SPOT LIGHT

Entering an era of new biology

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How seeing cells in context is changing the course of science and medicine

Spatial biology is becoming an essential tool for advancing precision medicine, learning about cell behavior, predicting future states and so much more – a technological advancement that will inevitably change how science is done.

We recently had the privilege of sitting down with Hartland Jackson, PhD, to find out his thoughts on the excitement around spatial biology and why he uses Imaging Mass Cytometry™ (IMC™) in so many facets of his research.

Jackson, an investigator at the Lunenfeld-Tanenbaum Research Institute, Sinai Health, aims to better understand cancer at the single-cell level by investigating how the tumor microenvironment drives disease progression and therapeutic resistance. Before starting his own lab, Jackson worked with the team that pioneered high-plex single-cell analysis with IMC while completing his postdoc in the Bodenmiller Lab. He applied IMC to breast cancer, performing large retrospective studies of clinical samples to inform patient-specific diagnosis. He brought his expertise back to Canada, where his group is advancing methods for tissue imaging and its application to precision medicine and discovery biology. “We’re going after it all,” Jackson says. This statement is itself a clear indicator of what’s to come.

The Jackson Lab was recently awarded a grant from the Canadian Cancer Society as part of the largest collective multidisciplinary research team of clinicians, scientists and patient partners focused on high-performance research to improve outcomes for low-survival cancers. This will leverage IMC in a multipronged approach to accelerate the translation of preclinical findings to the next generation of patient-centered clinical trials.

Spatial biology opens the door ...

Spatial analysis offers significant value for investigations into how diseases are initiated and progress. Looking at disease in the context of localized tissue uncovers what architectural and cellular changes are associated with the disease in question, a genetic modification or other trigger. And right beside it, healthy tissue provides an internal control and clear frame of reference.

“Incorporating spatial biology and focusing on location is really important,” Jackson says. “This is a big next step with single-cell technologies, providing this high-parameter information. But it’s very hard to do this at the scale of what’s needed to look at human disease, which is really variable person to person.”

IMC breaks down the wall

The ability to thoroughly analyze large numbers of samples and parameters provides the statistical power to ask different questions and find those rare or more complex events. Since IMC uses antibody-based proteomics, it can measure things that you would not get with sequencing technologies, such as fibrosis and extracellular matrix targets or signaling pathway regulation through post-translational modification and subcellular localization.

"Now, everyone wants to measure everything, but you have to have a strategy to focus on, examine relevant questions and take advantage of the benefits of the technology, such as expanding the types of patient samples we can use, and the skills you have. How can these combine to answer something new?"

Getting the most out of limited clinical samples

Patient samples are precious, whether new or dated, fresh or frozen. Typical experiments require samples to be processed and broken down into a form that can be used with a chosen technology. But cells and even whole samples can be lost along the way. Not to mention that samples must be large enough to process. This alone restricts sample sets to those that can be used within the limits of an approach.

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IMC enables the use of smaller samples as well as sample types that are usually not available for research, since many other technologies require fresh samples for analysis. This is a major advantage to accelerate a variety of studies. "When it takes 20 years to accrue enough samples to run a unique set of patients and ask a question, it's no wonder studies take so long. Because we can go into the biobank and pick any set of samples, maybe one from 1996, one from 2003 and one from this year, we can build new cohorts for a very unique question," Jackson explains.

The ability to use sample types directly from patients and biobanks is important, as the accompanying patient history helps inform which samples can provide the most information for the specific question being asked.

"Another big benefit from using IMC is that we get 100% of the cells that we're given, meaning we actually measure every cell from these valuable samples," Jackson says. This translates to getting more information from less material. "Since only one layer of a sample gets used in IMC, it's much easier to go to the clinical team and say, look what I can do with this little bit of material. That's a key benefit, especially when biopsies are super small."

Smaller sample size provides another benefit to investigating processes like tumor growth as they occur. This enables a look at new types of biology such as initiation stages and progression. For cancer, most studies require a larger tumor size to perform any kind of analysis – so large, in fact, that biologically, a lab-grown tumor can be disproportionate to its natural growth. "With the ability to use smaller samples, we're able to study these more disease-relevant stages because we can analyze the tumor at all growth phases. We can compare small tumors and micro-lesions and look at how those differ from the large tumors that most projects study."

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Context is critical

"So, we get to use a wider variety of samples, we get more from these samples by using multiple markers at once and we get the spatial information. This is a key step to find out what's happening with a biological system." Right now, immunotherapy efficacy or resistance is determined based on the presence of cells. Jackson notes that adding their context – are they interacting with something that enables those cells to fight the tumor or that stops them? Where are they localized in the tumor, or is the tumor excluding them? – provides a more systems biology or wholistic view of what's going on.

For science, space is a new dimension, and you can use that new dimension in different ways. IMC is a way to expand the number of measurements, sample types or functional tests that you can do. With it, we can define different dimensions, even time, in the spatial organization of molecular and cell biology.

References

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