UC San Diego
UC San Diego News Center

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Bioengineers Receive $12M Grant from NIH to Further Research on Building Blocks of Human Metabolism

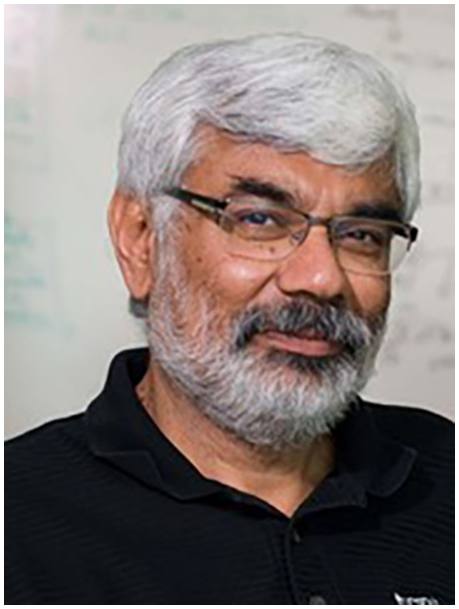
The Metabolomics Workbench will make data from tens of thousands of studies available to researchers and clinicians

The University of California San Diego has received a $12 million, four-year grant from the National Institutes of Health to expand the Metabolomics Workbench, a searchable, interactive repository of data for all research in the field of metabolomics—the study of the small molecules called metabolites that are found within cells and biological systems.

The Metabolomics Workbench project, led by bioengineering professor Shankar Subramaniam at the Jacobs School of Engineering at UC San Diego, launched in 2012 with a $6 million grant from the NIH. This new infusion of funds will allow Subramaniam and colleagues to add a wide range of clinical data to the Workbench and take the project into the clinic itself. This in turn will allow researchers and physicians to develop better tools to diagnose diseases through metabolite markers in blood.

Subramaniam is one of the pioneers of the field of developing data and analysis environments for metabolomics. His research group focuses on systems biology and systems medicine, including diseases of the liver, muscles, brain and vascular system.

Metabolites are produced and consumed in the chemical reactions that take place in the body to sustain life. Today, some metabolites are used to diagnose a range of diseases—think of blood sugar being used to diagnose diabetes and cholesterol for heart disease, for example. But Subramaniam said researchers want to be able to analyze the collection of all metabolites at any given moment — the metabolome — as a chemical readout of the state of health of the cell or body. He calls this “metabo-typing.”



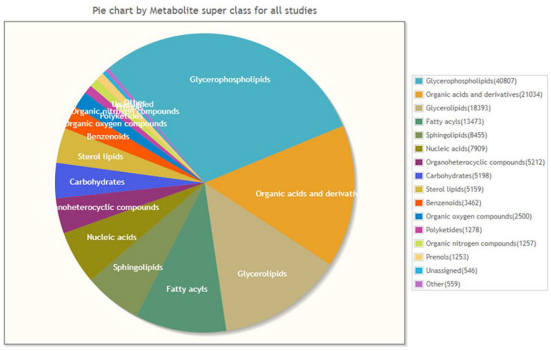
Bioengineering professor Shankar Subramaniam is the principal investigator for the $12M million grant.

Over the past six years, the Workbench has helped scientists elucidate the role that metabolomics play in diabetes and cancer. Researchers are now hoping to do the same for other conditions, such as obesity, heart disease, liver disease and more. Subramaniam himself is trying to determine if any metabolomics markers could help diagnose Alzheimer's disease in its early stages.

Metabolomics used to be considered the missing piece in the puzzle that systems biology is trying to solve, Subramanian said. But a series of advances in mass spectrometry—a technique that can elucidate a molecule's mass and chemical structure—has made it possible for researchers to better analyze metabolites and understand the role they play in human health.

The NIH funds will allow Subramaniam to hire more personnel for the Workbench, doubling the group's size to about a dozen experts in computer science, computational biology and of course metabolomics. Workbench data are housed in the cloud at the San Diego Supercomputer Center, with support from Christine Kirkpatrick, SDSC's division director for IT Systems & Services.

Asking better questions



A breakdown showing all studies categorized by metabolite super class.

Researchers at the UC San Diego School of Medicine said they are looking forward to using the next generation of the Metabolomics Workbench.

Subramaniam and his team are uniquely placed to identify novel prognostic biomarkers of disease severity of chronic metabolic diseases such as nonalcoholic fatty liver disease (known as NAFLD), said Dr. Rohit Loomba, director of the UC San Diego NAFLD Research Center.

“This grant provides an innovative platform to discover and validate novel biomarkers of disease severity and progression of chronic diseases,” Loomba said. “Using the resources from the NAFLD Research Center at UC San Diego and Subramaniam’s deep expertise in metabolomics, the stage is now set to unravel new discoveries that are likely to impact and transform clinical medicine in the coming years.”

Dr. Gabriel Haddad, chair of UC San Diego’s Department of Pediatrics and Chief Scientific Officer at Rady Children’s Hospital San Diego, is also excited about the Workbench’s transformative potential.

“The Workbench will allow us to ask better questions and pose new hypotheses,” he said.

Haddad’s research focuses on cardiovascular disease and atherosclerosis. Gaining information about the patient’s metabolome and microbiome in the human gut is key for this work—and that’s exactly what the workbench delivers.

Content and analysis tools

Since its inception in 2012, the Metabolomics Workbench has made available data from more than 1,000 projects around the nation and the world. It has established the only national metabolomics database with over 50,000 experimentally annotated metabolites along with over one million computationally generated metabolites described in terms of their structure, classification and computed spectra.

The project’s next generation will house enormous amounts of clinical data from human subjects, as metabolomics measurements are increasingly being used in epidemiological, observational, and interventional clinical studies. The clinical metadata will include elaborate demographic information for patients and participants as well as other relevant clinical data that are part of the study. Clinical study designs and protocols will include vital information on the study size; specifics related to study components; randomization process, nature and duration of the intervention; and other critical information, including subject exclusion and inclusion criteria. The Workbench will accumulate and provide human subjects data based on proper IRB protocols and approvals in a HIPPA-compliant manner.

To make a powerful impact, these data need to be easily accessed for analysis, computation and integration with other data. The Workbench is already a robust infrastructure that provides seamless access via web browser for clients to analyze and compute data on-the-fly as well as tools to interpret the data in biologically meaningful formats. These features will be enhanced in the next-gen Workbench, with embedded technology that will make it easier to customize

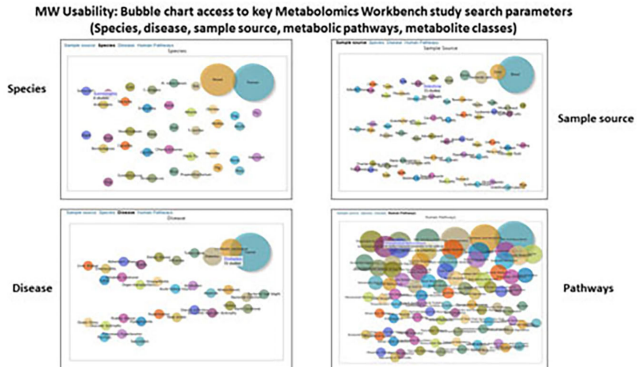
tools for analysis and computation. The Workbench will deploy cutting-edge strategies to support a data repository that allows easy data deposition; searchable access; and retrieval of datasets. Computational analysis will be possible within the cloud environment to avoid issues associated with downloading very large datasets. This will usher the data repository into the personalized computing and big data environment.

The project will develop a robust metabolomics data repository to store raw and primary metabolomic data with the metadata necessary for analysis. The required extent of metadata will be determined by community input and guidance from the Governance Core established by the UC San Diego Principal Investigator and the Program Officers of the National Institutes of Health. The data repository will have flexibility to accommodate metabolomic datasets of multiple formats, including spectrometric, spectrographic and chromatographic information derived from MS, NMR and gas chromatographic platforms and the associated unique chemical entities (UCE) and quantitative values where appropriate.

Metabolomics experiments stored in Workbench may include ion mobility or other orthogonal chromatographic information; topological information with mass spec imaging; isotopic information including isotopoloques and isotopomers; and qualitative and quantitative values requiring unique data formats. As metabolomic technologies continue to evolve, additional formats and information content will be accommodated.

The National Metabolomics Data Repository will work with the Stakeholder Engagement and Program Coordination Center (SEPCC) to ensure that the appropriate computational tools are available and, when possible, can be used in the cloud environment. The Repository Governance Core and the SEPCC, in consultation with the NMDR PD(s)/PI(s), will develop strategies to ensure that data formats meet evolving community standards.

Many datasets



Datasets charted across different search parameters.

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