eurofins | DISCOVERY

BioMAP Diversity PLUS Panel

Translational Insights with the Speed and Ease of *In Vitro* Evaluation

Human disease biology is complex, making it difficult to predict the impact of a molecule or biologic in the absence of a clinical trial. While animal testing answers some *in vivo* questions, most animal models do not mimic true human physiology. Common *in vitro* methods of screening and characterizing potential drugs are often one-dimensional and rarely reflect the complexity of biology seen in patients. The BioMAP® Diversity PLUS® Panel for phenotypic evaluation of candidate drugs brings drug testing as close to the clinic as possible. This approach combines predictive human primary cell-based disease models with a powerful suite of bioinformatics tools to help you make better, more clinically-relevant decisions earlier in the drug development process.

PHYSIOLOGICALLY RELEVANT PHENOTYPIC DATA PRIOR TO ENTERING THE CLINIC

The Diversity PLUS Panel was built out of a need for better *in vitro* models of human disease and is used by industry, government and academic scientists to better understand their candidate drugs, from discovery to preclinical safety and even through clinical trials. Whether rank ordering or screening thousands of compounds, Diversity PLUS phenotypic profiling and screening provides the data on efficacy and safety to enable informed decisions that move the right molecules to progress to the clinic.

BioMAP Profile of Trametinib Provides Insight into Efficacy, Safety and Mechanism of Action

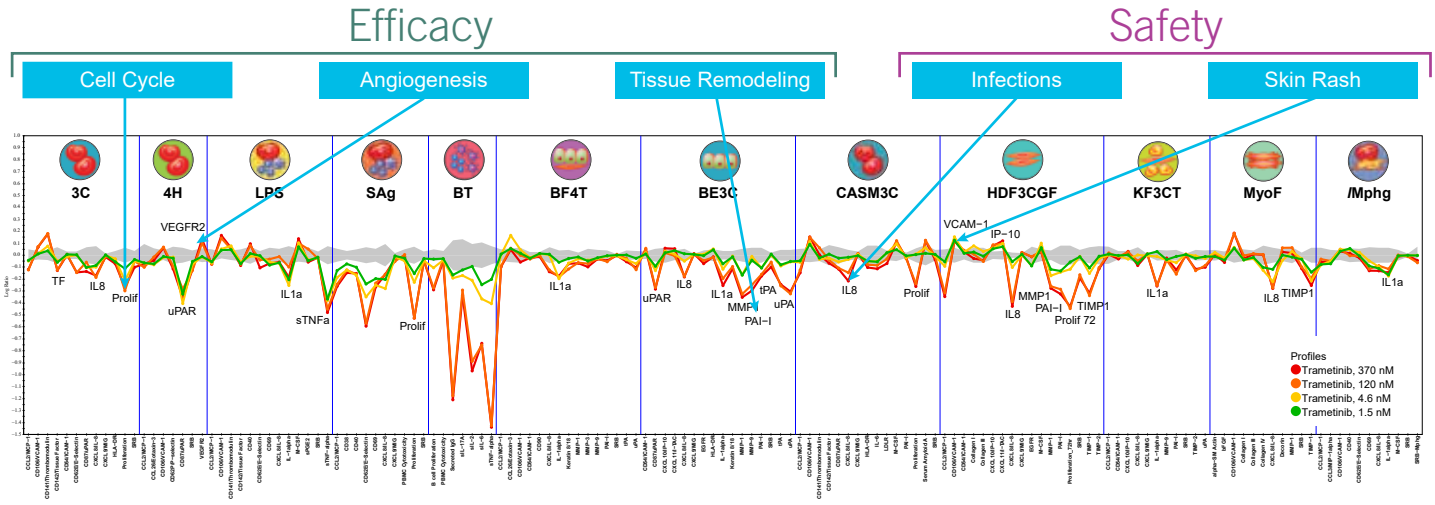

Figure 1. Trametinib (Mekinist™ or GSK-1120212), a MEK1/2 inhibitor approved for the treatment of metastatic melanoma, profiled at 4 concentrations (red, orange, yellow and green) in the BioMAP Diversity PLUS Panel. Trametinib decreased proliferation and increased VEGFR2 expression in two models of vascular inflammation (3C and 4H), and decreased PAI-1 in a lung inflammation model. These changes can be attributed to efficacy of trametinib in patients. Additionally, decreased IL-8 and increased VCAM-1 have been identified as important signatures in drugs associated with infections or skin rash, respectively. The remaining annotated peaks represent biomarker readouts that demonstrate statistically significant change during treatment as compared to historical controls (the range of historical vehicle control data is represented by the grey region closest to the axis).

WHAT IS THE BioMAP PLATFORM?

The BioMAP® Platform is a method of phenotypic profiling of candidate drugs that enables correlation of compound activity with clinical outcomes by providing insight into mechanisms of action, dosing, efficacy, and safety-related effects. To achieve this, the platform uses stimulated human primary cell-based assays (BioMAP systems) to recapitulate human disease that can be "treated" with your compound. The resulting changes in up to 148 biomarkers form a biomarker profile for the compound. By comparing your compound's biomarker activity profile against a database of more than 4,500 reference benchmark compounds, the BioMAP platform can provide you with the highly valuable insights needed to make the best decisions regarding compound advancement.

WHAT IS Diversity PLUS?

THE Diversity PLUS® PANEL CONSISTS OF:

- 12 individual human primary cell-based co-culture systems combined into one service to predictively model drug effects on multiple tissues and disease states
- 148 clinically relevant biomarker readouts determined by careful curation of clinical data
- Data from >4,500 reference compounds which underpin powerful and predictive bioinformatics tools

WHAT CAN Diversity PLUS DO FOR YOU?

THE Diversity PLUS PANEL IS USED BY INDUSTRY AND GOVERNMENT LEADERS TO:

- Prioritize candidates based upon on- and off-target effects, cell potency, and mechanism of action
- Predict safety and toxicity prior to initiating *in vivo* testing or clinical trials
- Perform competitive benchmarking to thousands of clinical compounds
- Identify new indications for drug repurposing and repositioning

BioMAP Diversity PLUS Panel Service Details

Service	Compound profiling (chemicals or biologics) of 148 biomarker readouts across 12 systems at 4 concentrations.
Examples of Analysis Performed	Identification and biological interpretation of relevant biomarker activities that are increased or decreased in comparison to vehicle control. Unsupervised search for phenotypically similar compounds from the BioMAP Reference Database of more than 4,500 reference compounds, approved drugs, and experimental agents. Benchmarking (optional). A direct comparison of test compound to a specified reference compound from the BioMAP Reference Database.
Report Details	Eurofins Discovery provides a study report that includes: Annotation of biomarker activities with respect to biological significance, profile plots, graphical overlays of test and reference compound profiles, results of similarity search, mechanism heatMAP analysis, network cluster analysis (for three or more test agents), and expert data interpretation and analysis.

Biology Modeled by the Diversity PLUS® Panel

BioMAP System			Description
3C		Th1 Vascular	The Th1 Vascular (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
4H		Th2 Vascular	The Th2 Vascular (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: Th2-Type inflammatory conditions such as allergy, asthma, and ulcerative colitis
LPS		Monocyte Activation	The Monocyte Activation (LPS) system models chronic inflammation of the Th1 type and monocyte activation responses. This system is relevant for inflammatory conditions where monocytes play a key role, including: atherosclerosis, restenosis, rheumatoid arthritis, and other chronic inflammatory conditions, as well as metabolic diseases
SAg		T Cell Activation	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 for inflammatory conditions where T cells play a key role including: organ transplantation, rheumatoid arthritis, psoriasis, Crohn's disease, and multiple sclerosis
BT		B and T Cell Autoimmunity	The B and T Cell Autoimmunity (BT) system models T cell dependent B cell activation as would occur in a germinal center. This system is relevant for diseases/conditions involving B cell activation and antibody production, including: autoimmune disease, oncology, asthma, and allergy
BF4T		Lung Disease	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, asthma, pulmonary fibrosis, as well as COPD exacerbations
BE3C		Lung Inflammation	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
CASM3C		Cardiovascular Disease	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
HDF3CGF		Wound Healing and Inflammation	The Wound Healing and Inflammation (HDF3CGF) system models wound healing, fibrosis and matrix/tissue remodeling in the context of Th1 type inflammation. This system is relevant for various diseases including: fibrosis, rheumatoid arthritis, psoriasis, and stromal biology in tumors
KF3CT		Psoriasis and Dermatitis	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 psoriasis and dermatitis
MyoF		Fibrosis	The Fibrosis (MyoF) system models the development of pulmonary myofibroblasts. This is relevant for: respiratory disease settings, as well as other chronic inflammatory settings where fibrosis occurs, such as rheumatoid arthritis
/Mphg		Macrophage Activation	The Macrophage Activation (/Mphg) system models chronic inflammation of the Th1 type and macrophage activation responses. This system is relevant for: inflammatory conditions where monocytes play a key role including atherosclerosis, restenosis, rheumatoid arthritis, and other chronic inflammatory conditions

For more information and to request a customized quote, visit discoverx.com/diversityplus or contact us at phenotypicsupport@eurofins.com