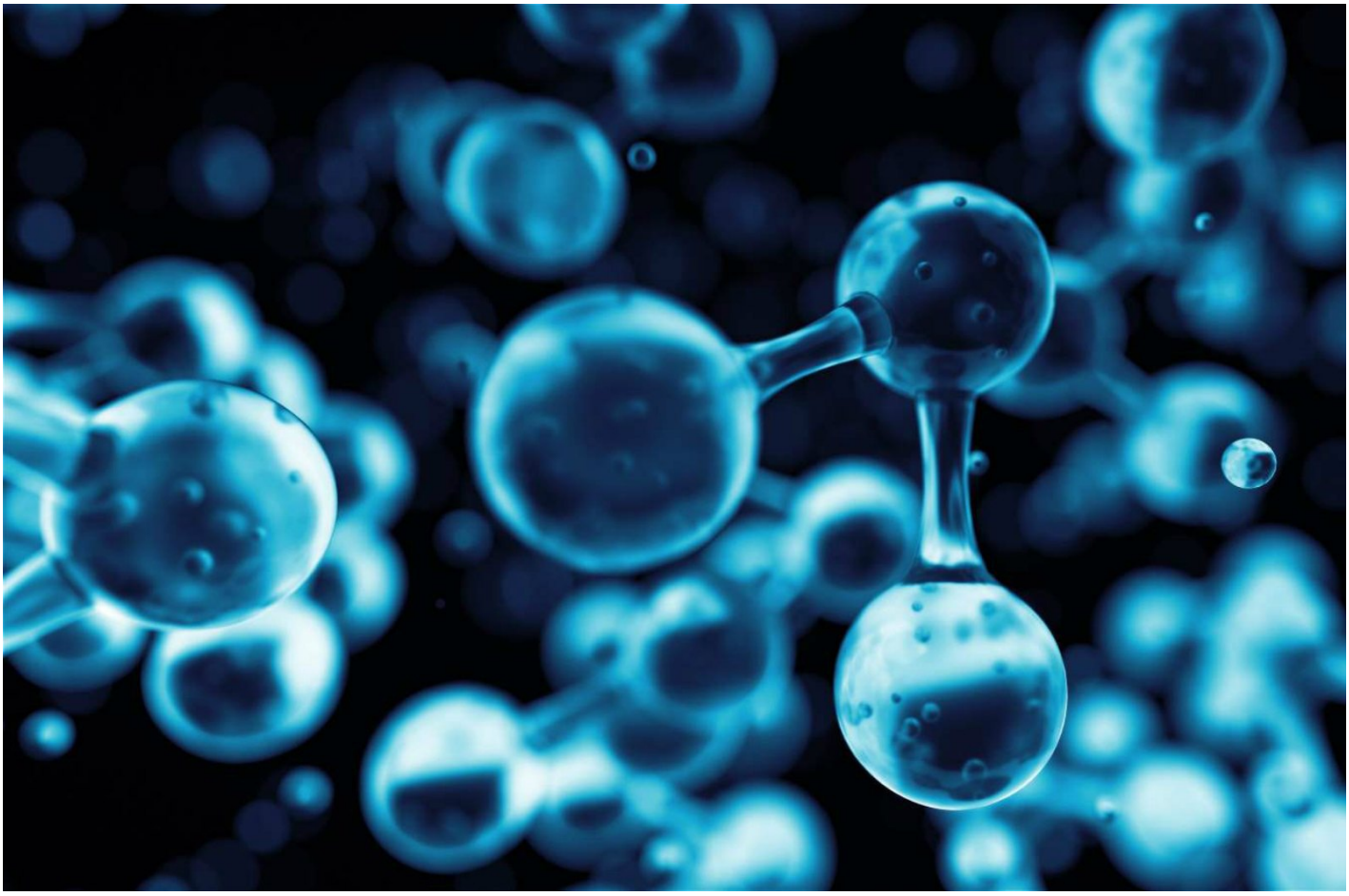
KineMed Offers Kinetic View Of The Body

University of California, Berkeley (UC Berkeley)



KineMed is a drug development company built upon a new way of seeing the inner workings of the human body and thus predicting clinical outcomes.

KineMed intends to change the way the world sees health and disease. The biotechnology company, based in Emeryville, Calif., has developed a technology that allows researchers to monitor and measure the myriad dynamics taking place at the cellular and molecular levels in the human body. The unique vantage point offered by KineMed's technology enables researchers to understand the full landscape of dynamic pathways of disease and thus predict the onset and monitor the course of an illness. These tools also enable researchers to discover new uses for drugs and expedite the drug development process.

David Fineman, co-founder of KineMed, explains: "To understand biological systems, you have to understand the dynamics of those systems. You have to understand the functional relationships that drive important clinical outcomes. KineMed enables seeing the multiplicity of drug effects in the biochemical and physiological pathways in the body."

Measuring exactly what drugs do in living systems leads to a more comprehensive understanding of a drug as it acts within the complexity of a human being. Most importantly, the KineMed technology accomplishes this with no effect on the system itself.

“It’s like having a ghost observer in the body – something that can observe every- thing that’s taking place but have no impact on the process,” says Fineman.

Using non-radioactive, or stable, isotopic labeling, a scientist can measure the rates of flux, or change, as the label is incorporated into molecules in the body.

“The label is a biochemical tag,” says Marc Hellerstein, M.D., Ph.D., the inventor of the technology. “It is an atom that is part of one molecule, and is transferred to another molecule when some biochemical event occurs.”

The tag provides researchers with a record of that event.

One way that KineMed achieves this is by administering to a patient a small dose of deuterium in a glass of water. Deuterium, a “heavy” form of hydrogen, is naturally occurring in nature and harmless at low levels. Deuterium has an extra neutron in the nucleus that does not change its chemical behavior in the body, but allows its fate to be monitored. The additional weight of the neutron makes it distinguishable by mass spectrometry, providing scientists with a way to “light up” pathways so they can see exactly what effects their drug is having on target cells, where the drug acted, and what the consequences are within the whole body system.

“For drug discovery, this is a ‘systems biology’ approach, which provides authentic biomarkers of the actual processes involved in disease or health,” says Fineman.

Hellerstein, who is a professor of nutrition at the University of California, Berkeley, professor of medicine at University of California, San Francisco, and a physician specializing in diabetes treatment at San Francisco General Hospital, had long been interested in metabolism. He also has a lifelong interest in translational medicine, which, loosely defined, is the process of bringing new tests and therapies out of the laboratory and into the clinic.

Hellerstein was struck by the differences he encountered between standard medical care and biological laboratory research.

“I couldn’t understand why we were not measuring the same cellular and molecular processes in a human being that we could do routinely with cells in the lab,” he says.

Hellerstein’s uncle, a cardiologist in Cleveland, had told his nephew the story of a researcher who had catheterized his own heart and injected himself with dye — and discovered that he could visualize the entire circulatory system of the heart. Today that’s known as angiography. For years, the discovery was only used as a laboratory research tool, until its value for diagnosing coronary heart disease was recognized.

“A mindset exists that prevents us from translating research tools to the clinic,” Hellerstein says. “But I was convinced that the type of tools I had been working on to answer questions in human metabolism could be used in medical diagnostics and drug discovery.”

Hellerstein patented his first invention through University of California, Berkeley. The first patent was on a method for non-invasively measuring the synthesis of polymers, such as proteins, cholesterol and glycogen, in the body. Prior to the invention, these measurements had some fundamental limitations.

“We could give a label to a person, but how could we figure out how much of the label really made it into the cells?” he explains. “You never knew how much label got into the biosynthetic machinery that generated a polymer, because it was non-accessible.”

He solved the problem by developing a combined mathematical and mass spectrometric approach to calculate definitively how much of the label was being delivered into the cells.

While his research was largely funded by National Institutes of Health (NIH) grants at the time of his discovery, the research into kinetic measurements was “sort of between the cracks,” while he was involved in AIDS research.

Today, there are more than 100 patents in the portfolio, the core technology having been licensed to KineMed. Hellerstein and Fineman, who are longtime friends, co-founded the company. The technology works by measuring the flow of molecules through pathways, like a motion picture capturing the dynamics of a good billiards break.

“It’s like being able to see the entire table, and watch all the balls go in different directions, seeing where they hit each other and what path they travel across the table, all at the same time,” says Fineman.

“The molecules in the body don’t just sit there,” says Hellerstein, “yet most diagnostic tests today are static measurements. You can see an X-ray or CT-scan of a structure, or measure the level of messenger RNA in a cell, but these types of measurements do not show movement, and in truth, everything is dynamic. So it was clear that there was a huge gap in the tool kit.”

Applying new strategies for tagging key processes in the body with non-radioactive tracers, combined with new mass spectrometric and mathematical analyses of these dynamic processes, enabled Hellerstein to see the kinetics of various biological pathways and processes. He characterizes most diseases as disorders of kinetics and the control of kinetics.

“Cancer is related to the production rate of cancer cells,” he says. “Liver cirrhosis is about the production and breakdown rates of collagen; AIDS is about the production and death rates of T-cells. Biochemistry is regulated through rate control,” that is, kinetics.

> *KineMed is now investigating the dynamic basis of various diseases by isolating specific molecules and looking at them through a kinetic lens.*

The company has hired dozens of researchers with various specialties to develop its own drugs and has relationships with more than 20 drug companies that are using KineMed’s platform in combination with other methods of drug discovery and testing.

“Kinetic medicine adds a new dimension in biology by including the measurement of time, the element that’s been missing in the area of drug development and molecular biology,” says Hellerstein.

KineMed is already making a difference in research, having developed assays for several major disease states, including cholesterol metabolism, insulin resistance, neuronal dysfunction, fibrosis and inflammation. That’s powerful technology that can lead to more powerful medicine.

This story was originally published in 2007.

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