AGILENT CASE STUDY: EMPOWERING RESEARCHERS

ROOM FOR DISCOVERY
AGILENT AIDS RESEARCH INTO THE ROLE OF LIPIDS

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The surprising thing about lipids is how little we know about them. Even cholesterol metabolism, which researchers have studied extensively, is not fully understood.

As a result of large-scale studies, high levels of cholesterol are considered a risk factor for cardiovascular disease in the population as a whole. Look closer, however, and the picture begins to blur.

"At the family and individual level, we can't necessarily make this correlation," says Markus Wenk, who is spearheading novel approaches to lipidomics at the National University of Singapore. "You might have some other characteristics in your metabolism that we don't know about, which might explain and go hand in hand with the high cholesterol."

Dr. Wenk and his team are part of an international research consortium using Agilent technologies—primarily liquid chromatography and high-resolution mass spectrometry—to advance the world's understanding of lipids.

Cholesterol is merely the most famous lipid. There are tens of thousands of others, and no one is quite sure why there are so many. (Lipids include fats, waxes, sterols, fat-soluble vitamins, mono- , di-, and triglycerides ...)

"We have only a few examples in nature where there is specific interaction of a lipid molecule and a receptor," Wenk says. "There are some, but it certainly wouldn't explain why there are so many different lipids."

While there has been an explosion of new information about genes and proteins over the past decade, Wenk notes that there has not, so far, been a corresponding advance in knowledge about lipids.

The first step: build a database showing the fat levels of healthy people in various ethnic groups—and Singapore just happens to have a diverse population with Chinese, Indian, and Malay ethnicities all well represented. This kind of data, which is also being gathered in other countries, will establish a baseline.

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"Understanding natural variations among healthy individuals will provide a foundation for understanding the onset of cancer, diabetes, and neurodegenerative diseases," Wenk says. "The next step is to connect our studies of lipids with studies that address variability at the level of genes, proteins, and sugars."

He believes that the approach described above—call it integrated biology—may be the best way to discover new biomarkers and develop more effective therapeutics.

"For us it would mean: How do we make sense out of this biochemical data in connection with genetic variation and these variability studies we're doing? How do we associate changes in lipid levels to other body parameters? Cholesterol is just one example. We can measure the number of red blood cells, the number of platelets, inflammatory markers ... That's the kind of granularity the field will be moving to," he says.

That level of detail is being made possible by innovations in bio-analytics instruments from companies like Agilent.

"We have been working closely with Agilent in setting up very sensitive and reproducible methods for measuring small amounts of these low-abundance metabolites," Wenk says. "Agilent has also helped us ensure cross-site reproducibility and integration of platforms, so we can easily exchange protocols and incorporate data from consortium colleagues in Korea and Australia."

Not only do Agilent instruments provide the resolution and accuracy his team needs, but the company has a proven capacity to optimize its tools for specific workflows.

"It really helps to have a strong technology partner behind you," Wenk says.

"We've found some chemistries that have not been described before, so there is room here for discovery. There is room for finding, not necessarily a new cholesterol but a 'brother' or a 'sister' to cholesterol. This is still out there. It leaves you with a feeling of excitement that there are still areas that can be discovered. Maybe the whole picture, the way we read about it in text books, is not fully accurate and may need to be adjusted. That's part of research and new knowledge, and that's still very much going on through technologies that are available now."

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