Radioluminescence tells the story of single cells

June 9 2014

With a new molecular imaging system powerful enough to peer down to 20-micrometer resolution, researchers can now use radioluminescence to examine the characteristics of single, unconnected cells. The result is a fascinating picture of diversity among cells previously assumed to behave the same, revealed researchers at the Society of Nuclear Medicine and Molecular Imaging's 2014 Annual Meeting.

A resolution of 20 micrometers or microns—about a quarter of the diameter of a single human hair—is made possible with an imaging technique that unites the physics of nuclear medicine with optical imaging. Researchers inject a radioactive material that acts upon an ultrathin scintillator, which fluoresces when it detects charged particles. The fluorescent signal is then picked up by a specialized radio-luminescence microscope.

"Our research seeks to answer the question: In a population of cells, how important is individuality? Are the cells so similar that just knowing the average of a cell population is sufficient, or is there a need to look at individual cells, one by one?" These are the questions being answered by Guillem Pratx, PhD, assistant professor of radiation physics and radiation oncology at Stanford University, Stanford, Calif., and principal investigator of the study.

Imaging the physiological functions of the body is possible with radiotracers, imaging agents that combine a radioactive material and molecular compound that interacts with biochemical processes. For this

study, radiotracers interact with live cells viewed by radio-luminescence microscopy. The specialized microscope's CdWO4 scintillator captures beta particles as they are emitted by the radiotracer in the cell sample. By compiling these atomic events, the scintillator can reconstruct the data into an image that nuclear medicine physicians use to interpret disease pathology and response to drug treatment.

"Our goal is to characterize radiotracers from the perspective of how they interact with single cells," said Pratx. "The conventional methods used in nuclear medicine use large numbers of cells to produce measurements of cellular characteristics, because they do not have the spatial resolution to see single cells. Very little research, if any, has looked at what happens at the scale of a single cell."

The innovation of this particular microscope is not only its detector but its ability to capture optical brightfield and fluorescence images. The two models differ only by their lens—one includes a commercial grade 0.2X tube lens and the other a custom 1X tube lens. Researchers used these systems to image how single breast cancer cells used a radiotracer called F-18 fluorodeoxyglucose (F-18 FDG), a molecular compound that mimics glucose as fuel for cellular processes. The breast cells showed unexpected and intense variation. The team also imaged a human antigen called CD20, which can signal cancer of the blood, or lymphoma, on a transplanted sample of small animal spleen tissue, and assessed how the sample responded to a simultaneous radionuclide and antibody lymphoma therapy called Zr-89 Rituximab. The radioluminescence microscope was able to clearly visualize the expression of CD20 from malignant B cells in the spleen sample.

"This new tool will help nuclear medicine and molecular imaging advance toward more personalized radionuclide imaging," Pratx explained. "Since we are able to see how properties of single cells impact their interaction with radiotracers, there is an opportunity to develop new

radiotracers that are biologically optimized to target specific disease pathways."

Further studies are required to validate the research for radioluminescence microscopy in order to secure regulatory approval for commercial use.

More information: Scientific Paper 42: Guillem Pratx, Silvan Turkcan, Marian Axente, Lei Xing, Radiation Oncology, Stanford University, Palo Alto, CA; Arutselvan Natarajan, Laura Sasportas, Sanjiv Gambhir, Radiology, Stanford University, Stanford, CA, "A novel radioluminescence microscope for imaging radiotracers at the single-cell level," SNMMI's 61th Annual Meeting, June 7, 2014, St. Louis, Missouri.

Provided by Society of Nuclear Medicine