they will affect us. “That,” he says, “is the grand challenge of genomic medicine: Which persons have problematic mutations, and what could those mutations ultimately cause?”

To address that challenge, Kumar practices “phylomedicine,” which involves sifting through tremendous amounts of genetic data from human beings; our closest relatives, the apes; and many other species to assess the impact of mutations we each harbor. “We are essentially mining the outcome of nature’s experiments from a large number of species to inform human medicine,” he says.

Kumar’s institute will also engage in related activities, such as phylogenetics, to develop species trees and analytics to better process genomic data. Software tools Kumar has developed have been cited more than 70,000 times. That includes TimeTree, a public database he and Hedges created that allows users to quickly calculate divergence times among various species—92.3 million years ago, for example, for humans and dogs.
Says Kumar: "We want to build tools for biologists throughout the world to do analyses easily and to discover scientific knowledge efficiently."

SMARTER, BETTER MATERIALS

The Center for Materials Theory, led by Laura H. Carnell Professor of Physics and Chemistry John Perdew, focuses on materials theory and density functional theory. Members include Dean Klein and professors Peter Riseborough, Adrienn Ruzsinszky and Jianwei Sun. The group develops the fundamentals and approximations of density functional theory for atoms, molecules and solids. For practical electronic structure calculations, both materials physics and quantum chemistry now usually rely on this theory—which can predict a molecule's shape or the energy of a bond.

Perdew’s innovations include the development of a "Jacob's ladder" of approximations. As the ladder’s rungs (three so far, with more under development) go higher, they describe with increasing accuracy a material’s exchange-correlation energy, which is "nature's glue" for interatomic binding.

Perdew’s group is also probing what is termed the van der Waals interaction. "It’s an interaction that produces an attraction between atoms, but one that is much weaker than a chemical bond," he says. "It’s the interaction that binds carbon atoms in graphite in flat, two-dimensional layers that are easy to break apart.

That’s why you can write on a piece of paper with a pencil.” The same force, adds Perdew, holds together molybdenum disulfide, which has potential applications in solar cells and for hydrogen fuel production.

Perdew also leads Temple’s Center for the Computational Design of Functional Layered Materials, one of 10 new Energy Frontier Research Centers announced by the U.S. Department of Energy. The $12 million award will support the design of materials that could potentially have applications in energy production or storage. (See page 7.)

BIOLOGICAL AND GENOMIC ARCHAEOLOGY

Hedges’ Center for Biodiversity explores such questions as how many species there are on Earth and what they need to continue to exist in the face of environmental degradation. Much of his work focuses on the Caribbean islands, including helicoptering into remote sections of Haiti that harbor the last remaining 1 percent of that country’s original forests in order to determine how best to keep frogs, butterflies and other species that depend upon those forests from going extinct.

Collecting frogs and snakes has its own charms, but the big data sets he and Kumar have gathered in their TimeTree program provide him with an essential tool to help pinpoint when two species diverged.
“If once there was one population of lizards,” Hedges explains, “but 1 or 2 million years ago two populations said goodbye to one another because some lizards rafted on litter during a storm over to another island, the tree-of-life data tell us when they became different species.”

Over in CCGG, Assistant Professor Alexander Platt is currently engaged in what he calls genomic archaeology—using genomic data sequenced from the teeth of three 50,000-year-old Neanderthal fossils to learn much more about that species and how it differed from Homo sapiens. Last year, Hey co-authored a separate study that concluded a small amount of gene sharing that took place between Neanderthal-like hominids and Homo sapiens occurred not, as some had speculated, in Africa more than 100,000 years ago, but later, possibly in the Middle East between 47,000 and 65,000 years ago, after humans began migrating out of Africa.

“Everyone wants to know where they come from, and human evolution is one of the greatest stories,” Hey says. “But much of the story remains untold. What were archaic Homo sapiens like, and where and when did the transition to modern humans occur, and what happened to cause that? It’s the most fundamental and exciting story to tell about our history.”

—Bruce E. Beans

Carnell Professor John Perdew and researchers at the Center for Materials Theory probe what is termed the van der Waals interaction (far left), named for Dutch theoretical physicist and thermodynamicist Johannes Diderik van der Waals, whose career spanned the late 19th and early 20th centuries. “It’s the interaction that binds carbon atoms in graphite in flat, two-dimensional layers that are easy to break apart,” says Perdew. “That’s why you can write on a piece of paper with a pencil.” The same force holds together molybdenum disulfide, which has potential applications in solar cells and for hydrogen fuel production.

(Left) The crystal structure of graphite, its layers held together by the universal glue of the material world, a weak set of forces generated by fluctuations in the electric field of molecules.

CST’S NEW RESEARCH ENTITIES JOIN A STRONG STABLE OF EXISTING CENTERS AND INSTITUTES

Center for Advanced Photonics Research
Director: Robert Levis, Professor of Chemistry
Focuses on understanding photochemistry and photophysics of molecules interacting with ultrafast, ultra-intense laser pulses, leading to new ways to diagnose disease, detect improvised explosive devices, classify tissues and phenotypes, and synthesize monodispersed nanomaterials.

Center for Data Analytics and Biomedical Informatics
Director: Zoran Obradovic, Laura H. Carnell Professor of Data Analytics
Advances research at the interface of information management, retrieval and analysis, including investigations of data mining, machine learning, databases, pattern recognition and computer vision.

Center for Networked Computing
Director, Jie Wu, Laura H. Carnell Professor of Computer Engineering
Investigates cloud computing, cyber-physical systems and sensor networks to develop new technologies such as wireless fetal heart monitors.

Institute for Computational Molecular Science
Director Michael L. Klein, Laura H. Carnell Professor of Science
Applies principles from quantum mechanics and statistical thermodynamics to model molecular phenomena using computer simulations, accelerating the development of new medicines and technologies.

Sbarro Institute for Cancer Research and Molecular Medicine
Director: Antonio Giordano, Professor of Biology
Conducts advanced research into cures for cardiovascular conditions, cancer and other diseases through the identification of their underlying molecular mechanisms.