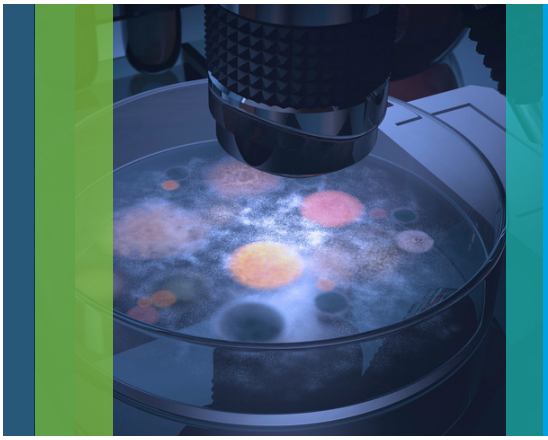

Agilent case study: Professor Jens Frisvad, PhD

The Good, the Bad, and the Mysterious

Professor Jens Frisvad and his colleagues at the Technical University of Denmark spend their days looking for small wonders.

By analyzing the biology of algae, bacteria, and especially fungi, they believe they can unlock the secrets of the metabolites, enzymes, and bioactive proteins that these micro-organisms produce.

Some of which may be toxic, which is bad — but can also be good.

"We're very interested in trying to avoid problems caused by these toxin producers," Frisvad says. "We are also interested in finding new and fantastic antibiotics or other drugs from all these organisms."

To that end, Frisvad, along with fellow scientists Thomas Larsen and Christopher Phippen, are using an array of Agilent instruments and software solutions.

One of the specific problems they have been addressing lately is a fish-killing algal toxin that has plagued fish farmers and mystified scientists.

"We are seeing increased fish farming in Denmark and all over the world, so blooms of micro-algae around the waters of many countries are more and more important to understand," says Larsen, who is a professor of microbial chemistry. "We have now described a new kind of compound and are basically explaining why people have not been able to understand the nature of the bloom for the past 20 years."

Larsen notes that the team has been able to characterize the complex isotopic patterns of toxins that have a mass of only about 2,000 daltons, using mass spectrometers and software from Agilent.

"Through chemical analysis or genotyping, we can have an early warning system," he says. "So if you have lots of fish in a cave by the sea, when the blooming is just about to start, you can catch the fish and avoid having them die."

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Another key aspect of the team's research is food safety. They are using their growing knowledge of taxonomy, for example, to predict and even prevent the production of mycotoxins in the food supply.

"This has been an important part of our work for many years, and after we got new instrumentation from Agilent, we really found out a lot of interesting things," Frisvad says. "We didn't know before that fungi produce very interesting mycotoxins, so we are now looking at emerging mycotoxins—those that may be next in line for having to be monitored—so we can be sure that our foods and feeds are healthy."

Frisvad notes that about 25 percent of the world's food supply is discarded or burned because of contamination or spoilage.

"In the future, when we will need to feed so many more people, it would be fantastic if we could rescue some of these foods and feeds," he says.

Perhaps the most exciting aspect of the team's research, however, involves early stage drug discovery and the vast potential of genetic engineering.

Recently, everyone on the team has been involved in sequencing the genomes of *Aspergillus and Penicillium* species, and they have uncovered a number of hidden or silent gene clusters—as many as 62 in one particular Penicillium.

"That represents tremendous potential for the future because, in all those gene clusters, we might find a new drug that could fight cancer or Alzheimer's or other diseases," Frisvad says. "Then we have some tricks to help those fungi produce compounds that they will not produce normally."

Christopher Phippen, who is in charge of the team's metabolomics platform, is especially excited about the possibilities.

"With all the recent advances in genetic engineering, we can make these organisms produce a lot more of these compounds, or find ones we didn't know that they were producing, or possibly engineer them to make different but related compounds. With a combination of bioinformatics and genetic engineering and chemical analysis, we'll be able to produce beautiful chemical compounds more predictably and more quickly."

So, how do you know if you have a compound that might help people who suffer from, say, a central nervous system disorder?

Zebra fish larvae.

"You can induce strokes and then introduce one of our fungal compounds to see whether it can reduce convulsions in such larvae," Thomas Larsen explains. "The way it moves around—the pattern of that—can indicate whether you hit a certain receptor in the brain. It gives a good indication of whether a given fungal compound might become a CNS [central nervous system] drug."

This test, performed in collaboration with researchers at the University of Leuven, in Belgium, has already yielded one jointly patented compound, which, after further testing, could lead to a spin-off company—not their first.

Small wonder the team is excited.

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