Biomarkers Predicting Response to Therapy

PamGene’s Biomarker Services in Immuno Oncology & Diagnostics Development

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PamGene’s approach

PamGene has developed a unique peptide-based microarray technology that can be used for the rapid development of mechanistic insight into signaling cascades and biomarkers. The aim herein is to support translational and (pre)clinical research. PamGene focuses its activity-proteomics services on the rapidly expanding immuno oncology area (I-O) and/or personalized anti-tumor drugs (i.e. kinase inhibitors, monoclonal antibodies).

PamGene is involved in several clinical biomarker studies in which retrospectively or prospectively tumor and blood samples of patients, including kinase (vemurafenib, dabrafenib, trametinib) and immune checkpoint inhibitors (ipilimumab, nivolumab, pembrolizumab), were analysed for their kinase and phosphatase activity profiles. These studies showed that for several cancer types the observed activity profiles of the tissues or blood could be correlated to the (non) response to specific therapies.

The substrate-specific protein tyrosine phosphatase assay is a new tool for biomarker discovery in I-O, because the I-O targets - checkpoint and immune receptors like PD1, CTLA4, LAG3, 4-1BB, CD40, CD20, OX40, TIGIT and GITR - are controlled by phosphatases.

For our services we most often use very small amounts of lysates obtained from treated and untreated cell lines, xenografts, tumor grafts and human tissues or blood samples.

Applications in Fundamental & Discovery Research
- Pathway elucidation
- Compound mode of action
- Target discovery and interaction analysis

Applications in Biomarker & Clinical Research
- Classification biomarkers
- Prognostic biomarkers
- Therapy-predictive biomarkers
- Pharmacodynamic biomarkers

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**Biomarker Development**

**Spotlight on 6 cancer types for diagnostics applications**

**PamGene’s approach**

PamGene’s unique peptide-based microarray technology enables researchers to determine the activity of kinases in tumour cells of cancer tissues. Cancer is a top priority disease worldwide, and using our platform, we can identify signaling defects in tumour cells by profiling kinase activities and test if kinase inhibitor drugs actually work on the tumour of the patient, thereby predicting drug effects prior to therapy. This approach is also effective in predicting immuno-oncology therapy.

**A step towards precision medicine**

PamGene’s technology enables translational medicine by starting with patient material and looking for the comparative effects of existing and new medicines. In this approach, we measure “drug on a chip” effects with small amounts of tumour tissue, cells, blood and other biopsy material. Through collaborations in various national and international clinical centers, we have shown the predictive value of this method to distinguish (non-) responding patient populations especially for some cancer types, where there is a very poor chance of survival due to the inadequacy of current treatments.

Our biomarker tests can also provide alternatives to fine-tune existing treatments such as chemotherapy and radiation, to reduce over treatment. Here we can exclude non-responders to therapy so that patients could experience less discomforts from side effects. PamGene intends to further develop a diagnostics pipeline for cancer treatment.

**Projects and Partnerships**

PamGene’s diagnostics portfolio is rapidly evolving, and we have shown proof of concept now in several cancer programs and with various clinical partners in The Netherlands and abroad. We are currently embarking on verification and validation studies in lung and melanoma patients. Please contact us on these partnerships or to learn more on the application of the peptide platform in clinical practice.

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1. Melanoma THerapy respOnse Diagnostics
2. Markers of Response to chemoradiation on Esophageal cancer

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**Phase 1**

**Phase 2**

**Phase 3**

**Discovery**

- Proof of Concept
- Candidate BM

**Verification**

- Confirmation trial
- Retrospective

**Validation**

- Multi-center
- Prospective
- Regulatory approval

From a candidate biomarker to diagnostics tests

**Breast cancer**

With Dutch healthcare insurer CZ, the Center for Personalized Cancer Treatment (CPCT) and VitrOnics Healthcare (VHH) as partners, PamGene aims to develop a new protocol which will preselect women who will have a higher chance of benefitting from treatment with exemestane and everolimus.

**Lung cancer**

In an EU Eurostars project with UMC Groningen and GenXPo GmbH, Germany as partners, PamGene aims to develop protocols to preselect patients benefitting from targeted lung cancer therapy with new kinase inhibitors and immuno-oncology therapy.

**Melanoma**

In the METHOD1 project with Jules Bordet Institute Brussels, Radboud UMC Nijmegen, LUMC Leiden, VitrOnics Healthcare (VHH) and Dutch Enterprise Agency (RVO) as partners, PamGene aims to develop methods to preselect patients benefitting from targeted and immuno-oncology therapy.

**Oesophagus cancer**

In the MORE2 project with Medisch Centrum Leeuwarden (MCL), Radboud UMC Nijmegen and Stichting De Friesland as partners, PamGene will contribute in co-investigating oesophageal cancer patients who will have a higher chance of benefitting from surgery after chemo-radio therapy.

**Renal cancer**

In the Euro TARGET project (TArgeted therapy in Renal cell cancer: GEnetic and Tumour related biomarkers for response and toxicity), in partnership with 10 EU groups in the EU FP7, PamGene aims to investigate new strategies for targeted therapy of patients with renal cell carcinoma.

**Uveal melanoma**

In the new European Horizon project UM Cure 2020 (New therapies for Uveal Melanoma), in partnership with 12 EU groups, PamGene aims to identify and validate novel therapeutic approaches for the treatment of uveal melanoma patients.

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PamGene’s Services and Products

Our Partnerships

PamGene technology has numerous applications in diagnostics and clinical research.

Our Services

Our kinase activity profiling services are fully tailored to your needs. We offer Services in immuno oncology as well as diverse preclinical and clinical research.

Our Products

The PamStation®12 and PamChip®4 products can be purchased worldwide through us or our distributor network.

Please contact us for more information about Partnership opportunities, Services, and Products at info@pamgene.com.