AGILENT CASE STUDY: EMPOWERING RESEARCHERS

SOLVING MICROMYSTERIES
AGILENT HELPS RESEARCHERS MAKE BIG DISCOVERIES IN TINY ORGANISMS

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Muriel Bardor finds microalgae fascinating, particularly the way these tiny organisms process sugars.

"It seems that microalgae are providing some bio-specific pathways for synthesizing their sugars, also called glycans, that are a mix of what happens in higher plants and what happens in humans," she says.

This interests Dr. Bardor in terms of both evolution and the production of biopharmaceuticals.

A leading researcher with the Glyco-MEV laboratory at the University of Rouen, Bardor has been studying glycosylation pathways within plants and microalgae in the context of producing plant-made biopharmaceuticals.

Bardor describes her team's latest findings as strange and difficult to comprehend at the moment—also well worth investigating. After all, sugars, or glycans, are known to prolong the half-life of biologic drugs, which means they can be taken less often and in smaller doses. They are also known to be essential for the biopharmaceutical's biological activity.

The work requires super sensitive equipment to characterize the structure of minute amount of sugars.

"This is where Agilent is helping us," Bardor says. "We are using a lot of Agilent LC/MS systems [including the 1290 Infinity UHPLC-Chip/MS] to do really in-depth characterizations of the oligosaccharides we are interested in."

The Agilent equipment is hosted by the PISSARO proteomic platform from the University of Rouen, which is also involved in the work.

Over the past year, Bardor and her team have been collaborating with Agilent via regular teleconferences.

"Agilent people have provided quite a lot of tricks so we can tweak the parameters of our experiments and really optimize our workflow," Bardor says. "They have also come out with some new, customized chips, as they are always striving to achieve better results."

When her investigation on microalgae began five years ago, Bardor recalls, little was known about the biology of microalgae. "We didn't even know what kinds of glycans microalgae were able to synthesize," she says. "We had to start from scratch, so it was challenging. Now we have proved that they are able to synthesize some glycans and transfer them to their proteins."

That understanding is vital because of the various roles sugar plays, both in how cells interact with each other and how they interact with viruses and bacteria.

The team started out using plants such as tobacco as models, demonstrating how they can act as factories to produce recombinant glycoproteins. These include monoclonal antibodies, used in many of today's blockbuster drugs, as well as erythropoietin, typically used to treat anemia. Such biologics, used in combination with vaccines, can prevent or treat a variety of serious medical conditions such as cancers, immune disorders, and infectious diseases.

"It's challenging for a plant to produce such complex proteins," Bardor notes. "Once it does, it also needs to add on top of the protein some specific sort of sugar, because sugar plays a crucial functional role. So you not only need to make sure the protein itself is produced correctly, but you also have to carefully characterize the sugar it adds. Most of the time the challenge comes from the fact that this sugar is completely different from the ones found in humans, which can induce an unwanted immune response."

Which, again, is why super sensitive equipment is needed for in-depth characterization.

Now the team has moved to microalgae as its main model, largely because microalgae can be easily and cheaply grown in a bioreactor.

"Now we have reached the point where we want to prove that microalgae can be used to produce glycosylated biopharmaceuticals," Bardor says. "We want to create a proof of concept, showing that the protein of interest we produce is correctly glycosylated and functional. At the moment I would say we are in the optimization phase, and we are getting good support from Agilent."

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