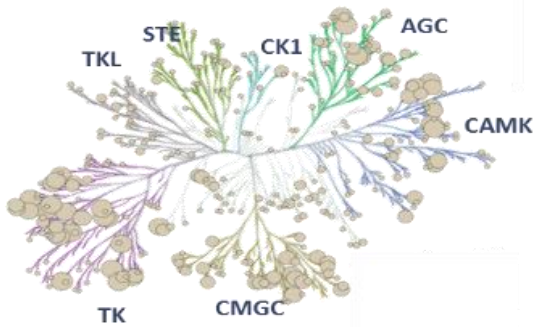
Gain ‘Kinome’ insights with the PamStation®

Measuring kinase activity provides deeper understanding of cellular signaling and target interaction, allowing pathway elucidation and biomarker discovery.

Kinases are the most intensively studied protein targets and the basis of numerous targeted therapies. However, traditional approaches study the abundance of proteins rather than their activity. This results in a knowledge gap on how cell signaling really works and only a partial understanding of your clinical samples.

Building on 15 years of experience, PamGene has developed a unique technology with unprecedented sensitivity, making real-time measurement and understanding of kinase activity possible. Our technology opens up opportunities for a wide range of rapid and non-invasive applications in the areas of fundamental science, translational research and diagnostics.



PamChip Kinome coverage

Based on current online knowledge, we compiled a comprehensive, integrated database of potential kinases that are linked to the peptides on the PamChips. This corresponds to ~350 unique kinases in literature, covering the majority of the Kinome.

The benefits our technology brings to your research

- **Wide coverage** – 380 Phosphosites are used to cover the majority of the Kinome.
- **Kinase activity-based** – Direct inhibitor effects on kinases can be measured.
- **Sensitive** – Only small amounts of protein input (0.5 to 5 µg per array) are required, thus making the assay more sensitive than alternative approaches.
- **No specific antibodies** – The quality of the data is not dependent on the specificity of phospho-antibodies since specificity is derived from the 380 phosphosites.
- **Full-length kinases** – We can measure kinase activity of full-length proteins from lysates of several cell lines and tissues, not offered by other recombinant-based kinase activity assays.

Get in touch with our team to learn how to apply our technology in your research.

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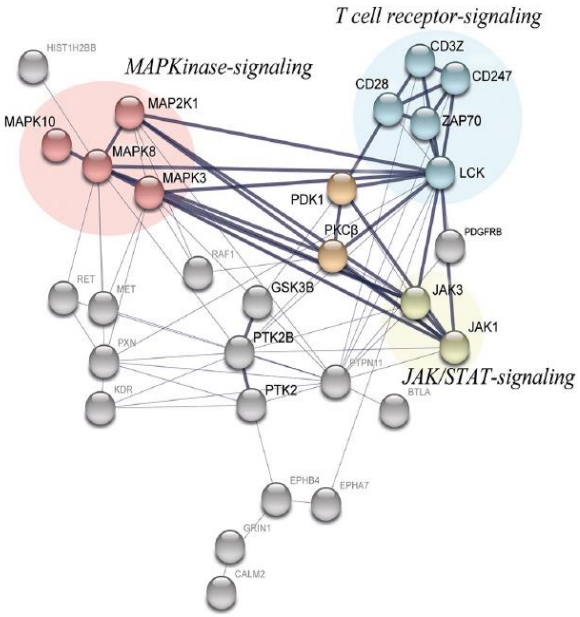
Numerous applications

Our unique and proven technology will provide you with robust measurements, and novel insights. PamGene's technology has been applied in hundreds of published studies. A selection of these studies can be found on the PamGene website.

Pathway Elucidation



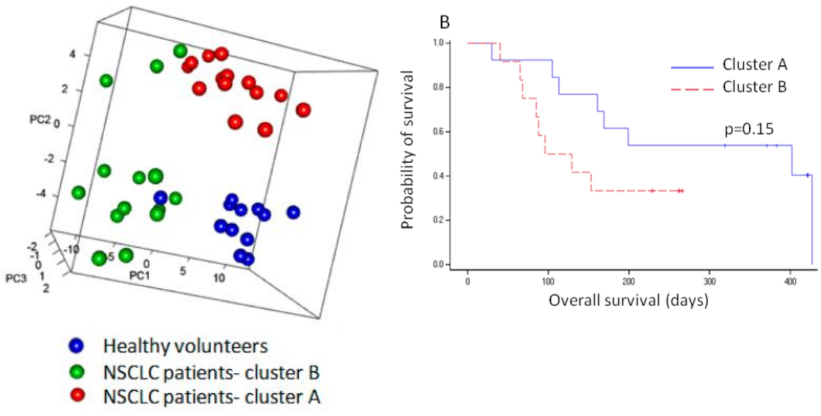
Dive deeper into relevant pathways in immune signaling, cancer, CNS, metabolic disorders or cardiovascular diseases. Elucidate pathways in mutants, knockouts, or as a result of *in vitro* treatments. Deduce pathways altered in drug responses or drug resistance Discover a broad range of pathways *apriori* without knowledge of key players and without depending on specific antibodies.

Example: PamGene's Kinome activity profiling was used to obtain a molecular understanding of TNFα signaling on IL-17 expression in the human effector T-cells (Treg). Strong associations were revealed with kinases involved in TCR, JAK, MAPK, and PKC pathway signaling in the involved networks, and were confirmed by small-molecule-based inhibition of TCR and JAK pathways that prevented IL-17 expression. These findings have implications in optimizing anti-TNF-based therapy and Treg-based cell therapy.

Source: TNFa-Signaling Modulates the Kinase Activity of Human Effector Treg and Regulates IL-17A Expression. P. Urbano, et. al. Front Immunol. 10:3047 (2020).

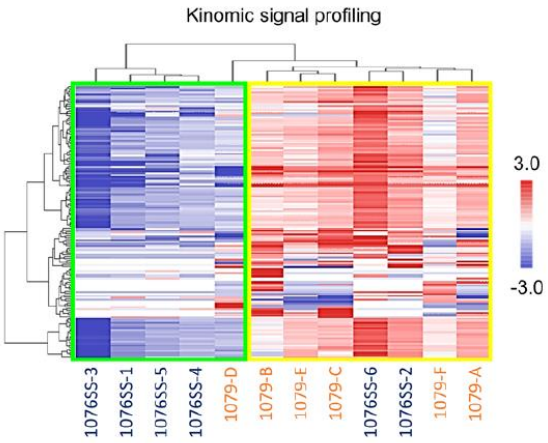
Biomarker Discovery

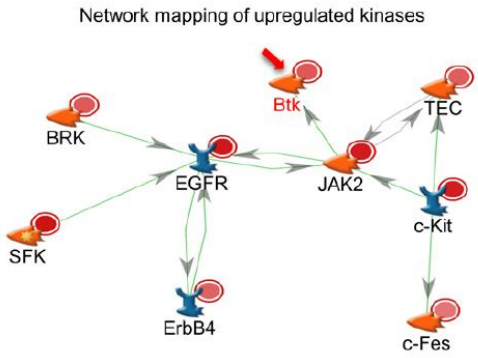
Use our on-chip pharmacology capabilities that lend a new approach to discovering therapy-predictive, disease specific and prognostic or pharmacodynamic biomarkers.



Example: Biomarkers of response to nivolumab therapy were investigated using PamGene's serine/threonine kinase (STK) activity assay in PBMC from lung cancer patients before nivolumab initiation and on day 14 after the first administration. Two clusters of patients (A and B) were identified that differed in overall survival (OS), PD-L1 tumor cell score and CD8+ cells, highlighting the benefit of basal Kinomic profiling to identify therapy response biomarkers.

Source: Differential Kinase Activation in Peripheral Blood Mononuclear Cells from Non-Small-Cell Lung Cancer Patients Treated with Nivolumab. G. Noé et. al. Cancers (Basel). 11, 762 (2019).





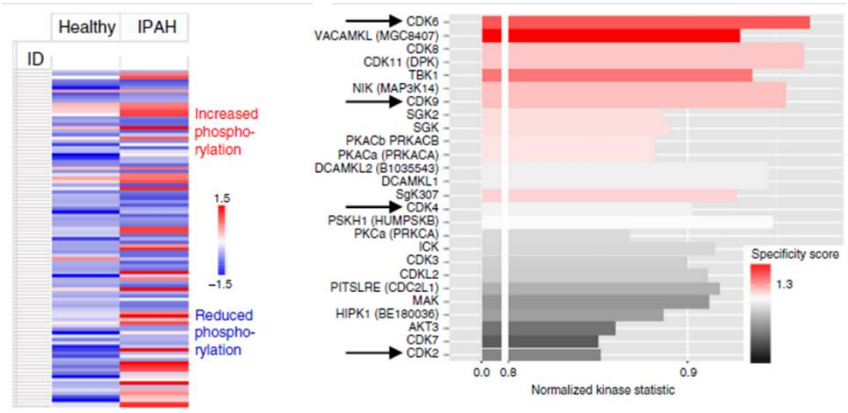
Disease model characterization

Perform comparative analysis of your diseases model (disease or mutant with healthy or wild type counterparts) to gain information related to the disease-specific Kinome or signal transduction pathways.

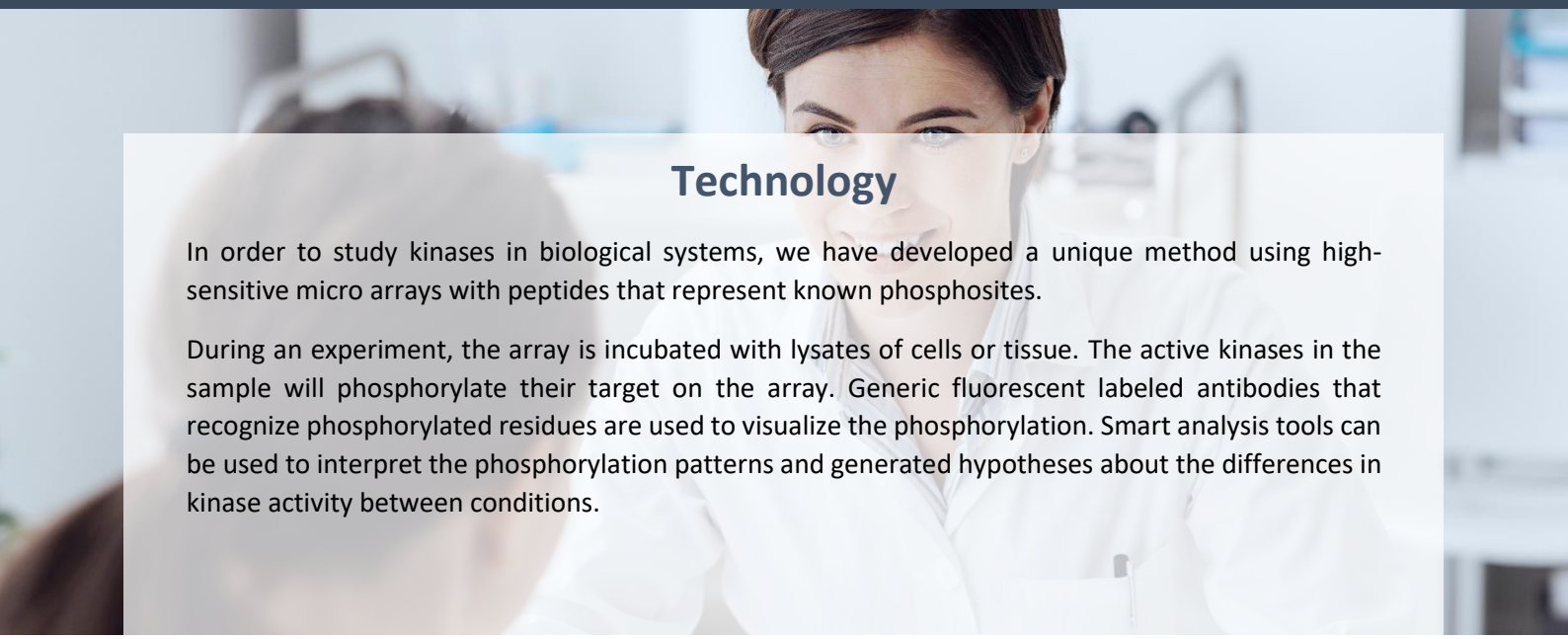
Example: Distinctive Kinomic profiling in glioblastoma demonstrated spatial heterogeneity, with elevated activity of BTK kinase in the classically hypoxic and therapy-resistant GBM tumor core compared to the infiltrating edge, indicating that selective inhibition of BTK may prove highly beneficial, to guide new therapeutic approaches**.** *Source: Intratumoral spatial heterogeneity of BTK kinomic activity dictates distinct therapeutic response within a single glioblastoma tumor. A. Ibrahim et. al. J Neurosurg. Oct 18:1-12 (2019).*

Target Discovery & Interaction

Discover novel drug targets to guide therapeutic options and drug development, where no prior target information is required. Find the mechanism of action of small molecule inhibitors or develop (surrogate) PD-markers.



Example: Kinome profiling revealed increased activity of the cyclin-dependent kinases (CDKs) signaling pathways in pulmonary arterial smooth muscle cells, from Idiopathic pulmonary arterial hypertension (IPAH) patients compared to healthy cells. This was further confirmed by specific CDK inhibition by dinaciclib and palbociclib which decreased PASMC proliferation via cell cycle arrest and interference with the downstream signaling. In two experimental models of IPAH, palbociclib showed beneficial effects, demonstrating that inhibition of CDKs may be a therapeutic strategy in IPAH. *Source: Targeting cyclin-dependent kinases for the treatment of pulmonary arterial hypertension. A. Weiss et. al. Nat Commun. 10(1):2204 (2019).*



Technology

In order to study kinases in biological systems, we have developed a unique method using high-sensitive micro arrays with peptides that represent known phosphosites.

During an experiment, the array is incubated with lysates of cells or tissue. The active kinases in the sample will phosphorylate their target on the array. Generic fluorescent labeled antibodies that recognize phosphorylated residues are used to visualize the phosphorylation. Smart analysis tools can be used to interpret the phosphorylation patterns and generated hypotheses about the differences in kinase activity between conditions.

PamStation

The CE-marked PamStation is a fully automated instrument designed for processing PamChip microarrays. The PamChip is available with either phospho-tyrosine kinase (PTK) or serine-threonine kinase (STK) substrates. 12 PamChip arrays can be processed simultaneously on the PamStation. It is operated through a dedicated computer with access to advanced software for data acquisition and analysis, called: Evolve and BioNavigator.

Kinase assay workflow

Step 1
<1 mm^3 tissue
or ~10.000 cells

Step 2
Instrument operation

Step 3
Data analysis and pathway knowledge