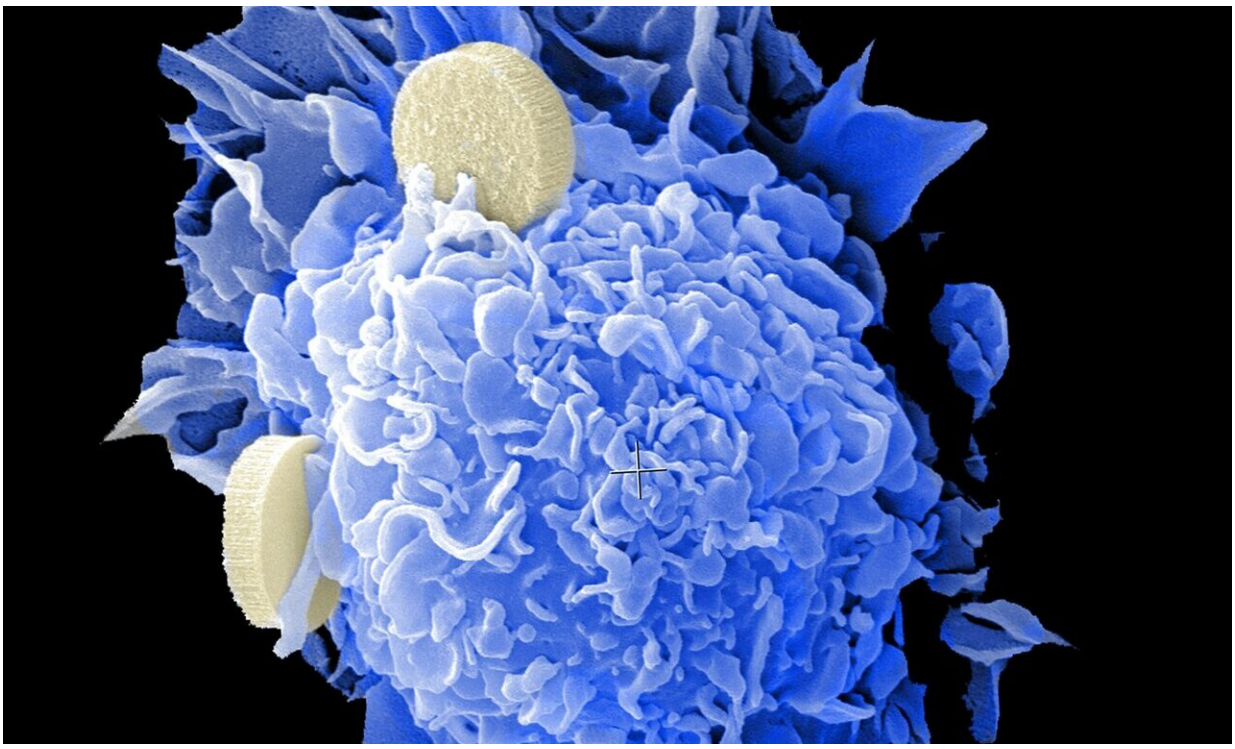
Capturing origins and early adaptive processes underlying therapy response to cancer treatments

September 17 2021, by Bob Yirka



Credit: Unsplash/CC0 Public Domain

A team of researchers with biotechnology corporation Genentech Inc., has developed a new way to capture the origins and early adaptive processes that are involved in therapy responses to cancer treatments. In

their paper published in the journal *Nature Biotechnology*, the group describes how their new system can be used to help treat resistant types of cancer.

As the researchers note, the current approach to treating patients with cancer is to give them therapies that their doctor believes are best suited to the kind of cancer they have and then watching to see how well it works—and then modifying the approach if the outcome is less than hoped due to resistance. To improve the process, the team has developed a system that is able to take into account pre-existing features of cancer cells and the changes that might have come about because of them that could lead to treatment resistance. The new system, called TraCe-seq involves analyzing clonal responses to various treatments applied to mutated lung cancer cells—using a single-cell RNA sequencing method. As part of its development, the researchers used EGFR-targeting therapies, which included kinase inhibitors that have been shown to disrupt enzyme binding.

The researchers note that the system is reliant on combinations of different cellular barcoding along with sequential single-cell sequencing. The bar-coding, they further note, allows for using clonal fitness with untreated cells along with those that are exposed to a variety of different therapies. It was created as a way to provide the best type of therapy available in resistant cases, without having to go through a long trial and error process. By taking into account the genetic history of the cells as they have mutated, the system is able to accurately predict which sorts of therapy will work best at stopping its growth.

Testing of the system showed it capable of providing more pronounced treatment fitness in lung cancers treated with GNE-104 or EGFR inhibitors than cells treated with more traditional options. They suggest the new system is likely just the first of many that will be developed along similar lines—all with the goal of better predicting which therapies

will work best on different types of resistant cancers.

More information: Matthew T. Chang et al, Identifying transcriptional programs underlying cancer drug response with TraCe-seq, *Nature Biotechnology* (2021). DOI: 10.1038/s41587-021-01005-3