BAY AREA

From COVID to cancer, gene-mapping tool could 'revolutionize' treatment, UCSF studies say

Danielle Echeverria

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Nevan Krogan is director of Quantitative Biosciences Institute and professor of cellular molecular pharmacology at UCSF.
Stephen Lam/Special to The Chronicle 2020

New research by UCSF and UC San Diego scientists involving techniques also deployed to fight COVID-19 has the potential to revolutionize cancer treatment by creating opportunities for more precision treatments, they say — which can be far less harmful than chemotherapy.

The collaborative effort — called the Cancer Cell Map Initiative — found that mapping the protein disruptions caused by DNA mutations, rather than just the mutations themselves, is very useful for grouping different kinds of cancer-causing mutations together. That opens up the opportunity to create precision treatments that can target groups of mutations, rather than just one.

On Thursday, the group released three papers in the journal Science describing how the maps work for breast cancer and cancers of the head and neck.

The research itself does not present a treatment for cancer. Rather, it is a tool that scientists can use to find better treatments, the researchers explained.

And it's "disease-agnostic," Nevan Krogan, director of the Quantitative Biosciences Institute in the School of Pharmacy at UCSF and one of the senior authors on the project, explained. That means it can be used to better understand and treat almost any disease.

Krogan's lab already has used the techniques, which have been in development for cancer research for about 10 years, to understand and work on treatments for infections from SARS-CoV-2 — the virus that causes COVID-19.

"We are going to revolutionize drug discovery going forward," he added. "I know that sounds like a lofty goal, but I truly believe that."

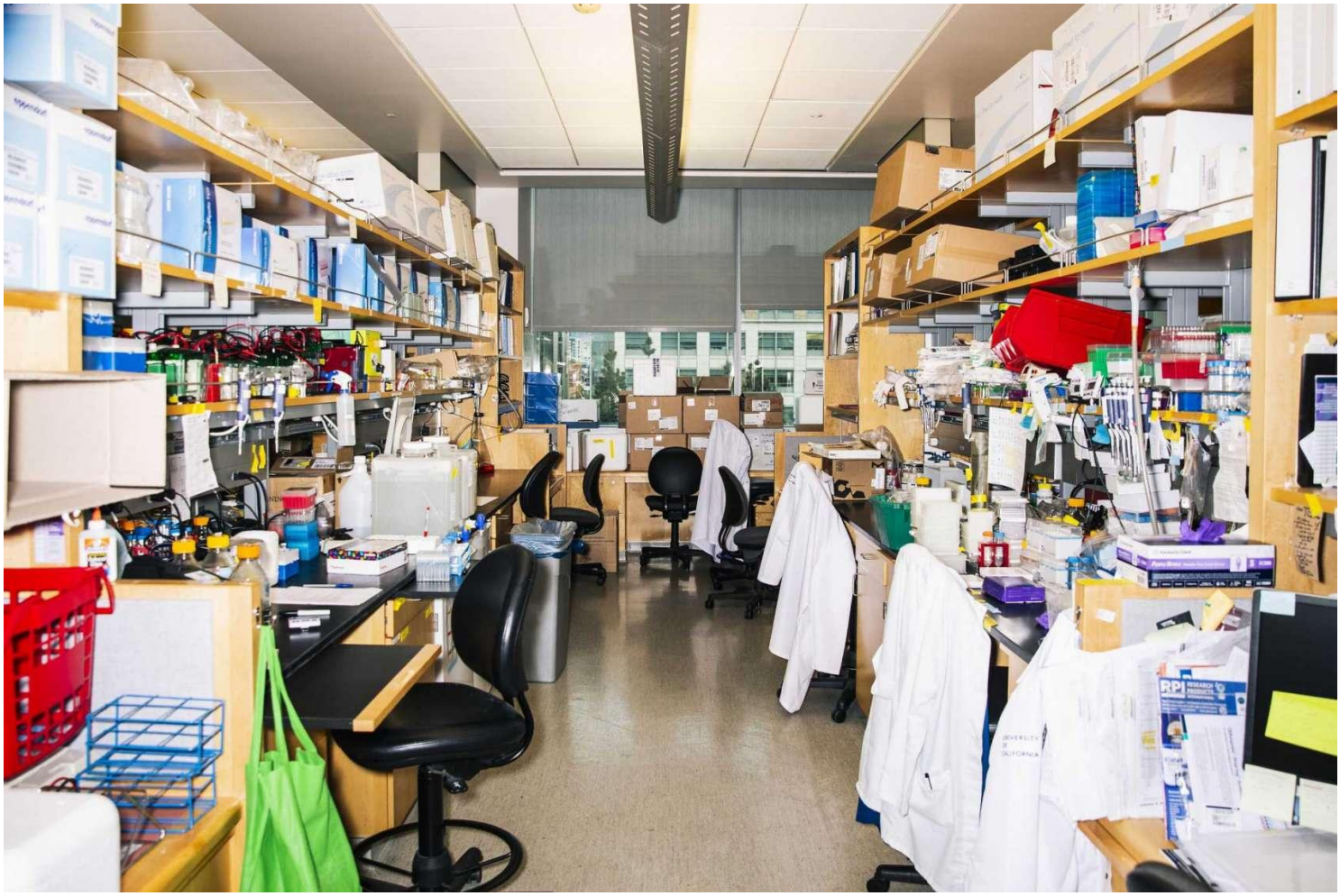
Previous cancer research looks only at the DNA mutations that cause cancer, which isn't always useful, since hundreds of sequences can lead to cancer, said Trey Ideker, a senior co-author of the papers and professor at the UC San Diego School of Medicine and Moores Cancer Center.

For example, scientists know that the BRCA gene causes breast cancer, he said, and there are precision treatments for that. But only about 4% of women who have breast cancer also have the BRCA gene. This research seeks to understand what the mutation in something like the BRCA gene actually does, so that similar mutations can be treated in "one fell swoop."

"It really is moving towards a more holistic view," Ideker said. "Rather than looking at one gene at a time, we look at the systems those genes create."

He described it as an IKEA manual — the human genome, or DNA sequences, are the first page, showing you the parts of a piece of furniture. CCMI seeks to be the next several pages, with the instructions for how the pieces actually fit together.

"We're seeing disease as a network, not just an individual gene," Krogan said.



The lab led by Nevan Krogan, director of Quantitative Biosciences Institute and professor of cellular molecular pharmacology at UCSF.
Stephen Lam/Special to The Chronicle 2020

Drought Map

The shift "opens up a new door for cancer research," said Dr. Howard Chang, a professor of cancer research and genetics at Stanford School of Medicine.

Chang's Stanford colleagues Ran Cheng and Peter Jackson agreed — writing that the protein interaction maps could be "a framework for future analyses that could drive our understanding of oncogenic transformation and identify therapeutic targets" in a perspective piece that ran alongside the studies in Science.

"It's a very powerful hypothesis-generating tool," Chang said. But that still leaves the question of how many of those hypotheses about treatments actually pan out, he said. He'd also like to see how the tool works outside a lab setting — which could take some time, depending on advances in the type of technology used to build these protein sequences.

Both Ideker and Krogan also noted that this is only a first step, and that there's much more work to be done to get this tool into a clinical setting.

Still, Chang said the papers are an important "building block" in cancer research, and the team working on it should "be applauded for their effort to really systematically go at this question" about how mutations affect protein interactions.

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