SPOT LIGHT

Paving a new road for spatial biology in precision medicine

JANA FISCHER, PhD

STANDARD BIOTOOLS™

How to find the right treatment for every patient

Ensuring the optimal outcome for every cancer patient – that's the promise of personalized medicine and the goal of the new company Jana Fischer, PhD, helped build. Navignostics AG, founded in 2022, aims to standardize the use of spatial biology data in better informing the most effective treatment decisions for patients, work that could be pivotal in the fight against cancer.

Fischer and her team are breaking ground by taking spatial biology to the clinic. In the last decade, research has seen an explosion of single-cell tissue imaging applications focused on detailing the interactions and behavior of immune and cancer cells in the tumor microenvironment. Understanding the spatial context of cells can provide critical insights into disease progression and response to therapeutics. The team at Navignostics has developed a rapid workflow that generates actionable clinical data from high-dimensional images, filling a gap that current methods have not been able to bridge. "Using this type of spatial single-cell proteomics-based approach to support clinical decisions is a road that we're paving to firmly establish relevant associations and better translate to treatment outcome," Fischer explains. Typically, pathologists use genomic analysis and immunohistochemistry, performing single stains on tissue sections and analyzing single proteins. This offers a restricted view of what's happening in a tumor and can be limiting if there is minimal tumor material available. High-plex spatial analysis offers a unique opportunity to expand the number of protein markers, and thus data, from a single slide – getting the most out of limited tissue samples.

The basis of their work is Imaging Mass Cytometry™ (IMC™), an imaging technology that can simultaneously quantitate 40-plus protein markers without the inherent challenges of fluorescence.

In prior studies using IMC, the team demonstrated the utility of high-dimensional proteomic imaging for stratifying patient populations and detecting the molecular properties of different tumors. They used this data to explain why there are patient groups with apparently similar tumors that react differently to treatment or have varying clinical outcomes.

Foundational knowledge gained from these experiments provided the bridge they needed to develop a novel method that can predict individual patient response to treatment.

Transferring spatial research to actionable data

In a significant advancement for clinical research, the team created a streamlined imaging strategy combined with fully automated data analysis, demonstrating the ability to go from samples to data reporting in under 72 hours, with efforts to further reduce this time. This is faster than genomic analysis of tumors, so information for decision-making strategies can be interpreted sooner by clinicians.

"With our extensive experience using IMC technology, we've been able to optimize and standardize our experimental workflows and computational analysis, which has enabled us to now bring our approach into a clinical space to help inform treatment decisions for cancer patients – and it's incredibly exciting to be able to do that. This is a big step in precision oncology," Fischer says.

The imaging pipeline currently includes two 40-marker panels, one to characterize immune cells and their interaction with the tumor and one focusing on tumor cell features, for broad characterization of targetable properties informing tumor-targeted and immunotherapy treatment decision-making. Given such high-parameter results, reporting must be simplified so it can be interpreted quickly and easily. Information about protein overexpression or absence of expression relative to a background dataset integrates with a score of how strong the correlation would be between the proteins and a given treatment outcome. This helps indicate the likelihood of success of different therapy options and can even suggest options that wouldn't otherwise be considered.

Speeding acquisition and eliminating complexity

Enhancements made to the next-generation Hyperion XTi™ Imaging System, including faster run times and long-term system stability, are critical to the team's success.

Minimizing the complexity of such an intricate process by using IMC on Hyperion™ XTi helps reduce any margin of error, possible biases or unwanted effects that can pose a challenge with fluorescent technologies to get the same plexity.

"With IMC data, we see none of the fluorescence-specific artifacts like autofluorescence; spectral overlap; cyclic fluorescence issues ... and this significantly reduces the complexity of what we are doing."

For example, FFPE tissue sections are routine in clinics and can be imaged with IMC, so no extra effort is needed from pathologists to work with alternative sample types. IMC also enables a single staining and measurement step, which reduces potential artifacts prevalent in repetitive cyclic staining or other fluorescence-based methods.

"With IMC data, we see none of the fluorescence-specific artifacts like autofluorescence; spectral overlap; cyclic fluorescence issues such as degrading of the tissue and signal loss over staining rounds; or stitching effects from microscopes – and this significantly reduces the complexity of what we are doing."

"Our extensive experience using IMC technology ... enabled us to now bring our approach into a clinical space to help inform treatment decisions for cancer patients – and it's incredibly exciting to be able to do that. This is a big step in precision oncology.

Real outcomes that make a difference

Fischer notes that Navignostics has recently been involved in several collaboration studies that evaluate alternative therapy options using spatial data for those patients who have been unsuccessful with standard-of-care treatments.

"In beyond standard-of-care settings, we often find proteins overexpressed that are not considered as part of the standard treatment guidelines but against which there are targeted therapies available, reopening an opportunity for treatment for patients who would otherwise receive palliative care," Fischer says.

Spatial information offers a significant step up, especially in context of immunotherapy decisions where more comprehensive questions can be asked: Where are the immune cells? Which phenotypes have which immune cells? Are they in contact with tumor cells? Which immune checkpoint proteins are expressed?

"Our goal is to inform personalized treatment decisions for cancer patients, and with the wealth of information contained in spatial single-cell proteomic data, we are getting to a place where we can do that."

Get more information:

nature.com/articles/s41586-019-1876-x

cell.com/cell-reports-medicine/fulltext/S2666-3791(23)00083-6

open.spotify.com/episode/7w0p0Y6rOpctPulwcdtFn2?si=xkymt8AHQv6fKxrxtlNElQ&nd=1

pubmed.ncbi.nlm.nih.gov/33482122/

Explore more applications using Imaging Mass Cytometry: **standardbio.com**

Unleashing tools to accelerate breakthroughs in human health™