World Pancreatic Cancer Day provides another occasion for Lab members to educate the public about one of the most lethal cancers.

Not just animal models. While still in Cambridge, then continuing in his new lab at CSHL, Tuveson and collaborator Hans Clevers, president of the Royal Netherlands Academy of Arts and Sciences, developed a method to grow pancreatic tissue in the form of hollow spheres called organoids.

Pancratic cancer cells had always been hard to grow in culture, slowing research. Until the advent of organoids, scientists had to rely on cells grown in flat culture dishes and depended on samples from genetically engineered mice, which take a year to generate. Organoids, which grow in a 3D medium, develop in days.

In addition to enabling researchers to observe pancreatic cancer from its beginnings, pancreatic organoids have where they faithfully recapitulate the course of the illness. Extrapolating from the new knowledge gained in organoids to preclinical experiments “is really the foundation of our laboratory,” Tuveson says.

One of Tuveson’s insights while still at Cambridge centered on the role of antioxidants in pancreatic cancer. This work, taken up by postdoc Christine Chio in his CSHL lab, has led to another new therapeutic idea. Chio has led experiments showing how reducing antioxidant levels in cancer cells provides a powerful way to get the cancer, in her words, “to burn itself out.”

This work stems from Tuveson’s research on Nrf2, a master regulator of the delicate oxidant-antioxidant balance in cells. Chio is testing combination therapies to reduce antioxidants in cancer cells while leaving healthy cells unharmed. Her team is learning that some of these combinations work better than others and is trying to optimize the approach.

Another team, led by Tuveson lab postdoc Danielle Engle, is finding ways to detect pancreas tumors while they’re still small and treatable. “Current technology shows us tumors that are golf-ball sized,” says Tuveson. “I would love to have a way of seeing them when they’re the size of blueberries or grapes.” Tuveson hopes Engle and her team will devise “a dipstick test,” i.e., one that can be given routinely at trivial cost to people at their annual physical exam. Early signs of abnormality would call for a more expensive and detailed anatomical examination of the pancreas using functional MRI scans.

“Our lab has a remarkable amount of freedom to find answers,” Tuveson reflects. “Strong support from Bruce Stillman and the very generous contributions made by Lustgarten allow us to be fearless as we pursue things we think important. Waking up every morning, I can’t wait to get to the lab to see the results of the previous day’s experiments. The science we’re doing is so exciting. This is the best time I’ve ever had as a scientist!”

Peter Tarr

In November 2016 Dr. David Tuveson was named Director of the Laboratory’s National Cancer Institute (NCI)-designated Cancer Center. “What a privilege,” he later commented. “I feel as if I have been asked to come in and take the baton of the New York Philharmonic! For the last 25 years Bruce Stillman has ensured the Center’s greatness by appointing rising stars. Our opportunity is to continue to excel in discovery science while translating our insights into diagnostics and therapies to defeat cancer.”

Of Tuveson’s three predecessors, Stillman has shaped the Cancer Center as it exists today, having guided it through five NCI sponsorship renewals. During this time, basic research has revealed cancer’s genetic roots, making possible a first generation of targeted therapies.

Basic insights won’t only be leading to experiments in animal models “but also in patients who have cancer. It’s going to be meaningful and productive and I hope many of our scientists will get to participate in that, while they continue to pursue the fundamental research that they are world leaders in.”

Peter Tarr