New 3-D imaging method for tumour samples to be used for studying COVID-19

June 30 2020, by Johanna Bylund

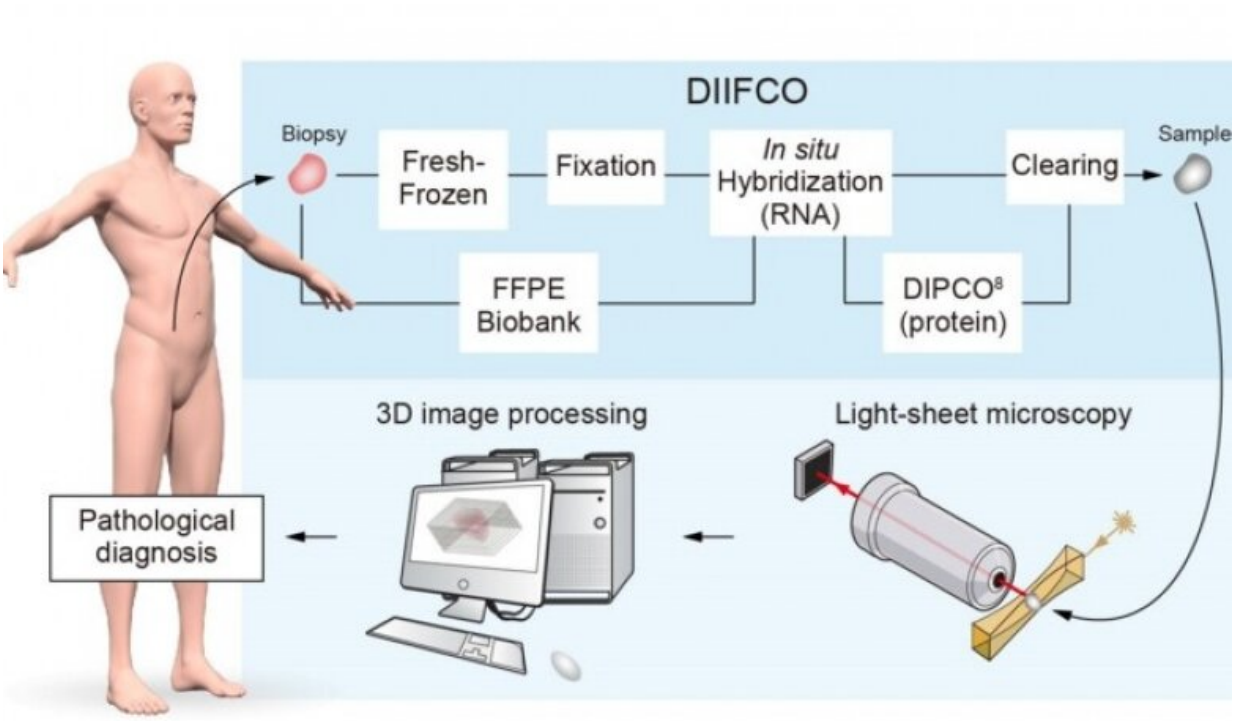

Figure 1. The method, called DIIFCO, facilitates the study of cancer-related mechanisms and enables more exact diagnoses of tissue samples from cancer patients. Credit: Mattias Karlén

Researchers at Karolinska Institutet in Sweden have developed a new method for analyzing intact tumor samples in 3-D on a molecular level.

The study is a collaboration with Karolinska University Hospital and is published in *Nature Biomedical Engineering*. Now the researchers are planning to use the method to study tissue samples from COVID-19 patients in the hope that it will provide information on where and how the new coronavirus attacks different organs.

Cancer is caused when vital molecular mechanisms in cells stop operating normally. To better understand these pathological processes, scientists need to study what occurs in tumor cells at an RNA and protein level. RNA acts as a messenger between the genes and the proteins that they code for, and there are different kinds of RNA involved in cancer.

The researchers have applied a new imaging technique, which is used in basic research, to study intact—rather than sectioned—human tumor tissue. The technique involves making the tissue transparent, staining different kinds of RNA and proteins, and then imaging the tissue in three dimensions using an instrument called a light-sheet microscope. Doing this, it is possible to determine where in the tumor there are abnormal amounts of RNA or protein. The method, called DIIFCO, facilitates the study of cancer-related mechanisms and enables more exact diagnoses of tissue samples from cancer patients (see figure 1).

More exact cancer diagnoses

"For years, clinicians have used the labeling of specific proteins to diagnose tissue samples from tumors," says principal investigator Per Uhlén, professor at the Department of Medical Biochemistry and Biophysics. "Being able to specifically stain RNA in intact tumor samples opens up entirely new opportunities for clinical specimen diagnosis."

Working with pathologists and surgeons at Karolinska University Hospital, the researchers studied digital 3-D images of tumors using

advanced image processing software. In this way, they managed to identify each individual cell of a tumor and to analyze how the cells cluster as well as how specific cell populations arrange themselves in relation to the tumor's blood vessel structure (see figure 2a). In another experiment, they studied the presence of so-called cancer stem cells in a highly aggressive form of breast cancer by specifically staining PROM1 RNA, a biomarker for cancer stem cells. Cancer tumors contain a very small number of cancer stem cells, which are thought to play a significant part in cancer formation. The DIIFCO method revealed small clusters of cancer stem cells deep inside the tumor samples from breast cancer patients (see figure 2b).

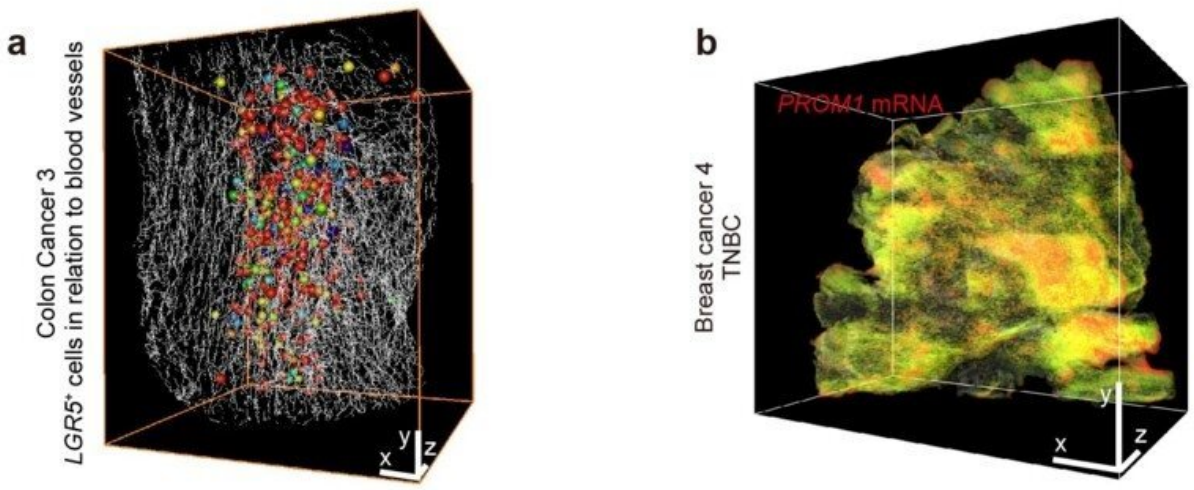

Figure 2a and 2b. Credit: Per Uhlén

COVID-19 samples next

Using the DIIFCO method, scientists can study RNA and proteins at a high resolution in all human tissue. The researchers are now planning to

use their method to study tissue samples from COVID-19 patients. PCR analyzes for detecting the RNA from the SARS-CoV-2 virus are frequently used in hospitals to test if patients have COVID-19, and the researchers now hope that the new imaging technique will be able to detect exactly where in the tissue the viral RNA is.

"Ours is one of the few labs in the world able to study intact tissue samples from humans," says Professor Uhlén. "This is particularly difficult when the tissue comes from elderly patients. I believe and hope that our method can provide important answers to where and how the new coronavirus attacks different organs."

More information: Nobuyuki Tanaka et al. Three-dimensional single-cell imaging for the analysis of RNA and protein expression in intact tumor biopsies, *Nature Biomedical Engineering* (2020). DOI: 10.1038/s41551-020-0576-z

Provided by Karolinska Institutet