

## Spatially Intelligent Platform

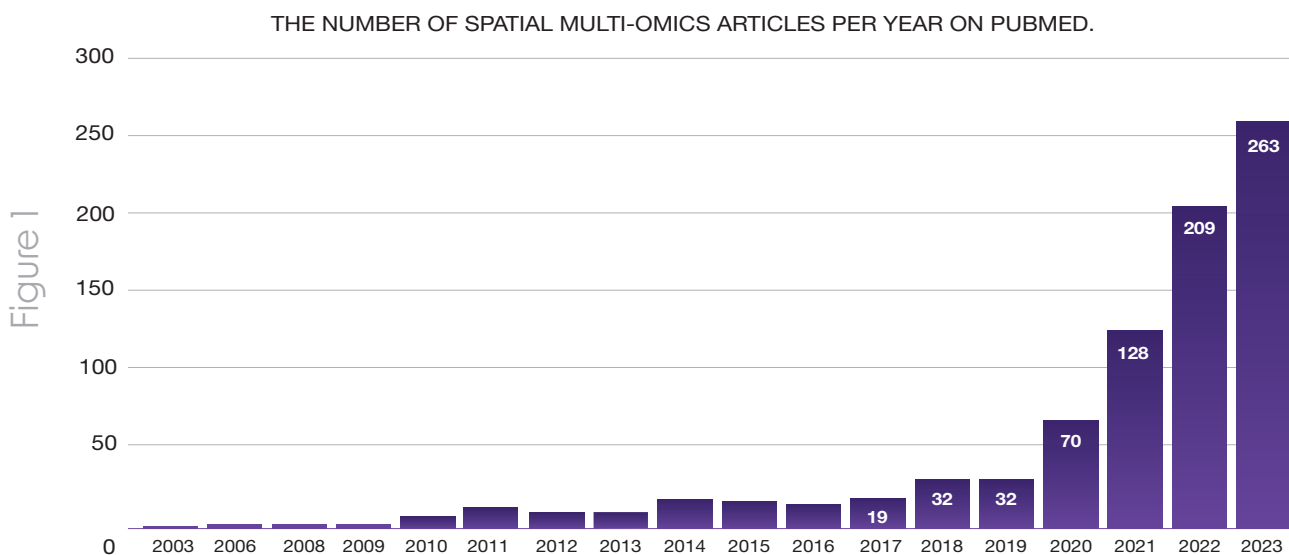
# WHITEPAPER

### The Why

Despite all of the recent advances in cancer treatment, immunotherapy has a response rate of only around 20%. This leaves patients, even with known biomarkers, with unpredictable treatment options. While pharmaceutical companies are working hard to bring an increased number of cancer treatments to market they face many challenges. One of those challenges is understanding the what and the why behind the mechanisms of cancer. PredxBio is focusing on utilizing multimodal spatial interrogation to unravel the

hidden circuitry of cancer and bring order out of chaos.

Spatial biology is a growing technology, recognized by the exponential growth in papers published regarding spatial multi-omics (**Figure 1**). It is understood that spatial orientation of cells matters more in terms of understanding intratumor heterogeneity. However, genomics have failed as a technology because genomics and transcriptomics only reveal ~5% of the hidden circuitry of cancer.

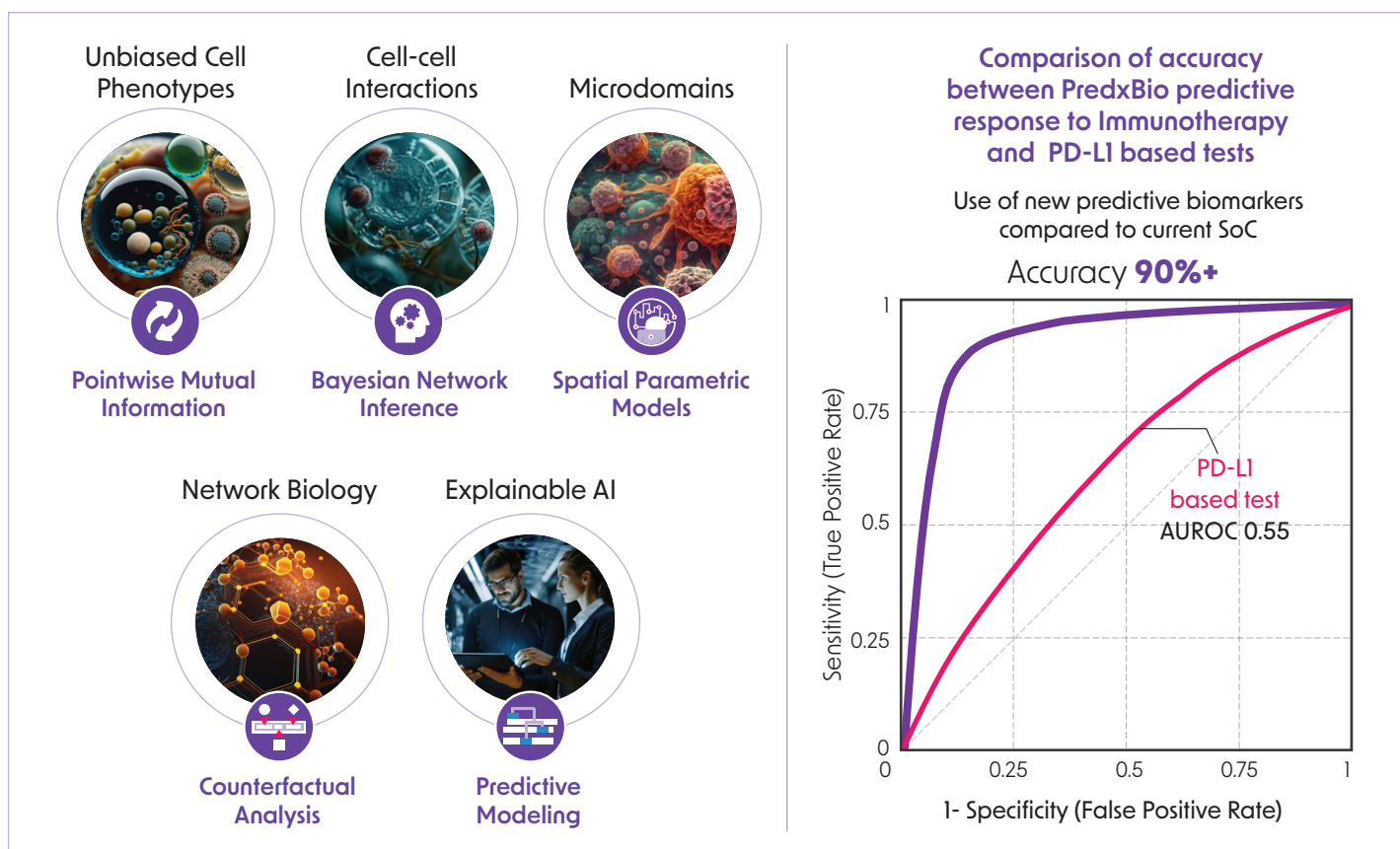


<https://thepathologist.com/diagnostics/future-trends-in-spatial-biology>

# PredxBio Solution

PredxBio is an AI platform that is transforming drug discovery and clinical development with spatially intelligent biology. Our platform has a greater than 90% accuracy in predicting patient response achieved through the use of explainable AI (xAI) and unbiased spatial analytics. The platform ingests spatial multimodal images to perform 1) cell phenotyping 2) cell-cell communication 3) microdomain discovery and 4) network biology. PredxBio's discovery of spatial biomarkers is based on relevant positioning of cells and the emergent network biology, which provides a holistic view of the tumor microenvironment. We capture protein-protein interactions to explore the dynamics of cell to cell communication.

PredxBio doesn't just quantify the cells in a tumor, but also explains the heterogeneity. We understand that there is an organizing principle within the tumor heterogeneity, and that's how we define microdomains. Microdomains are repeated spatial structures within a tumor. After finding microdomains we utilize them as pivot points to understand tumor initiation, tumor progression and a response to therapy. Microdomains allow us to extract [network biology](#) and explore the intricate interplay of genes, proteins, and signaling pathways, which ultimately help us and our partners to generate new hypotheses for drug design and target identification.



Microdomains are the landmarks to navigate the multimodal space. Once they are identified, we also offer utilizing additional technologies to interrogate the tumor microbiology within the microdomains as they provide the map for key landmarks in the tissue sample. The PredxBio

platform is agnostic to spatial biology imaging systems and takes tumor images from multiple modalities. As a solution, the platform is able to process and analyze large images acquired by any existing multi-hyperplexed imaging platform that generates extensive spatial data.

## Multimodal Interrogation

The PredxBio platform scales across a variety of spatial imaging modalities. Imaging modalities provide complementary insights when working to characterize cellular interactions and decipher the tumor microenvironment. While PredxBio starts with identifying the microdomains, the identified microdomains become the map for further investigating the tumor and the associated network biology.

### Spatial Biology

Spatial biology is a burgeoning field that advances our understanding of the intricacies of the tumor and associated network biology. Employing cutting-edge techniques, such as spatial transcriptomics, spatial genomics, proteomics and multiplexed imaging, to elucidate the spatial organization of cells within tissues. The PredxBio platform uses the spatial relationships of various cell types, gene expression patterns, and protein distributions within the tumor microenvironment. This comprehensive approach enables a holistic understanding of how immune cells, stromal cells, and cancer cells coordinate and communicate in the complex landscape of a tumor.

### Additional Modalities

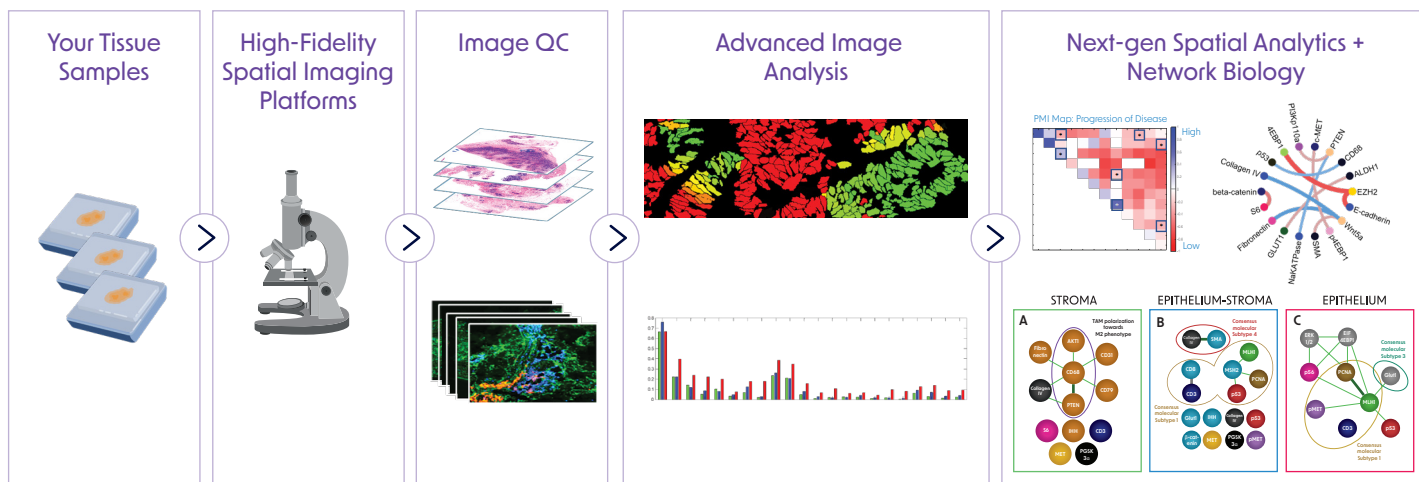
Cancer is a complex and dynamic disease requiring the continuous exploration and incorporation of additional

modalities. Therefore, in addition to spatial biology, PredxBio incorporates additional modalities, including transmitted light pathology, bulk and single cell genomics.

Recently, efforts have been made to integrate spatial transcriptomics and spatial proteomics to generate a complete picture of the biology of cancer in the tumor microenvironment, but these efforts have been hindered by lack of correlation between mRNA and protein expression. It is possible that microdomains derived from spatial proteomics would enable more informed and guided exploration of spatial transcriptomics yielding significantly greater insights into the network biology and pathways of cancer.

As this field progresses, PredxBio aims to remain at the forefront of innovation. Our spatially intelligent platform will continue to support additional imaging modalities including metabolomics, microbiome and radiological imaging. This will allow us to maintain our unmatched accuracy by providing the most comprehensive information on the tumor microenvironment, rigorous cell-cell communication with the goal of continuously improving prediction of response.

## From biopsy tissue to network biology



## Accuracy

While compatible across a multitude of toolsets the PredxBio platform maintains an unprecedented accuracy. To achieve this high accuracy, PredxBio platform relies on two key items: xAI and unbiased spatial analytics.

### Explainable AI

AI is typically known as being a black box, relying on an underlying algorithm that provides no reasoning on outcomes. PredxBio utilizes xAI, we provide the steps and reasoning behind each decision that is provided and you receive the detailed mechanistic explanations for disease progression and response to therapy.

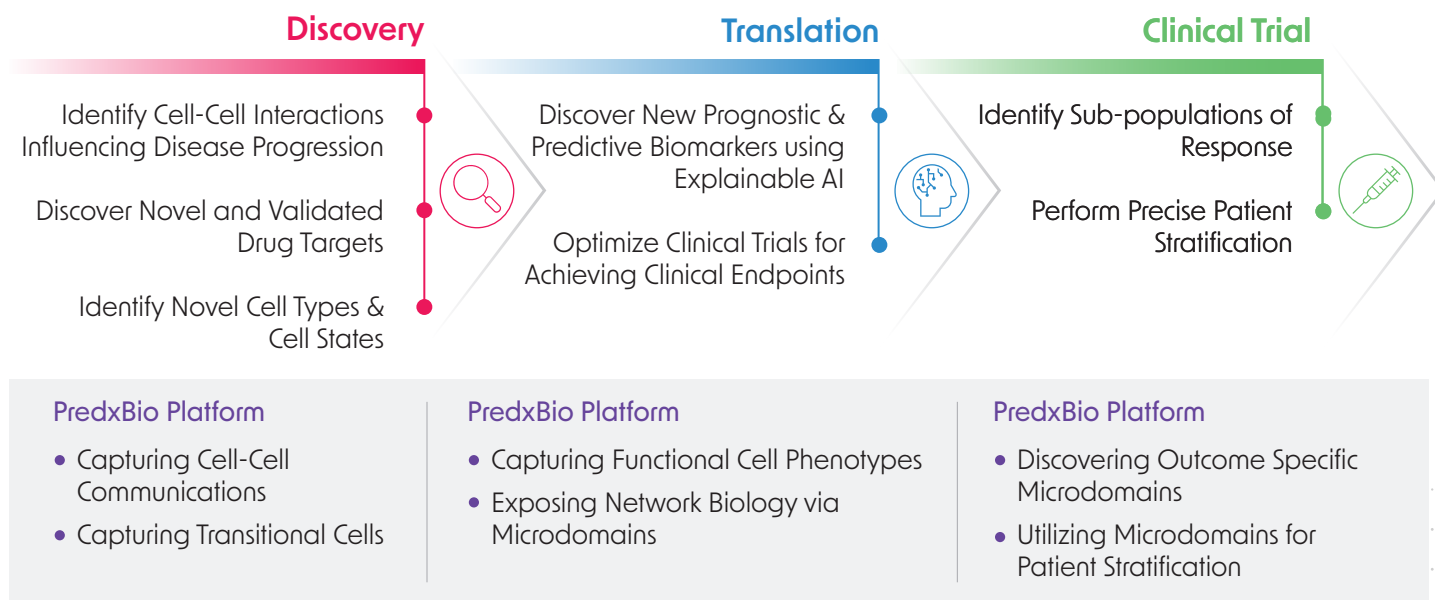
The application of xAI builds confidence in the algorithms and extends its utility in clinical and biomedical research. At any time, our platform will answer "why?" questions from users and can answer "what if?" alternatives. The lack of confidence in "black box" AI decisions has been a major roadblock to the adoption of computational

pathology, since additional studies may be required to verify an AI decision and may introduce inefficiency involving extra time and resources.

### Unbiased Spatial Analytics

PredxBio uses an unsupervised machine learning algorithm to build a hierarchy of functional cell phenotypes on a continuum. In combination with the pointwise mutual information (PMI) algorithm, microdomains are discovered. These algorithms allow the capture of a phenotypic continuum comprised of specialized, transitional, and multi-transitional cell states that accurately reflect the complexity of intratumor heterogeneity. More importantly, using spatial heterogeneity data determined by PMI, the PredxBio approach enables the discovery of microdomains, characterized by distinct compositions and spatial configurations of cancer and non-cancer cell populations.

## Address Challenges Throughout Drug Development



# Applications/Case Study

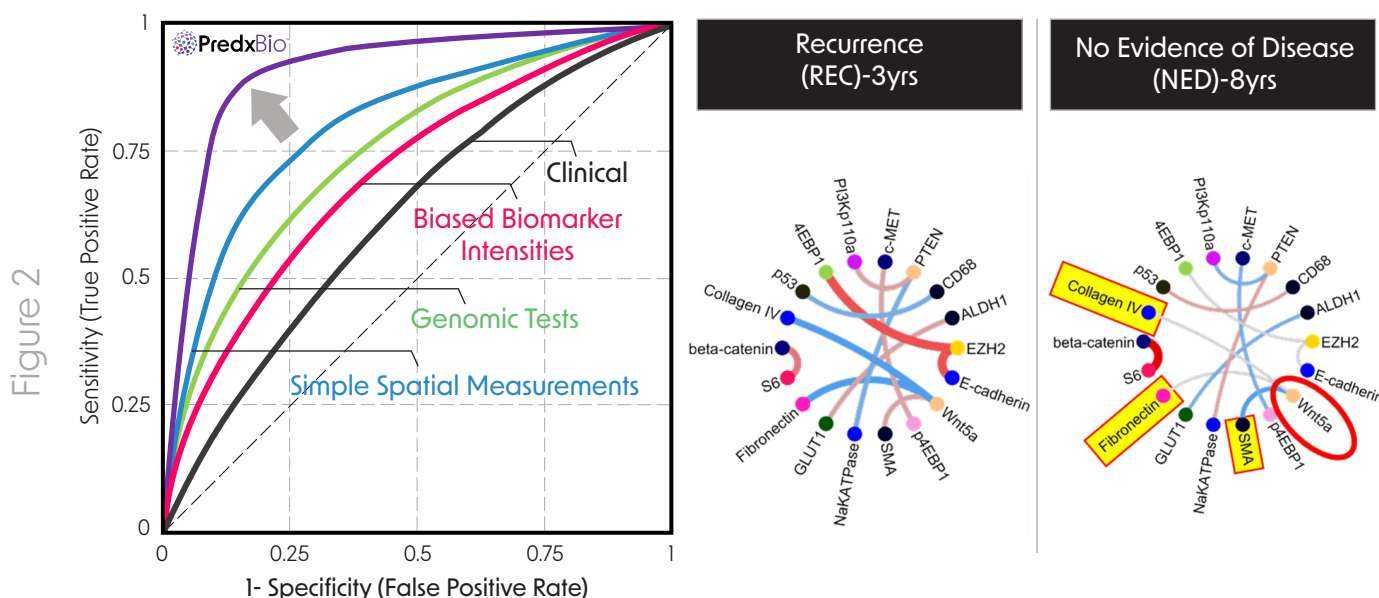
PredxBio's spatially intelligent platform has a proven accuracy over 90% from our study predicting the risk recurrence for colorectal cancer (CRC) patients. Currently, only 4% of the stage II high-risk and 25% of the stage III CRC populations benefit from adjuvant chemotherapy.

There is an urgent need to optimally evaluate the tumor biology to predict an individual patient's response to adjuvant chemotherapy. The goals within this study were: 1) Predict the risk of recurrence and 2) Identify network biology driving future risk to improve drug treatment.

Our 5-year risk of recurrence prediction accuracy for a cohort of 400+ CRC patients across stages I, II and III, dramatically shows the improvement in specificity and sensitivity of the prognosis (**Figure 2**). As you go from basic biomarker utilization, to genomic testing, to simple spatial measurements, to our approach of extracting

microdomain specific network biology from the samples – you can achieve over 90% accuracy compared to some of the other techniques, and we have seen this in colorectal cancer and across others as well.

On the right panel of **Figure 2** you can also see the data related to the various pathways that we were able to reveal through our approach. Defining microdomains with all the statistical weights and understanding spatial ITH allow us to define a network of interaction characteristic of each microdomain. Accordingly, our xAI approach identifies the statistically significant pathway crosstalk happening in the tissue samples to unravel the hidden circuitries of cancer. Please refer to our published studies to have a deeper dive into our technology [\[NATURE COMMUNICATIONS | \(2020\) 11:3515, Cell Rep Methods. 2021 Sep 27; 1\(5\): 100072\]](#).



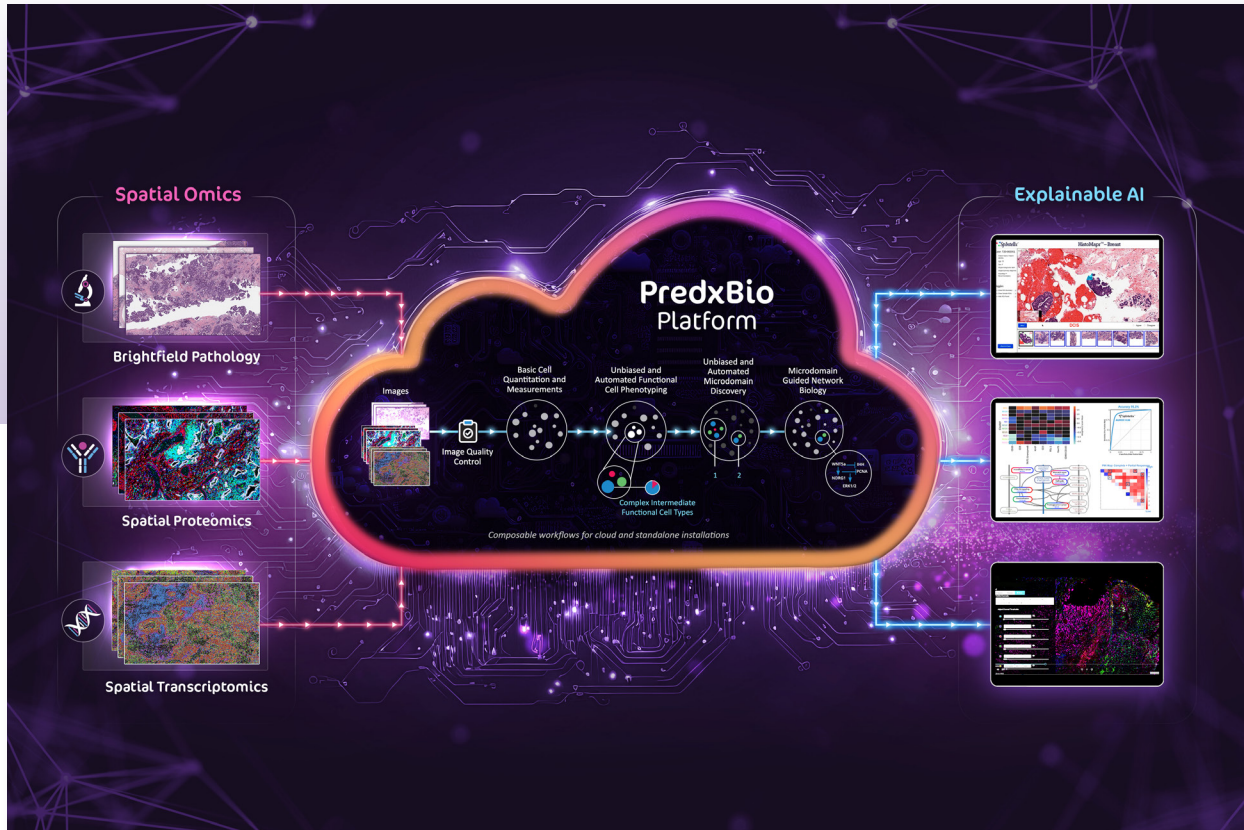
[NATURE COMMUNICATIONS | \(2020\) 11:3515](#)

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