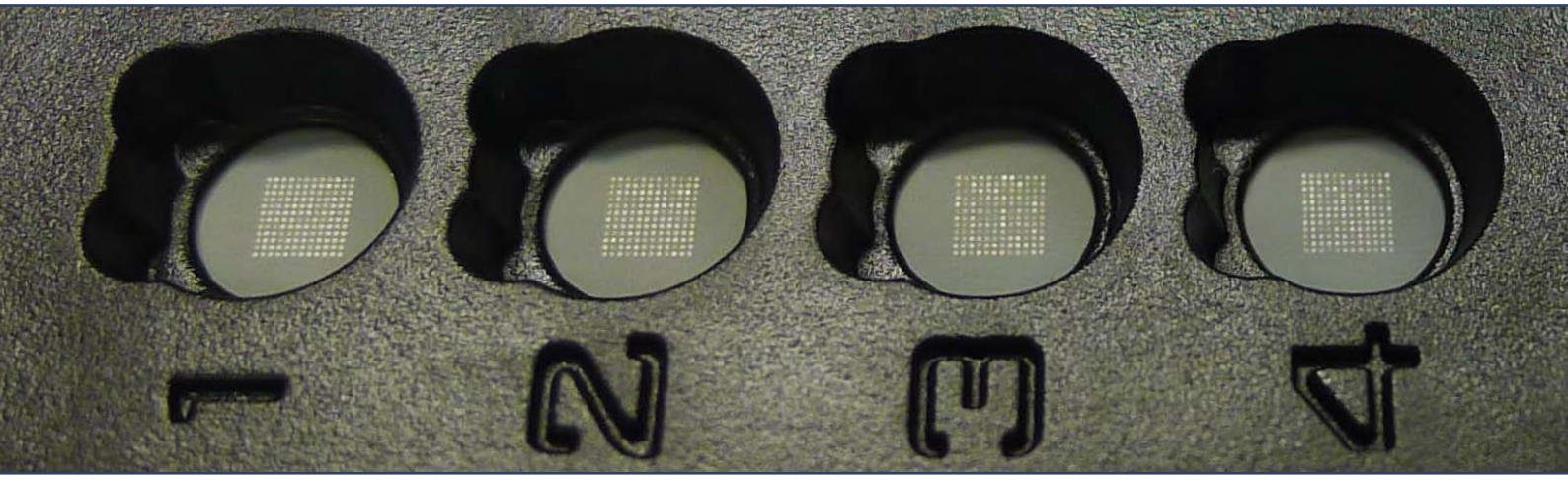
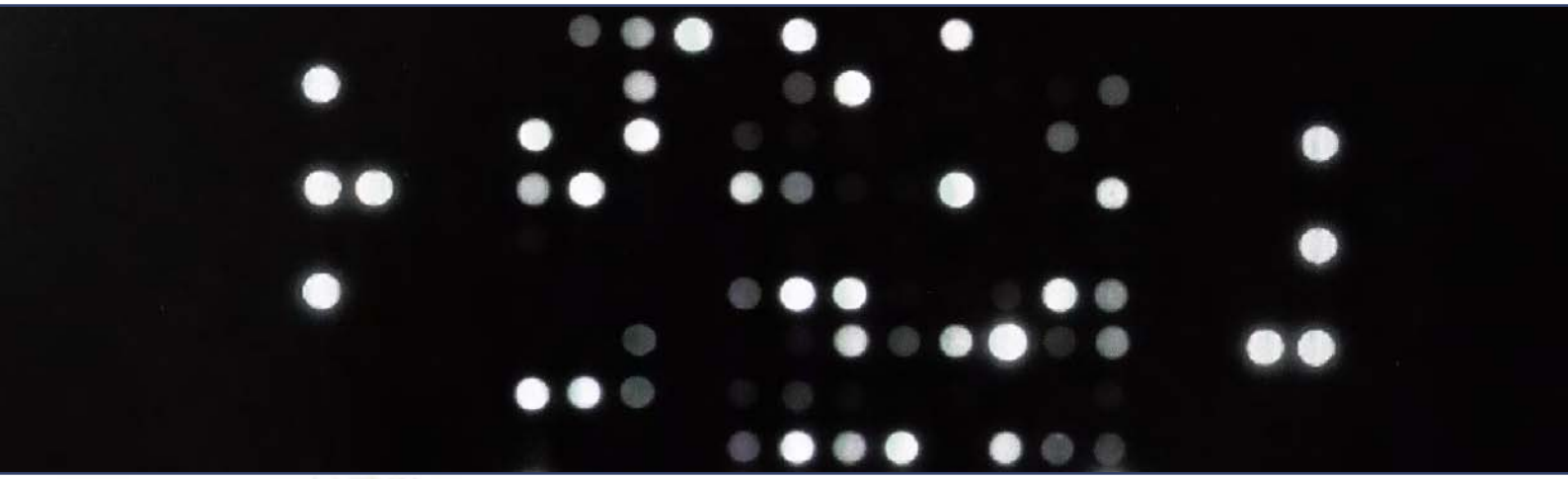
NUCLEAR RECEPTOR FUNCTION

PEPTIDE ARRAYS FOR MULTIPLEX KINETIC MEASUREMENTS

ROBUST INSTRUMENTATION • USER FRIENDLY SOFTWARE





PamGene

KINETIC DATA AT YOUR FINGERTIPS!

NOVEL PLATFORM FOR PROFILING NUCLEAR RECEPTOR FUNCTION USING PEPTIDE PAMCHIP® MICROARRAYS AND THE PAMSTATION® INSTRUMENT TO ACCELERATE CELL SIGNALLING RESEARCH.

Monitoring nuclear receptor activity

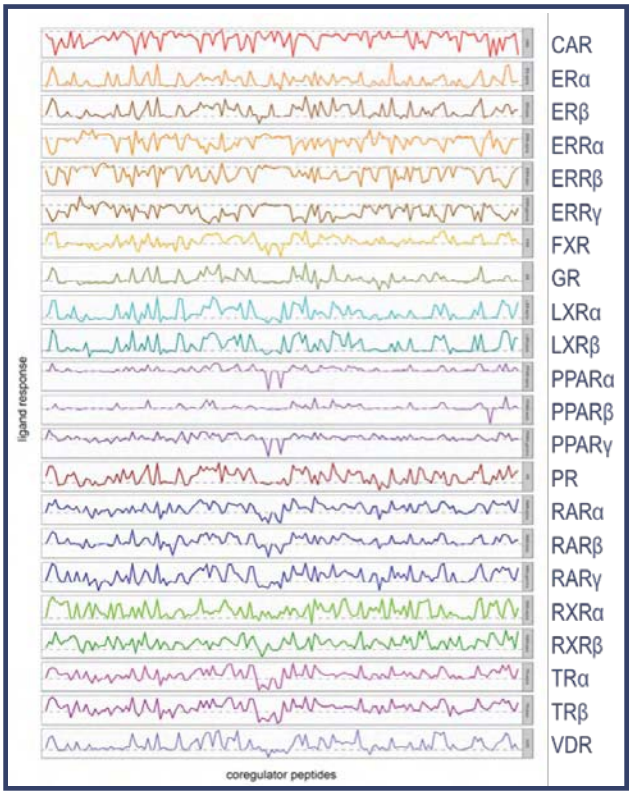
PamGene, an innovative biotechnology company in The Netherlands, has developed a new technology which enables researchers to monitor the functional properties (activity) of nuclear receptors (NRs) in recruiting cofactors. By investigating the broad spectrum of interactions of these receptors with multiple cofactors present on the PamChip®, this leads to further elucidation of normal and aberrant gene transcription. The functional read-out is especially relevant in investigations of ligand profiling, as both potency, efficacy and selectivity are monitored concomitantly.

Different research areas

Researchers worldwide are using this innovative platform to accelerate their research into NRs and NR ligands. The research areas vary from immunology, cardiovascular diseases to cancer and diabetes.

Variety of applications

The technology is used in a variety of applications, from basic research to applied pharmaceutical sciences. Recently it has been shown that beyond using purified proteins, it is now possible to test for receptor functionality in crude cell lysates, and even tumour tissue extracts from breast cancer patients. The chip can be used in research extending to other receptors and more types of biospecimens.



22 different NHR aplications

Assay protocols for 22 different nuclear receptors, have been developed. Modulation of receptor binding (y-axis) to each individual coregulator on the array (x-axis) by a reference (ant-)agonist is profiled. Modulation profiles of known and unknown profiles can be compared for compound classification and elucidation of mechanism of action.

A COMPLETE, MULTIPLEX SOLUTION FOR LOOKING AT NUCLEAR RECEPTOR FUNCTION:

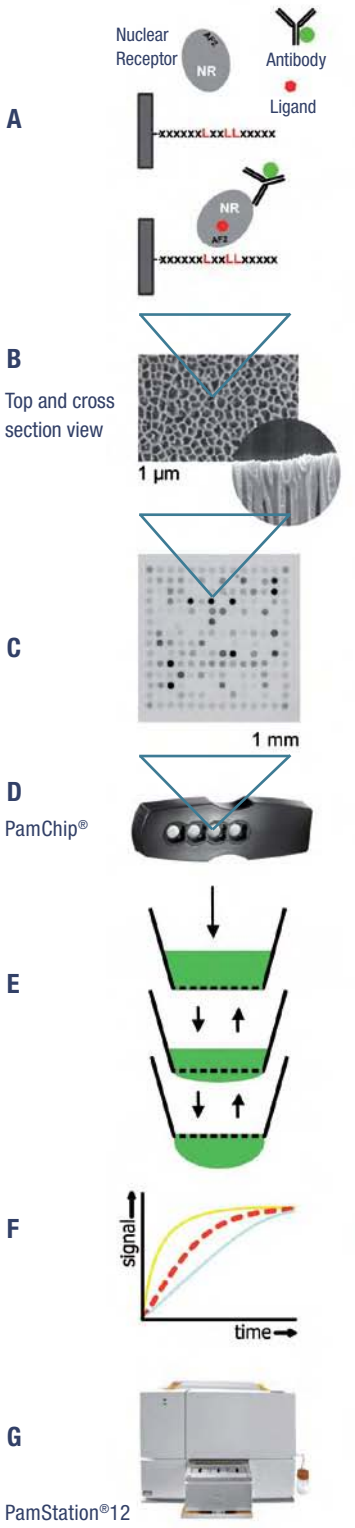
• TRUE FUNCTIONAL PROTEOMICS • HIGH THROUGHPUT KINETICS

Measurements - The technology is based on measuring nuclear receptor coregulator binding. The peptides are immobilized on a dedicated microarray which allows multiplex measurements. Fluorescently labeled anti-nuclear receptor antibodies are used to detect binding (fig A).

The microarrays are made of a highly porous ceramic membrane (fig B). Some 53 or 155 peptide coregulator motifs are immobilised per microarray (fig C). A PamChip® consists of four arrays (fig D).
The assay as shown in figure A detects NR binding present in cells or tissue lysates kinetically in about one hour (fig F).
The workstation does this by moving the sample solution up and down through the array providing the nuclear receptors maximal opportunity to bind with the peptides on each array (fig E).

Capture - When the sample solution is placed under the microarray, the CCD camera in the workstation takes an image of each array. A fully automated workstation called PamStation® 12 does the incubation, dispensing of reagents and imaging of the PamChip® array (fig G).

This workstation usually takes 15 images during the one hour incubation period. The data analysis workflow, which includes image quantification, quality control, statistical analysis, visualisation and interpretation, can be performed with especially developed software, called BioNavigator.

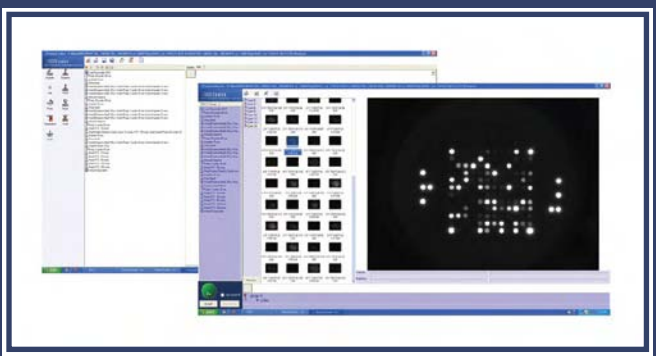


PamGene Technology

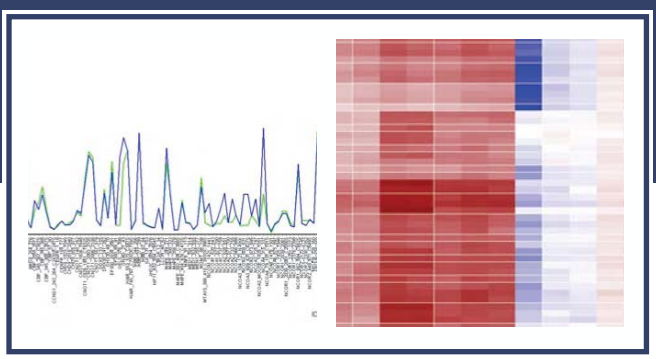
WORKFLOW FOR TESTING ON THE PAMSTATION®12

PamChip®

Pamstation®12: Load up to three PamChips®



Processing: incubate and read



Interpret data

Standard workflow - With the PamStation®12 workstation and PamChip® array you are able to measure nuclear receptor function. The measurements show the binding of the NR in the sample to coregulator driven peptides immobilized on the array. For the estrogen receptor, this assay can be performed with recombinant nuclear receptors and in lysates of cell lines or tissue via a real time fluorescent read-out, using labelled antibodies.
Between one and twelve arrays per run can be tested on the PamStation®12. A run takes about one hour. The progress of the reaction is monitored in real time by images taken every five minutes. The BioNavigator software suite, developed by PamGene, enables you to quantify binding and perform data analyses.

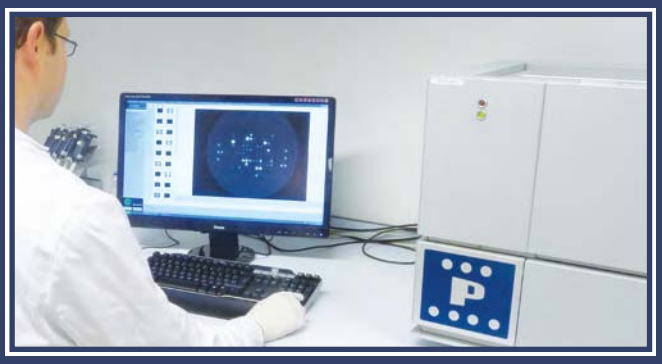
PamAcademy is one of PamGene's new initiatives to help you successfully apply our technology to enhance your functional proteomics research. We share our experience and expertise with you so that you can reach your goals faster. It covers a range of topics from sample preparation to interpretation of complex data. We offer training modules for protocols for each assay in our product portfolio. PamAcademy empowers you to use the capabilities of PamGene's BioNavigator software for data visualization, computation and interpretation. The BioNavigator education modules allow you to progress from a basic to an advanced user enabling knowledge integration of PamChip data. With hands-on training tailored to your own data, you can directly apply your knowledge to your research goals. PamAcademy will assure continued support for you, so that you know we are always interested in your success.

A FUNCTIONAL PROTEOMICS - A MULTIPLEX SOLUTION FOR NUCLEAR RECEPTOR BINDING:

- MULTIPLEX • HIGH THROUGHPUT KINETICS • USER FRIENDLY SOFTWARE
- RESULTS IN ONE HOUR

PamChip®

Pamstation®12: Load up to three PamChips®



Processing: incubate and read

Interpret data

PAMGENE PRODUCTS

Description	Article code
PamStation®12 instrument PamStation®12 Desktop PC Evolve Instrument Control software BioNavigator Data Analysis software	31500
Nuclear Receptor PamChips® (53) for PamStation®12 , 12 pcs	32502
Nuclear Receptor PamChips® (155) for PamStation®12 , 12 pcs	32503
BioNavigator 6 stand-alone version	59012
BioNavigator 6 renewal fee (per year)	59013
BioNavigator 6 additional user fee (per year)	59014
Bioinformatic support	59010
Basic training for Nuclear Receptor assays (instrument handling, assay training and data analysis)	33200

PamGene International B.V. offers advanced trainings for a broad range of PamStation®12 applications, please contact your local sales representative for further information.

CUSTOMER SUPPORT

PamGene International B.V.

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Since it was founded in 2001, PamGene has successfully developed and marketed its patented PamStation® instrumentation and the PamChip® arrays which are used in a variety of life sciences applications, especially in oncology. The company is now the #5 SME (Small and Medium Enterprise) in The Netherlands patent-wise and has introduced a number of significant innovations in its field. This work has been performed in close collaboration with many local and international partners in industry and academia.

PamGene