

New Techniques, Collaborations Push Patient-Focused Precision Oncology Forward

\$5.4M NCI award supports Dr. Chris Kemp's multi-disciplinary discovery platform for cancer-therapy targets.

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When scientists sequenced and mapped nearly all the DNA in humans — our genome — a new era dawned. It seemed that we'd have an easy-to-follow roadmap to better health, including better cancer therapeutics.

But scientists learned that often, the link between tumor genetics and tumor behavior is difficult to trace. To make precision oncology, or tailored treatments, a reality for most cancer patients, scientists are developing new tools to help them better understand how a tumor's genetic alterations underpin its behavior and potential vulnerabilities.

Fred Hutchinson Cancer Center's [Christopher Kemp, PhD](#), recently received a five-year, \$5.4 million grant from the National Cancer Institute to use [leading-edge functional genomics approaches to uncover new cancer therapy targets](#) in tumor tissues donated by patients. The team has developed a method to grow patient-derived tumor cells in tumor-like 3D structures called organoids, which better capture tumor behavior and enable them to uncover promising new vulnerabilities.

"We have an unbiased approach to search for new treatment targets beyond what we already have," Kemp said. "It's ground truth, directly from a patient. What could be more relevant than that?"

His vision extends beyond adding to the number of promising cancer drug targets.

"This research will make the search for better therapies better," Kemp said.

He envisions the team's organoid platform enabling scientists across the functional genomics field to identify targets with the most potential for successful clinical translation.

NCI offers the grant as part of its [Cancer Target Discovery and Development \(CTD²\) Network](#) (also

pronounced C-T-D-Squared). CTD² was created to bridge the gap between genomics (the study of all the DNA in a cell) and cancer therapeutics. It's an outgrowth of the NCI and the National Human Genome Research Institute's [The Cancer Genome Atlas](#), which has helped scientists chart the landscape of cancer-associated genetic abnormalities. As with TCGA, the data generated by CTD² participants is made publicly available to the research community.

This is the third renewal of Kemp's functional genomics CTD² team science. The latest project will incorporate new technologies, new computational tools, new methods and new collaborators. The researchers will focus their studies on tumor organoids derived from tumor tissue donated by cancer patients.

"We have clinical data, which is very important. These patients are undergoing treatment at the same time that we're studying their tumors," Kemp said.

This will allow the researchers to gain a wider and more-detailed picture of each patient's tumor: its genetic alterations, molecular differences and changes in gene expression patterns. They will be able to see which genes are critical for a tumor's growth and survival. The team will be able to compare primary and metastatic tumors, as well as look at the molecular changes a patient's tumors undergo in response to treatment. Their preliminary studies demonstrate that the patient-derived organoids behave very similarly to their primary tumors, such as exhibiting resistance to the same drugs.

Central to this patient-focused approach is University of Washington cancer geneticist and ovarian cancer researcher [Elizabeth Swisher, MD](#), who will lead recruitment and treatment of patients participating in the study.

"We're focusing on ovarian and pancreas cancers, but our approaches are applicable across tumor types," Kemp said.

New Fred Hutch collaborators will enable the team to incorporate innovative technologies to discover new targets and validate their worth. Fred Hutch cancer chemical biologist [Behnam Nabet, PhD](#), has developed a method that uses targeted protein degradation to pinpoint key cancer-causing proteins. This will allow the team to more easily determine whether a promising gene or protein plays an important (and potentially therapeutically relevant) role in a tumor's growth, survival or response to treatment.

They will also incorporate innovative tools developed in the lab of Fred Hutch genomicist [Steven Henikoff, PhD](#), that will allow them to study molecular modifications to DNA that don't change its sequence. Known as epigenetic modifications, these alterations can influence which genes are turned on and off. The team will use the tools to map the epigenome of individual patients' tumors and link different epigenetic patterns to tumor behavior and vulnerabilities.

Additionally, the team will use new computational tools to integrate this complex mix of genetic, epigenetic and functional data generated by their organoid models and pinpoint the most

promising therapeutic targets.

This spirit of collaboration has made the work possible, Kemp said. In particular, scientists at Seattle's Institute for Systems Biology and SEngine Precision Medicine, a cancer drug screening and development company Kemp helped found, contributed to the project, he said.

Of primary importance is the fact that all the data they generate will be available to the scientific community.

Kemp said researchers participating in CTD² projects upload their findings into a public database. This allows other investigators with different expertise to further investigate and pursue drug development strategies for targets discovered and validated by others.

"We're generating a resource for future research," Kemp said. "I hope it gets used for years to come."

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