



Pioneering the Science of Metabolomics for Better Diagnostics and Disease Treatment

Metabolon, Inc.

Studies on predicting the risk of obesity and age-related diseases launched Metabolon, Inc., a start-up company pioneering the application of the science of metabolomics toward the development of new or better diagnostics and treatments for diseases, located in Research Triangle Park, North Carolina. Metabolomics is the study of the metabolome, the collection

of all the small molecular substances produced by the body. Some examples of these substances, known as metabolites, are glucose, cholesterol, creatine, and fatty acids.

Throughout his career, Bruce Kristal, Weill Cornell Medical College, Neuroscience, has been working to understand what makes dietary or caloric restriction (defined as

“undernutrition without malnutrition”) the most potent and reproducible way to increase life span and reduce morbidity in laboratory mammals and to use this model for predicting diseases. Since caloric restriction affects the body’s whole metabolic network, he knew he had to develop a way to study all the metabolites in a sample in order to find the collective changes due to dietary restriction. Obtaining a sample’s metabolite profile was technically difficult. It required the separation and detection of metabolites—humans make about 2,500 such substances—and a way to analyze the massive amounts of data obtained. Kristal and his colleagues developed effective methods in his dietary restriction experiments with rats.

Scientific discussions between Kristal and Rima Kaddurah-Daouk, a biochemist with extensive experience in drug development and founder of the Avicena Group, led them to invent ways of using metabolic profiles of samples obtained from patients in different medical states. Patent applications for the technology, which uses comparative metabolic profiles to identify ways of diagnosing and developing better drugs for specific diseases, were filed.

The metabolites, which differ in specific ways in patients with a disease and those without, can be used collectively as “biomarkers” for detecting the disease. Depending on the samples compared, these profiles can also highlight differences in the metabolic response to a drug and help identify drug targets. In 2003 the entrepreneurial Kaddurah-Daouk founded Metabolon, Inc., with Paul Schimmel of the Scripps Institute, to commercialize the technology that she and Kristal had invented. That year Cornell licensed its rights to Metabolon, giving the company the exclusive use of the technology.

The company’s initial \$4 million funding was led by the Aurora Funds of Durham, North Carolina, with participation from the Trelys Funds of Columbia, South Carolina, Alexandria Real Estate Equities of Pasadena, California, and other investors. This funding enabled Metabolon to put together its management team, install the necessary instrumentation, and test the metabolomics platform in medical applications.



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biotechnology companies in specific disease or therapeutic areas to generate metabolite signatures for preclinical and clinical studies. With Metabolon's profiles these companies can save considerable development time in selecting the best new drug candidates, and they can reposition or rescue existing drugs. Complementing its technology, Metabolon has developed an extensive database of more than 1,000 compounds, which can identify the metabolites present in profiles and relate the profiles to defined biochemical pathways. The company is currently the top service provider of metabolic studies for pharmaceutical and biotechnology companies.

reliable analytical platforms have established Metabolon as the leading metabolomic discovery solution provider," says John Ryals, president and CEO of Metabolon. "In over 60 studies, we have identified biomarkers that are used to diagnose diseases, identify drug targets, select leading drug candidates, and discover the effects of drugs in humans."

The pioneering status of Kaddurah-Daouk and Kristal in the field of metabolomics is evident. Kaddurah-Daouk is president of the newly formed Metabolomics Society, Kristal serves as its secretary, and both are members of its board of directors. Both inventors are

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In September 2006, Metabolon launched its *mSelect™* service, the first in a pipeline of products to facilitate the discovery of new drugs. This service determines the metabolic profiles of cultured cells exposed to drug candidates and provides an unbiased and nontargeted assessment of a compound's intended effects and side effects. This enables the selection of the most promising, lowest risk drug candidates for continued development.

Metabolon has received grants from disease foundations and the U.S. government for metabolic profiling work in collaborative studies with other institutions, particularly Massachusetts General Hospital. The company has contributed to studies of ALS (ALS Association and National Institutes of Health), Huntington's Disease (High Q Foundation), diabetic nephropathy in type 1 diabetes (NIH), premenstrual dysphoric disorder (NIH), and preterm labor (NIH). For the latter study, Metabolon and their NIH collaborators received the 2005 March of Dimes award for Best Research in Prematurity. They were able to predict the outcome of patients exhibiting preterm labor from the metabolic profiles of their amniotic fluid.

"Our investments in a database of over 1,000 identified compounds, quality control, and

still involved peripherally in Metabolon: Kaddurah-Daouk is a member of Metabolon's scientific advisory board and Kristal is a consultant.

"We are happy to see Metabolon's success," says Brian Kelly, director of Weill Cornell Medical College's Office of Technology Development, the office that licensed Cornell's rights to the company. "This was a platform technology that needed to be licensed to a start-up company that could maximize its commercialization in many directions. Luckily, this technology had entrepreneurial champions that saw the technology's potential and made it come to fruition."

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