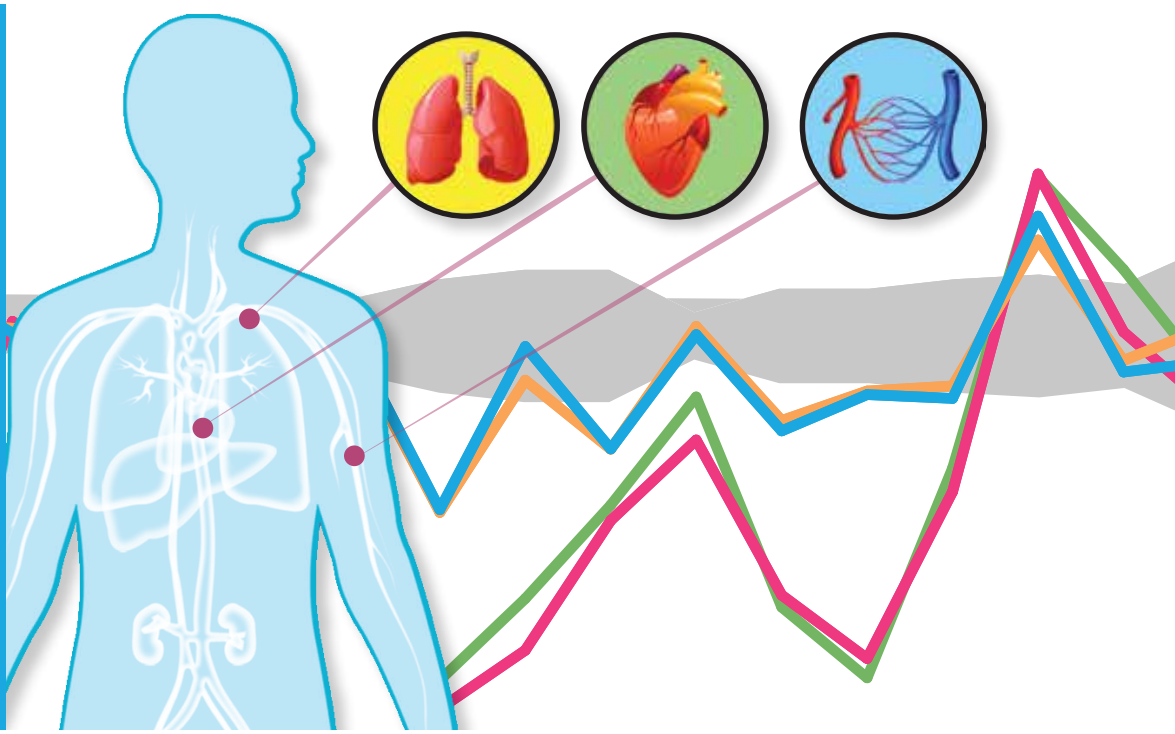
DiscoverX

BioMAP®
Phenotypic Profiling Services

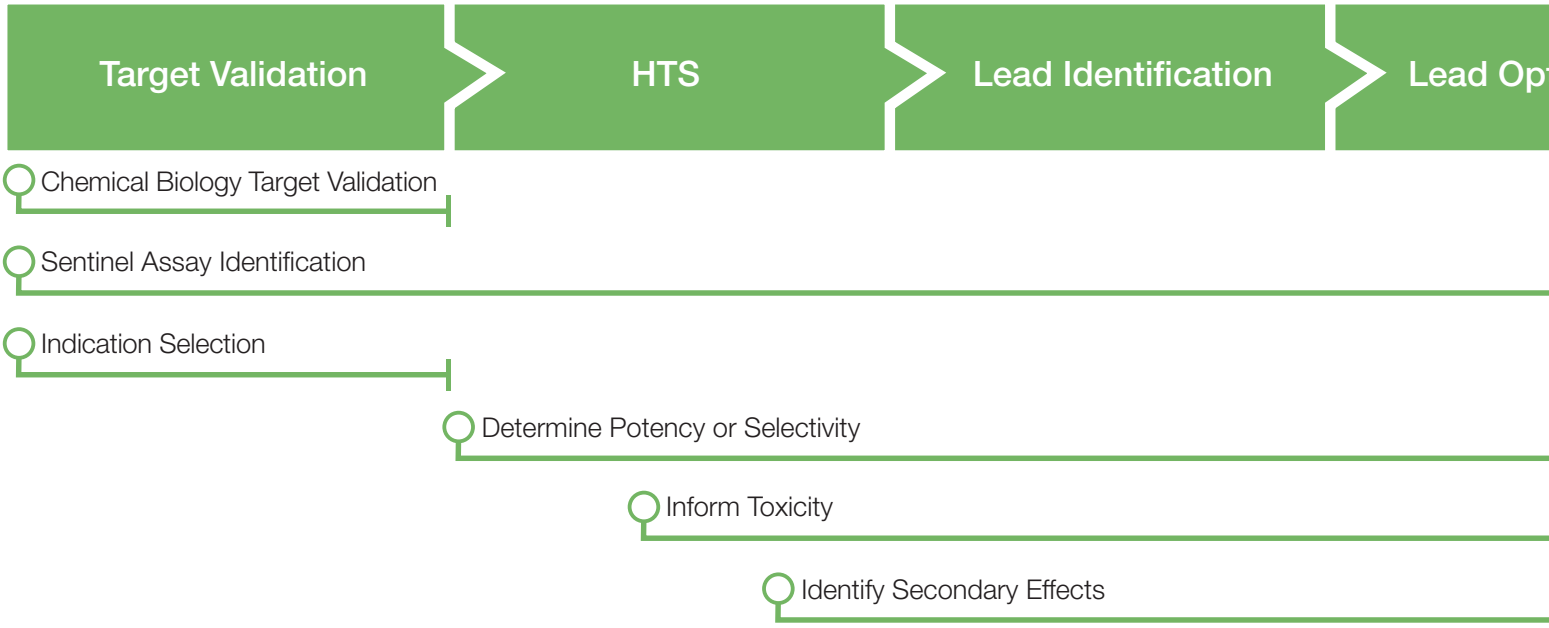
In Vivo Insights with the Speed and Ease of an *In Vitro* Assay

What's Inside:

- Triage drug candidates
- Test compounds for safety & efficacy
- Inform preclinical design
- Reposition existing drugs



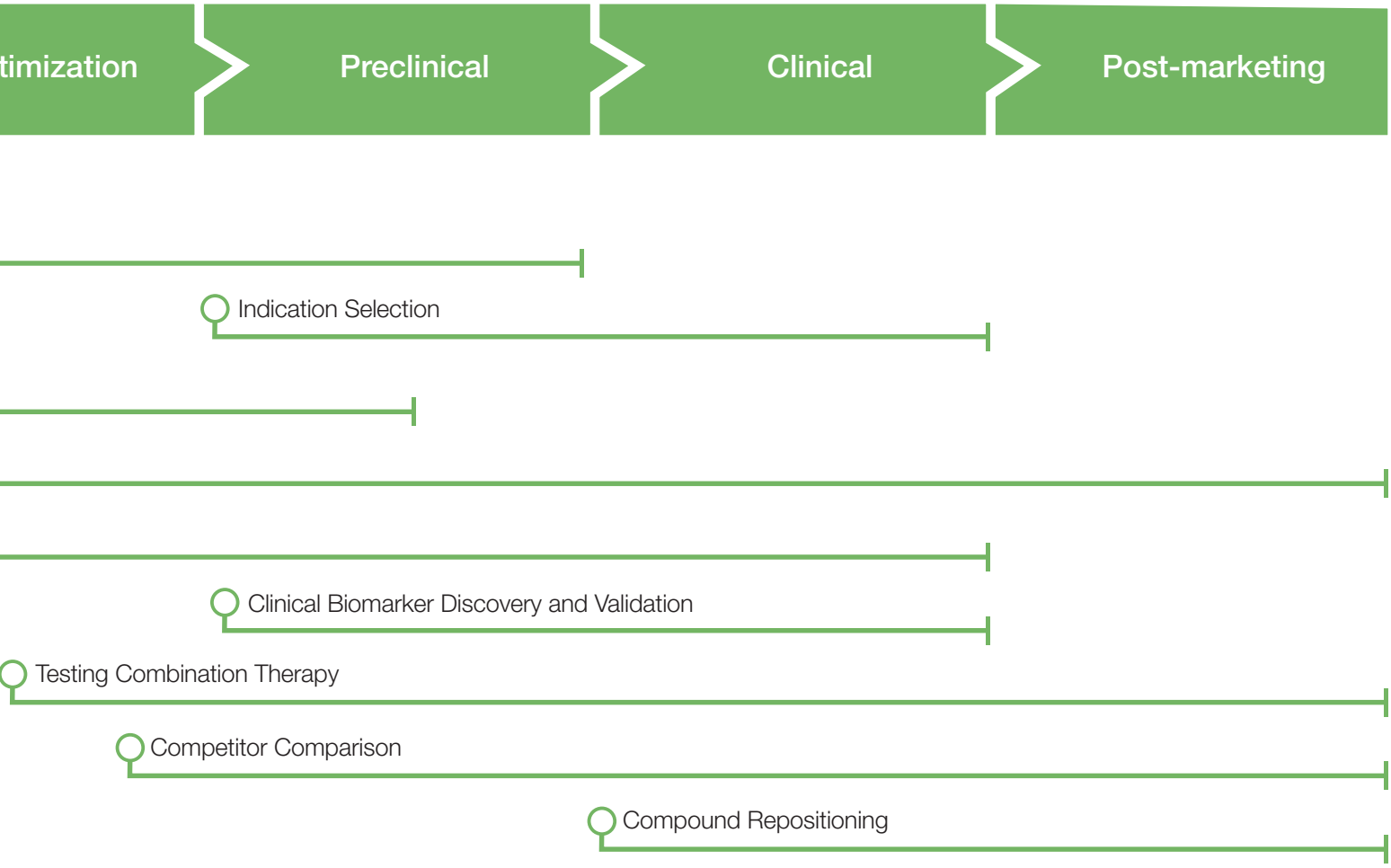
Applications of BioMAP® Systems in Drug Discovery



Phenotypic Drug Discovery

Human disease biology is complex and we are only now beginning to fully decipher the countless chemical and physical interactions that contribute to the disruption of normal processes to manifest in disease pathology. It is easy to understand why predicting the effects of a novel compound on disease biology remains a significant challenge. Numerous strategies have been developed for identifying the target, mechanism, selectivity, and potency of a compound, however, many approaches are one-dimensional and fail to capture the complexity of patient physiology *in vitro*. The BioMAP Phenotypic Profiling Platform overcomes these challenges by mirroring complex tissue and disease biology *in vitro* and has been validated using approved drugs and known test agents to recapitulate reported clinical outcomes. The BioMAP platform is the best available service to:

- Triage candidates prior to *in vivo* experiments or IND submission
- Test compounds for safety and efficacy
- Inform preclinical design and biomarker selection
- Manage product lifecycle and reposition existing drugs



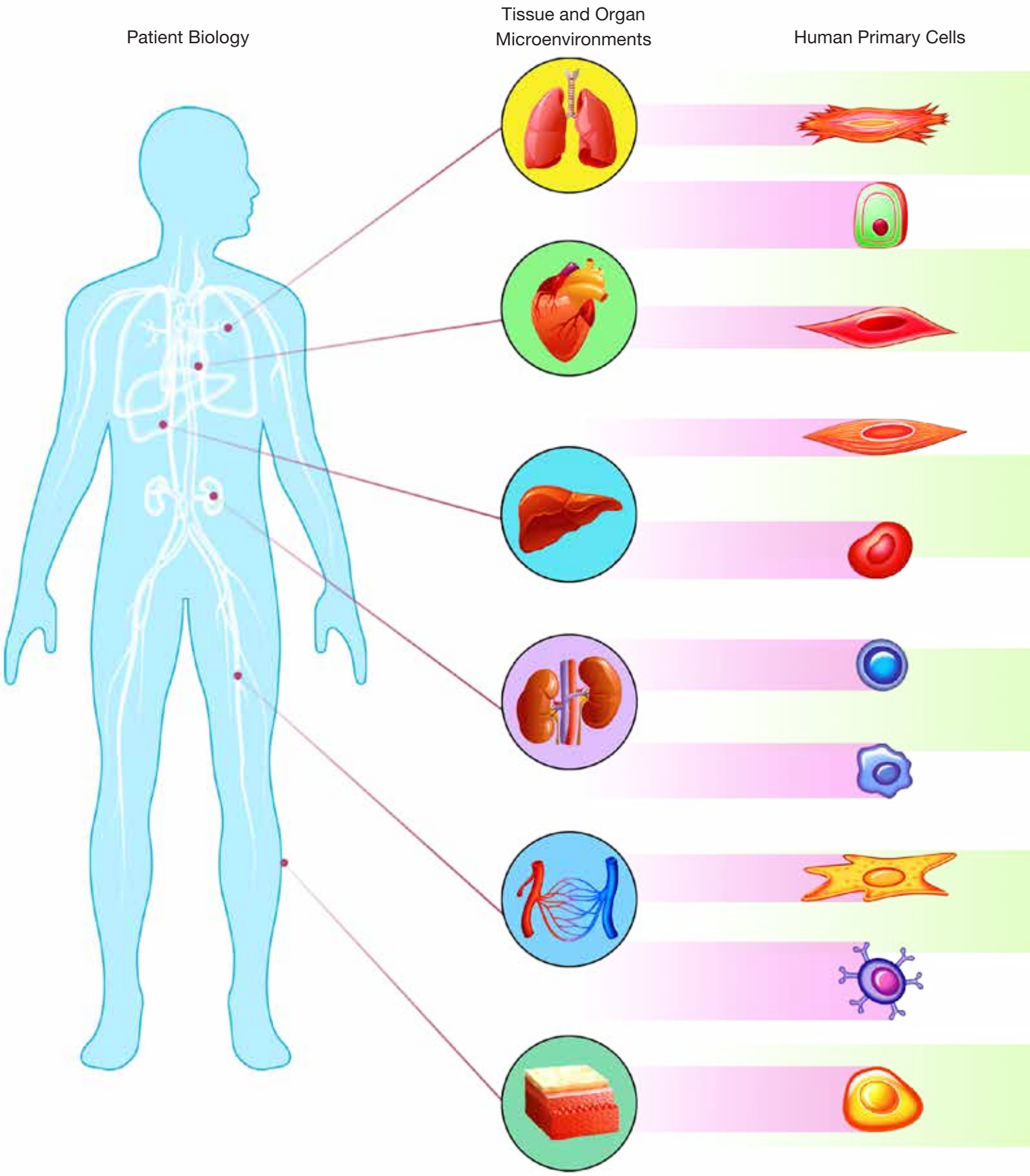
BioMAP Advances Drug Development

BioMAP systems come as close to testing on human patients as an *in vitro* assay can. When considering what method to use for your next screen or lead characterization, consider the following benefits of BioMAP.

What BioMAP Offers	Why It Matters in Drug Development
▪ Human primary cell-based assays	▪ Intact regulatory and feedback mechanisms
▪ Validated to recapitulate clinical results	▪ Predictive of clinical outcomes
▪ Automated assay platform	▪ Reproducible within and between assays
▪ Proprietary database and custom computational analysis	▪ The only platform to be able to predict safety and mechanism of action based on historical data
▪ Identification of secondary and off target activities	▪ Reveal potential assets or liabilities of test compounds that one-dimensional approaches may miss

Learn more about BioMAP and request a quote at www.discoverx.com/biomap

Modeling Human Biology for Phenotypic Drug Development



Co-Culture and Disease Relevant Stimuli

60+ BioMAP Systems

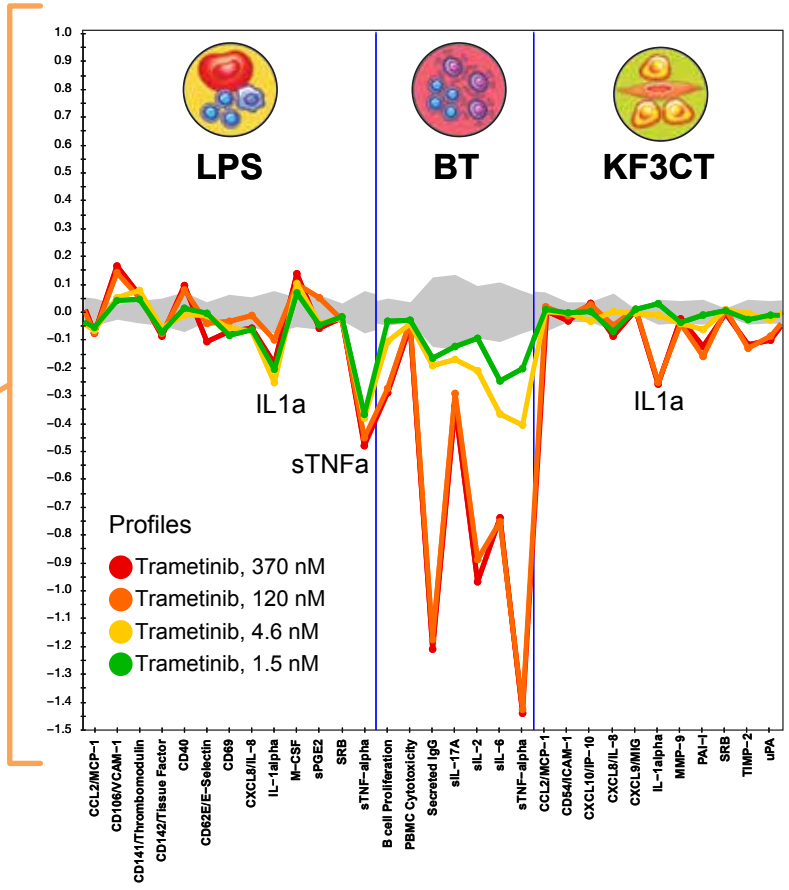
BioMAP® Phenotypic Profiling Platform

The broadest, most physiologically relevant method to quickly and robustly determine the efficacy, safety, and mechanism of action (MOA) of candidate drug molecules to support their pipeline progression. BioMAP Systems are composed of:

- Over 60 human primary cell-based models of tissue and disease biology
- Profiling with 100's of clinically relevant protein biomarkers
- Database of 4,500+ reference compounds and a suite of bioinformatics for in-depth prediction of safety and MOA

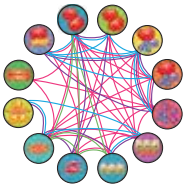
BioMAP informs decisions that accelerate drug candidates from testing to therapies.

Profile of Clinical Protein Biomarkers



The BioMAP® Service Offering

Diversity PLUS™ Panel



The Diversity PLUS panel contains 12 BioMAP Systems that allow unbiased characterization of test agents across a broad set of systems modeling various therapeutically relevant disease states. A profile of biomarker activity of each test agent is generated and compared against the BioMAP reference database of more than 4,500 BioMAP profiles of bioactive agents (biologics, approved drugs, chemicals, and experimental agents), clustered with other project compounds and compared against 19 consensus mechanism class profiles of well-characterized drugs.

Use Diversity PLUS to: Inform on the potency, selectivity, safety, mechanism of action, and disease indication of a test agent.

Oncology Panels

The BioMAP Oncology Systems model the complexity of different tumor microenvironments (TME) by combining primary human stromal or vascular cells with immune cells and human tumor cell lines to recapitulate the complex interactions and signaling pathways that occur during tumorigenesis.

Use Oncology Panels to: Gain insight into TME-specific mechanism of action, efficacy, and safety-related effects of test agents.

T Cell/Autoimmune Panel

The T Cell/Autoimmune Panel models the adaptive immune cell microenvironment, as well as the individual T and B cell responses during different types of inflammation.

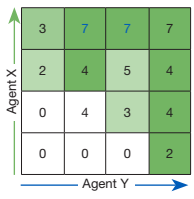
Use the T Cell Panel to: Gain insight into inflammation-related mechanism of action effects, indication guidance, and combination feasibility for a diverse set of target classes.

Fibrosis Panel

The BioMAP Fibrosis Panel contains systems modeling the tissue environments of the lung and kidney during the complex inflammatory and pro-fibrotic conditions that occur in fibrotic disease, wound healing, and extracellular matrix remodeling.

Use the Fibrosis Panel to: Gain insight into fibrosis-related mechanism of action effects, compound ranking, indication guidance, and combination feasibility for a diverse set of target classes.

Combo ELECT



The BioMAP Combo ELECT service allows statistical evaluation of drug combinations to determine additive or antagonistic differences between drug agents in a nominated system of interest. Each agent is analyzed individually and then statistically compared against a combination array of the two serially diluted agents.

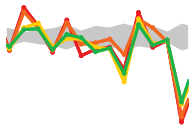
Use Combo ELECT to: Inform on the optimal dosing, potential synergy, or adverse effects of different drug pairings.

Results that Drive Decisions

Below are the types of data readouts you receive at the conclusion of a BioMAP project to assist in your drug development decision making.

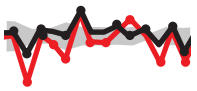
Profile Analysis

Concentration dependent response of biomarker activities of individual test agents.



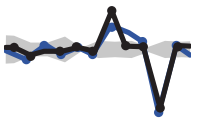
Benchmark Analysis

Concentration dependent response of biomarker activities of individual test agents.



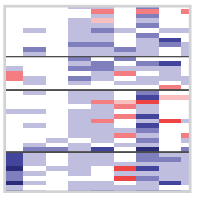
Similarity Analysis

Identifies agents with similar BioMAP profiles using an unbiased mathematical approach against a proprietary reference database of over 4,500 BioMAP profiles of bioactive agents (Diversity PLUS™ only).



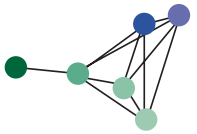
HeatMAP Analysis

Biomarker readouts of agents are compared against consensus mechanism profiles of well characterized drugs (Diversity PLUS) or selected reference benchmarks that are current standards of care (T Cell/Autoimmune and Fibrosis).



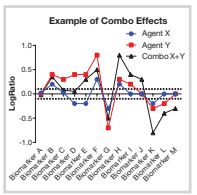
Cluster Analysis

Graphical representation of functional similarities between agents tested in BioMAP Systems using pairwise correlation analysis.



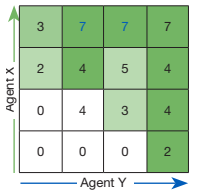
Combination Analysis

Comparative annotated overlays of biomarker readouts of the combinations that are specifically different than the individual test agents (Combo ELECT).



Checkerboard Analysis

Summary of the number of biomarker activities in the combination for each concentration pair that are significantly different than individual test agents (Combo ELECT).



Human Disease Modeled by the BioMAP® Platform

Panel		System	Cell Types	Diseases/ Tissues Modeled	Description	Protein Biomarker Readout
Diversity PLUS	3C	Th1 Vasculature	Venular endothelial cells	Cardiovascular Disease, Chronic Inflammation	The Th1 Endothelium (3C) system models vascular inflammation of the Th1 type, an environment that promotes monocyte and T cell adhesion and recruitment and is anti-angiogenic. This system is relevant for chronic inflammatory diseases, vascular inflammation and restenosis.	MCP-1, VCAM-1, TM, TF, ICAM-1, E-selectin, uPAR, IL-8, MIG, HLA-DR, Proliferation, SRB
	4H	Th2 Vasculature	Venular endothelial cells	Asthma, Allergy, Autoimmunity	The Th2 Endothelium (4H) system models vascular inflammation of the Th2 type, an environment that promotes mast cell, basophil, eosinophil, T and B cell recruitment and is pro-angiogenic. This system is relevant for diseases where Th2-type inflammatory conditions play a role such as allergy, asthma, and ulcerative colitis.	MCP-1, Eotaxin-3, VCAM-1, P-selectin, uPAR, SRB, VEGFRII
	LPS	Monocyte Activation	PBMC/Venular endothelial cells	Cardiovascular Disease, Chronic Inflammation	The Monocyte Activation (LPS) system models chronic inflammation of the Th1 type and monocyte activation responses. This system is relevant to inflammatory conditions where monocytes play a key role including atherosclerosis, restenosis, rheumatoid arthritis, and other chronic inflammatory conditions, as well as metabolic diseases.	MCP-1, VCAM-1, TM, TF, CD40, E-selectin, CD69, IL-8, IL1-α, M-CSF, sPGE2, SRB, sTNFα
	SAg	T Cell Activation	PBMC/Venular endothelial cells	Autoimmune Disease, Chronic Inflammation	The T Cell Activation (SAg) system models chronic inflammation of the Th1 type and T cell effector responses to TCR signaling with costimulation. This system is relevant to inflammatory conditions where T cells play a key role including organ transplantation, rheumatoid arthritis, psoriasis, Crohn's disease and multiple sclerosis.	MCP-1, CD38, CD40, E-selectin, CD69, IL-8, MIG, PBMC Cytotoxicity, Proliferation, SRB
	BT	B and T Cell Autoimmunity	B cells/PBMC	Asthma, Allergy, Oncology, Autoimmunity	The B and T Cell Autoimmunity (BT) system models T cell dependent B cell activation and class switching as would occur in a germinal center. This system is relevant for diseases and conditions where B cell activation and antibody production are relevant. These include autoimmune disease, oncology, asthma and allergy.	B cell Proliferation, PBMC Cytotoxicity, Secreted IgG, sIL-17A, sIL-17F, sIL-2, sIL-6, sTNFα
	BF4T	Lung Disease	Bronchial epithelial cells/ Dermal fibroblasts	Asthma, Allergy, Fibrosis, Lung Inflammation	The Lung Disease (BF4T) system models lung inflammation of the Th2 type, an environment that promotes the recruitment of eosinophils, mast cells and basophils as well as effector memory T cells. This system is relevant for allergy and asthma, pulmonary fibrosis, as well as COPD exacerbations.	MCP-1, Eotaxin-3, VCAM-1, ICAM-1, CD90, IL-8, IL1-α, Keratin 8/18, MMP-1, MMP-3, MMP-9, PAI-1, SRB, tPA, uPA
	BE3C	Lung Inflammation	Bronchial epithelial cells	Lung Inflammation, COPD	The Lung Inflammation (BE3C) system models lung inflammation of the Th1 type, an environment that promotes monocyte and T cell adhesion and recruitment. This system is relevant for sarcoidosis and pulmonary responses to respiratory infections.	ICAM-1, uPAR, IP-10, I-TAC, IL-8, MIG, EGFR, HLA-DR, IL1-α, Keratin 8/18, MMP-1, MMP-9, PAI-1, SRB, tPA, uPA
	CASM3C	Cardiovascular Disease	Coronary artery smooth muscle cells	Cardiovascular Inflammation, Restenosis	The Cardiovascular Disease (CASM3C) system models vascular inflammation of the Th1 type, an environment that promotes monocyte and T cell recruitment. This system is relevant for chronic inflammatory diseases, vascular inflammation and restenosis.	MCP-1, VCAM-1, TM, TF, uPAR, IL-8, MIG, HLA-DR, IL-6, LDLR, M-CSF, PAI-1, Proliferation, SAA, SRB

Panel	System		Cell Types	Diseases/ Tissues Modeled	Description	Protein Biomarker Readout
Diversity PLUS	HDF3CGF	Fibrosis and Inflammation	Dermal fibroblasts	Fibrosis, Chronic Inflammation	The Fibrosis and Inflammation (HDF3CGF) system models wound healing and matrix/tissue remodeling in the context of Th1-type inflammation. This system is relevant for various diseases including fibrosis, rheumatoid arthritis, psoriasis, as well as stromal biology in tumors.	MCP-1, VCAM-1, ICAM-1, Collagen I, Collagen III, IP-10, I-TAC, IL-8, MIG, EGFR, M-CSF, MMP-1, PAI-1, Proliferation_72hr, SRB, TIMP-1, TIMP-2
	KF3CT	Psoriasis and Dermatitis	Keratinocytes/ Dermal fibroblasts	Psoriasis, Dermatitis, Skin Biology	The Psoriasis and Dermatitis (KF3CT) system models cutaneous inflammation of the Th1 type, an environment that promotes monocyte and T cell adhesion and recruitment. This system is relevant for cutaneous responses to tissue damage caused by mechanical, chemical, or infectious agents, as well as certain states of psoriasis and dermatitis.	MCP-1, ICAM-1, IP-10, IL-8, MIG, IL-1α, MMP-9, PAI-1, SRB, TIMP-2, uPA
	MyoF	Fibrosis	Lung fibroblasts	Fibrosis, Chronic Inflammation, Wound Healing, Matrix Remodeling	The Fibrosis (MyoF) system models the development of pulmonary myofibroblasts, and are relevant to respiratory disease settings as well as other chronic inflammatory settings where fibrosis occurs such as rheumatoid arthritis.	a-SM Actin, bFGF, VCAM-1, Collagen-I, Collagen-III, Collagen-IV, IL-8, Decorin, MMP-1, PAI-1, TIMP-1, SRB
	IMphg	Macrophage Activation	Venular endothelial cells/ Macrophages	Cardiovascular Inflammation, Restenosis, Chronic Inflammation	The Macrophage Activation (IMphg) system models chronic inflammation of the Th1 type and macrophage activation responses. This system is relevant to inflammatory conditions where monocytes play a key role including atherosclerosis, restenosis, rheumatoid arthritis, and other chronic inflammatory conditions.	MCP-1, MIP-1α, VCAM-1, CD40, E-selectin, CD69, IL-8, IL1-α, M-CSF, sIL-10, SRB, SRB-Mphg
Oncology	StroHT29	Colorectal Cancer - Stro	HT-29 colon adenocarcinoma cell line/Primary human fibroblasts/ PBMC	CRC Oncology/ Immune Oncology: Host Stromal-Tumor Microenvironment Biology, Tissue-Remodeling, Wound Healing, Inflammation	The Colorectal Cancer - Stro (StroHT29) system models the host stromal-tumor microenvironment by capturing the complex interactions between tumor cells, the host stromal network, and infiltrating immune cells recruited into the tumor mass.	VCAM-1, uPAR, Collagen I, Collagen III, IP-10, MMP-9, PAI-1, PBMC Cytotoxicity, sGranzyme B, sIFNγ, sIL-10, sIL-17A, sIL-2, sIL-6, SRB, sTNFα, sVEGF, TIMP2, tPA, uPA, CEACAM5, Keratin 20
	VascHT29	Colorectal Cancer - Vasc	HT-29 colon adenocarcinoma cell line/Primary human endothelial cells/PBMC	CRC Oncology/ Immune Oncology: Host Vascular-Tumor Microenvironment Biology, Inflammation	The Colorectal Cancer - Vasc (VascHT29) system models host vascular-tumor microenvironment by capturing the complex interactions between tumor cells, the host vascular network, and infiltrating immune cells associated with angiogenesis.	MCP-1, VCAM-1, CD40, CD69, uPAR, Collagen IV, IP-10, MIG, PBMC Cytotoxicity, sGranzyme B, sIFNγ, sIL-10, sIL-17A, sIL-2, sIL-6, SRB, sTNFα, CEACAM5, Keratin 20
	StroNSCLC	Lung Cancer - Stro	NCI-H1299 NSCLC cell line/ Primary human fibroblasts/ PBMC	NSCLC Oncology/ Immune Oncology: Host Stromal-Tumor Microenvironment Biology, Tissue-Remodeling, Wound Healing, Inflammation	The Lung Cancer - Stro (StroNSCLC) host-NSCLC tumor microenvironment model system consists of human primary fibroblasts co-cultured with a NSCLC cell line, NCI-H1299, and human peripheral blood mononuclear cells. These conditions model the host stromal-tumor microenvironment by capturing the complex interactions between tumor cells, the host stromal network, and infiltrating immune cells recruited into the tumor mass.	VCAM-1, uPAR, Col-III, IP-10, EGFR, HGF, PAI-1, PBMC Cytotoxicity, SRB, tPA, uPA, sGranzymeB, sPGE2, sVEGF, sIFNγ, sIL-10, sIL-13, sIL-17A, sIL-2, sIL-4, sIL-6, sMDC, sTNFα

Human Disease Modeled by the BioMAP® Platform

Panel	System		Cell Types	Diseases/ Tissues Modeled	Description	Protein Biomarker Readout
Oncology	VascNSCLC	Lung Cancer - Vasc	NCI-H1299 NSCLC cell line/ Primary human endothelial cells/ PBMC	NSCLC Oncology/ Immune Oncology: Host Vascular-Tumor Microenvironment Biology, Inflammation	The Lung Cancer - Vasc (VascNSCLC) host-NSCLC tumor microenvironment model system consists of human primary vascular endothelial cells co-cultured with a NSCLC cell line, NCI-H1299, and human peripheral blood mononuclear cells. These conditions model the host vascular-tumor microenvironment by capturing the complex interactions between tumor cells, the host vascular network, and infiltrating immune cells associated with angiogenesis.	MCP-1, VCAM-1, CD40, CD69, uPAR,IP-10, PAI-1, PBMC Cytotoxicity, SRB, sGranzymeB, sIFNγ, sIL-10, sIL-13, sIL-17A, sIL-2, sIL-4, sIL-6, sMDC, sTNFα
Fibrosis	SAEMyoF	Pulmonary Fibrosis	Small airway epithelial cells/ Lung fibroblasts	Pulmonary Fibrosis, Chronic Inflammation, Wound Healing, Matrix Remodeling	The Pulmonary Fibrosis (SAEMyoF) system models the biology of fibrotic lung diseases such as idiopathic pulmonary fibrosis. This co-culture of pulmonary epithelial cells and myofibroblasts is relevant for evaluating wound healing and inflammation-related responses in the lung.	α-SMA, MCP-1, VCAM-1, Collagen-I, Collagen-III, IP-10, I-TAC, E-Cadherin, EGFR, M-CSF, MMP-1, MMP-9, N-Cadherin, PAI-I, sIL-6, sIL-8, SRB, sVEGF, TIMP-1, uPA
	MyoF	Fibrosis	Lung fibroblasts	Fibrosis, Chronic Inflammation, Wound Healing, Matrix Remodeling	The Fibrosis (MyoF) system models the development of pulmonary myofibroblasts, and is relevant to respiratory disease settings as well as other chronic inflammatory settings where fibrosis occurs such as rheumatoid arthritis.	a-SM Actin, bFGF, VCAM-1, Collagen-I, Collagen-III, Collagen-IV, IL-8, Decorin, MMP-1, PAI-1, TIMP-1, SRB
	REMyoF	Renal Fibrosis	Renal proximal tubule epithelial cells/Lung fibroblasts	Renal Fibrosis, Chronic Inflammation, Wound Healing, Matrix Remodeling	The Renal Fibrosis (REMyoF) system models the development of kidney fibrosis. This system is relevant for inflammatory kidney diseases, nephritis, and fibrosis.	α-SMA, MCP-1, VCAM-1, Collagen-I, Collagen-III, IP-10, I-TAC, E-Cadherin, EGFR, Ker8/18, M-CSF, MMP-1, MMP-9, N-Cadherin, PAI-I, sIL-6, sIL-8, SRB, sVEGF, TIMP-1, tPA, uPA
T Cell/Autoimmune	BT	B and T Cell Autoimmunity	B cells/PBMC	Asthma, Allergy, Oncology, Autoimmunity	The B and T Cell Autoimmunity (BT) system models T cell dependent B cell activation and class switching as would occur in a germinal center. This system is relevant for diseases and conditions where B cell activation and antibody production are relevant. These include autoimmune disease, oncology, asthma, and allergy.	B cell Proliferation, PBMC Cytotoxicity, Secreted IgG, sIL-17A, sIL-17F, sIL-2, sIL-6, sTNFα
	SAg	Chronic Th1 Inflammation	PBMC/Venular endothelial cells	Autoimmune Disease, Chronic Inflammation	The Chronic Th1 Inflammation (SAg) system models chronic inflammation of the Th1 type and T cell effector responses to TCR signaling with costimulation. This system is relevant to inflammatory conditions where T cells play a key role including organ transplantation, rheumatoid arthritis, psoriasis, Crohn's disease, and multiple sclerosis.	MCP-1, CD38, CD40, E-selectin, CD69, IL-8, MIG, PBMC Cytotoxicity, Proliferation, SRB
	ITH2	Vascular Inflammation	Venular endothelial cells/TH2 blasts	Asthma, Allergy, Oncology	The Vascular Inflammation (ITH2) system models vascular inflammation (mixed Th1 and Th2 types), an environment that promotes mast cell, basophil, eosinophil, T and B cell recruitment, vascular permeability, and is pro-angiogenic. This system is relevant for diseases where Th2 type inflammatory conditions play a role such as allergy, asthma, and ulcerative colitis.	MCP-1, Eotaxin-3, VCAM-1, CD38, CD40, E-selectin, P-selectin, CD69, uPAR, Collagen IV, IL-8, MIG, PBMC Cytotoxicity, sIL-17A, sIL-17F, SRB
	HDFSAg	Tissue Inflammation	Dermal fibroblasts/ PBMC	Autoimmune Disease, Chronic Inflammation, Rheumatoid Arthritis	The Tissue Inflammation (HDFSAg) system models chronic inflammation of the Th1 type and T cell effector responses to TCR signaling with costimulation. This system is relevant to inflammatory conditions where T cells play a key role including rheumatoid arthritis, psoriasis, Crohn's disease, fibrosis, and wound healing biology.	MCP-1, VCAM-1, Collagen I, IP-10, MMP-1, sIL-10, sIL-17A, sIL-17F, sIL-2, sIL-6, SRB, sTGFb, sTNFα, sVEGF, IL-8, MIG, MCSF

Learn More About BioMAP® from Scientific Literature

DiscoverX Publications

1 E. L. Berg, *et al.* "Elucidating mechanisms of toxicity using phenotypic data from primary human cell systems-a chemical biology approach for thrombosis-related side effects," *International Journal of Molecular Sciences*, vol. 16, no. 1, pp. 1008–1029, 2015.

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3 E. L. Berg, "Systems biology in drug discovery and development," *Drug Discovery Today*, vol. 19, no. 2, pp. 113–125, 2014.

4 E. L. Berg and A. O'Mahony, "Complex primary human cell systems for drug discovery," in Human-based Systems for Translational Research (R. Coleman, ed.), RSC Drug Discovery, pp. 88–109, *The Royal Society of Chemistry*, 2014.

5 N. C. Kleinstreuer, *et al.*, "Phenotypic screening of the ToxCast chemical library to classify toxic and therapeutic mechanisms," *Nature Biotechnology*, vol. 32, no. 6, pp. 583–591, 2014.

6 E. L. Berg, *et al.*, "Building predictive models for mechanism-of-action classification from phenotypic assay data sets," J*ournal of Biomolecular Screening*, pp. 1260–9, 2013.

7 J. A. Lee and E. L. Berg, "Neoclassic drug discovery the case for lead generation using phenotypic and functional approaches," *Journal of Biomolecular Screening*, p. 1087057113506118, 2013.

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9 G. Bergamini, *et al.*, "A selective inhibitor reveals PI3Kγ dependence of T(H)17 cell differentiation," *Nature Chemical Biology*, vol. 8, no. 6, pp. 576–582, 2012.

10 E. L. Berg, *et al.*, "Chemical target and pathway toxicity mechanisms defined in primary human cell systems," Journal of *Pharmacological and Toxicological Methods*, vol. 61, no. 1, pp. 3–15, 2010.

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13 E. L. Berg, *et al.*, "Approaches to the analysis of cell signaling networks and their application in drug discovery.," Current Opinion in *Drug Discovery & Development*, vol. 8, no. 1, pp. 107–114, 2005.

14 E. L. Berg, *et al.*, "Biological complexity and drug discovery: a practical systems biology approach," IEE Proceedings-*Systems Biology*, vol. 152, no. 4, pp. 201–206, 2005.

15 E. C. Butcher, *et al.*, "Systems biology in drug discovery," *Nature Biotechnology*, vol. 22, no. 10, pp. 1253–1259,2004.

16 E. J. Kunkel, *et al.*, "Rapid structure-activity and selectivity analysis of kinase inhibitors by BioMAP analysis in complex human primary cell-based models," *Assay Drug Development Technologies*, vol. 2, no. 4, pp. 431–442, 2004.

17 E. J. Kunkel, *et al.*, "An integrative biology approach for analysis of drug action in models of human vascular inflammation," The FASEB Journal, vol. 18, no. 11, pp. 1279–1281, 2004.

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Client-DiscoverX Co-Publications

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