

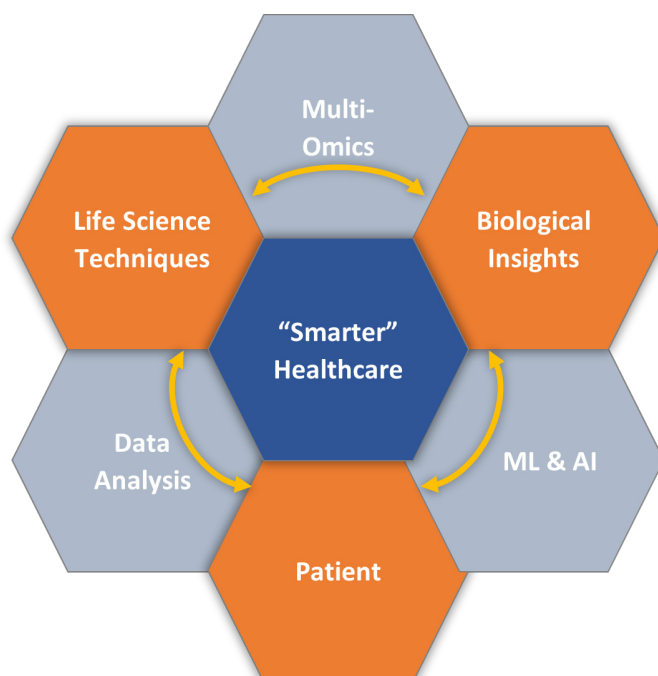
Biology & Digital Technology Merger Gives Rise to Spatial Biology

Craig Steger
Senior Vice President, Outcome Capital

Oded Ben-Joseph, PhD, MBA
Managing Director, Outcome Capital

Introduction

As a highly specialized life science advisory and investment banking firm, Outcome Capital looks to identify emerging trends that effect how researchers and clinicians understand, diagnose, and treat disease. One emerging trend we have noted is the integration of advancements in biological sciences, such as tools and techniques, and digital technologies, such as machine learning (ML) and artificial intelligence (AI). This merger has given rise to a new field - spatial biology.



Spatial biology examines the relationship between the location of cells within a tissue and disease pathology. Taken a step further, spatial transcriptomics looks to relate disease with specific gene expression or activity within a tissue or cell.

The advent and improvement in specimen workflow automation, precision multiplexed staining, spatial sequencing, digitization, and AI-assisted image analysis have enabled companies like 10x Genomics and Akoya Biosciences to create a market segment focused on spatial biology. For example, researchers and clinicians now have commercially available tools

Table 1

Spatial Biology Market Entrants

Company Name	Year Founded	Company Name	Year Founded
Vysis	1991	Visikol	2012
Angle (United Kingdom) (LON: AGL)	1994	Spatial Transcriptomics	2012
Fluidigm (NAS: FLDM)	1999	10x Genomics (NAS: TXG)	2012
Bio View (TAE: BIOV)	2000	Clarapath	2014
PathXL	2004	Enspectra Health	2014
Advanced Cell Diagnostics	2006	Ionpath	2014
Cartagenia	2008	Lunaphore Technologies	2014
Omnyx	2008	Proscia	2014
Flagship Biosciences	2009	Akoya Biosciences	2015
RareCyte	2009	Ultivue	2015
Viewics	2009	PathAI	2016
Ovizio Imaging Systems	2009	ReadCoor	2016
Digital Diagnostics	2010	S2 Genomics	2016
Celsee	2010	VistaPath Biosystems	2017
Biospyder	2011	Deep Lens	2017
Berkeley Lights (NAS: BLI)	2011	Paige	2017
Mission Bio	2011	Cartana	2017
Reveal Biosciences	2012	Resolve Biosciences	2020

Source: Pitchbook

to identify gene expression in specific locations within a single cell or multiplex up to 40 different immunofluorescent biomarkers in a single tissue section – abilities that profoundly improve their knowledge, treatment, and diagnosis of disease.

Combining Biological Sciences With Digital Technology

Because spatial biology brings together life sciences and digital technology, Outcome Capital has benchmarked private mid-market companies active within the spatial biology space (whether research or clinically focused) to get a snapshot on the flow of capital (Table 1).

Of the spatial biology-fo-

cused companies that we have identified, ~67% were founded after 2010. In the 20-year period prior to 2010, a mere \$300M was invested. Since 2010 more than \$780M has been invested, with an average investment of approximately \$33M. Of note, >\$400M of the \$780M was invested in 2019 and 2020. As anticipated, the degree of investment within spatial biology has correlated with the emergence of high-impact science and technology.

We can further dissect investments in spatial biology based on the companies' primary focus – life science technologies vs. digital technologies. Interestingly, we see about a 50/50 split with half the

companies focused on digital technologies as defined as those related to slide scanning, image capture, and data analysis. In addition, the \$400M funding in 2019 – 2020 was also evenly distributed amongst these two categories.

Not Everyone Has Open Arms

As spatial biology expands it drives not only the understanding of disease pathology but also the evolution of clinical molecular pathology or digital pathology. In general, the research and clinical market segments react differently to emerging technologies. The research market segment tends to contain early adopters who are looking to move their research

further and better understand the science in a shorter time. In comparison, the clinical market segment is composed of slow adopters who are looking to give accurate, precise, and actionable information to their patients and maintain control over healthcare spending.

Outcome Insight

Outcome Capital spoke with life science industry leaders to gain feedback on how they are looking at the emerging spatial biology space and penetration into the research vs clinical market segments.

Most industry executives see value in the spatial biology space

and are encouraged by how the evolution of both biological sciences and digital technology is driving actionable innovation. They note, however, that spatial biology to-date has been most successfully adopted by the research market.

Many executives cautioned that there is a large chasm between research and clinical markets requiring significant time and cost. This has slowed the momentum of companies entering the digital pathology market despite the advancements in life sciences and digital technology.

Several common themes emerged from our conversations:

- Slide scanning and image acquisition time is important for market uptake when digitizing slide images. This is potentially one of the obstacles slowing digital pathology uptake.
- Transitioning from a research-based tool to a clinical tool may not need multiplexing >10 items on a slide. The clinical market will need current clinical assays available on any platform for market acceptance.
- Image analysis and sharing is becoming more critical for market adoption. Proprietary formats may be limiting in the market.
- Enter the clinical market with



Akoya Biosciences

www.akoyabio.com

Merging Multiplex Staining and Spatial Imaging with Sophisticated Analysis

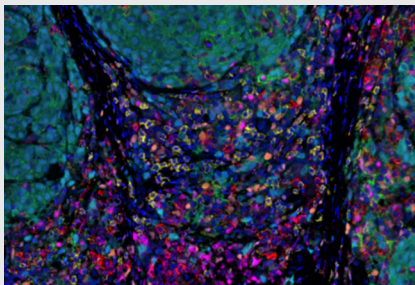


Image source: www.akoyabio.com/phenoptics

Akoya Biosciences, founded in 2015, focuses on accelerating biomarker discovery and translation to the clinic using an integrated set of tools including highly multiplexed staining, imaging and analysis. The Akoya offering has been both internally created and augmented via acquisition of the Phenoptics portfolio from PerkinElmer in 2018 and external partnerships.

Traditional immunohistochemistry (IHC) technologies retain the spatial context of the tissue but are limited to 2 to 3 biomarkers per sample. In contrast, next-generation sequencing (NGS) enables the analysis of far more biomarkers, but the spatial context is lost. Akoya's proprietary multiplex imaging enables the analysis of a multitude of independent cellular phenotypes within the spatial context of the tissue microenvironment which they believe is key to understanding disease pathology and progression.

CODEX, the initial research-focused product offering, is an integrated system from assays and reagents through image acquisition offering unique insights into the complexity of cellular interactions and their microenvironment via 40+ multiplex staining and imaging analysis.

Akoya has fostered relationships with researchers who are translating insights into the clinical market. This has allowed Akoya to build an impressive publication set (>120 since 2015 including several high impact journals). Moreover, many of these publications come from key clinical collaborations over the past 2 years, which is a critical part of the long road to entering the clinical market.



PathAI

www.pathai.com

*Artificial Intelligence
Decodes Pathology Images*

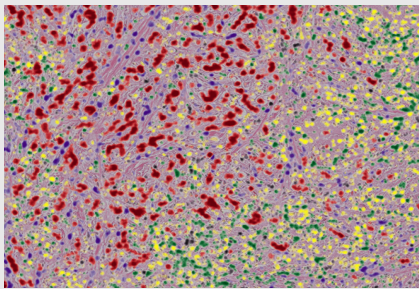


Image source: www.novartis.com/stories/discovery/artificial-intelligence-decodes-cancer-pathology-images

PathAI, founded in 2016, develops AI-powered technology that looks to assist pathologists in making rapid and accurate diagnoses – which to date is a daunting, highly-manual process. PathAI and several large pharmaceutical partners believe the addition of AI to clinical pathology has the potential to not only reduce errors, but also garner more in-depth information about disease pathology and patient response to treatment that is overlooked using traditional microscopic analysis.

PathAI quickly gained industry recognition by winning a global competition for the detection of metastatic lymph nodes. This led to a partnership with Philips Healthcare to further validate the impact of their digital technology on pathologists' capabilities.

They have continued to use partnerships with key industry veterans to accelerate their path to the clinical spatial biology marketplace. In collaboration with pathologists and data scientists at Novartis, PathAI used real-world clinical data sets to 'teach' their AI systems to identify cancer cells, cell phenotypes, and biomarkers associated with patient outcomes.

PathAI has on-going relationships with Bristol-Myers Squibb and Gilead in clinical trials ranging from PD-L1 expression to better understanding disease progression in liver disorders, such as NASH and Hepatitis B infections.

Further monetary investments from several partners are propelling PathAI technology towards clinical approval and ultimately use in diagnostic pathology.

all the needed material to capture customers. Generally, clinical labs need to compare current clinical techniques along with potentially new staining or imaging analysis techniques to understand the new capabilities of the platform. Clinical studies, peer reviewed publications and white papers will all be needed to gain customer confidence and will help drive market adoption.

Two approaches to penetrate the clinical spatial biology market are highlighted in the Akoya Biosciences and PathAI case studies: i) entry into the commercial research

market to build awareness, technology adoption, and assets needed for subsequent transition to the clinical market, and ii) collaborations with pharmaceutical and/or diagnostic partners to generate clinical use data to drive direct entry into the clinical market.

Planning for the Exit

Of the limited exits that we have seen in the spatial biology space (10), most have been research-oriented companies. 10x Genomics has solidified their beachhead in this space with 3 acquisitions since 2018, most recently acquiring Cartana and ReadCoor in

2020. These acquisitions have seen a healthy return for their shareholders ranging from 3x - >10x returns.

Overall, Outcome believes this will be a rapidly evolving field where we will see further industry consolidation, but also continued market entrants. As companies continue to mature and begin to enter the clinical markets, we believe we will also see an increase in acquisition prices as the technologies begin to impact how pathologist practice medicine and further impact patient care.



About Outcome Capital

Outcome Capital is a specialized life science and technology investment bank with a global reach, providing middle market group companies with a value-added approach to mergers and acquisitions, corporate finance and advisory services. The firm uses its proven 'strategy-led execution' approach to value enhancement by assisting boards and management teams in navigating both the financial and strategic markets and in implementing the best path for success. Outcome Capital's strength stems from its unique ability to draw on its wide range of operational, strategic and investment experience, its expertise across the value chain, and its broad industry relationships.



About the Author

Dr. Ben-Joseph is a Managing Director at Outcome Capital and co-lead of its life sciences practice. He brings a unique combination of executive, entrepreneurial, scientific and transactional experience to client companies. He is passionate about guiding cutting-edge life science companies through disciplined market-driven decisions toward strategic value enhancement and a path to liquidity.



About the Author

Craig Steger is the Senior Vice President of Life Sciences at Outcome Capital and brings corporate and commercial expertise in the diagnostic and life science space.

New York
555 Fifth Ave.
19th Floor
New York, NY 10017
(212) 350-8213

Boston
99 High St.
Suite 2900
Boston, MA 02110
(617) 431-4886

Washington, D.C.
12120 Sunset Hills Rd.
Suite 500
Reston, VA 20190
(703) 225-1500