

## Overview

varionostic is Europe's leading expert for **DNA methylation analysis** using pyrosequencing. We offer our customers from industry and academia outstanding tailored services from assay design to data analysis. Scientists can also profit from our predesigned methylation assays developed within our own research facilities. Our unique specialised competence is the basis for highest quality in **epigenetic research** and service to **oncology**.

Additional services for epigenetic research include genotyping, allele quantification, short read sequencing and species identification. With our state-of-the-art lab we can detect all types of snips, polymorphisms and mutations. Besides human samples, the company also runs typing of BACs and other species.

### Research:

Together with partners from clinical research, varionostic is performing its own epigenetic research. Our objective is to continuously improve our service, in particular by developing predesigned methylation assays.

Research partners include:

- Institute for Pathology, University Hospital Ulm
- Institute for Forensic Medicine, University Hospital Ulm

### Network:

We are member of an extensive scientific network and have continuous access to the latest technologies, research and developments. Our scientific network includes:

- EPIGENOME Network of Excellence - The focal point for the European research community
- German Genetics Society
- German Chemical Society (GDCh)
- Consortium of Genetical Diagnostics (AGD)
- BioRegionUlm
- BioRegioSTERN

varionostic is in strong cooperation with pathologists of Southern Germany: we perform validated molecular marker tests relevant in modern pathology.

## Profile

## Network / Partners

## Services

As with all scientific research projects, a thoroughly planned assay is key to success. When it comes to quantitative DNA methylation analysis the assay design is of high importance. Based on our experience we assist you from the very beginning of a project. We give advice on the complete assay design customised to the needs of your specific question, timeline and budget. This includes technical advice such as primer and PCR specifications to be used for best results as well as recommendations on how to best organise the project.

Within a certain project varionostic can cover the complete process from assay design to the interpretation of the data. It is also possible to share resources with customers if a partner wants to deliver parts of the workflow itself.

Quantitative DNA methylation analysis gives valuable information on the **gene activity** in the human genome under certain conditions. The methylation level of specific regions of the DNA is especially important for cancer research. varionostic, as THE methylation expert, gives you quantitative data on the methylation of the CpG regions and single CpGs you are interested in.

We use pyrosequencing as the "gold standard" of genetic analysis for methylation analysis. Pyrosequencing is an accurate and fast analysis method for quantifying CpG methylation in epigenetic studies. Quantification of methylation frequencies in individual CpG sites is highly reproducible due to its quantitative measurement principle, inherent quality controls, and few processing steps.

Quality controls are built-in as CpG sites are presented in the context of the DNA sequence, and controls for completion of the bisulphite conversion step can be integrated into the analysis process. Single CpG sites can be analysed as easily as the individual methylation levels of multiple consecutive CpG sites. We have also established methods for estimating global methylation.

Customized  
assay design

DNA methylation  
analysis

varionostic conducts research on its own to develop predesigned assays for cancer-relevant genes and their CpG sites. This enables you to conduct cost-efficient and high-quality methylation analysis. The following predesigned methylation assays are available i.a.:

- CDH-1, E-Cadherin
- GSTP1, Gluthation S-Transferase p1
- PTEN, Phosphatase and tensin homolog
- MGMT, O-6-methylguanine-DNA-methyltransferase
- p16, Cyclin-dependent kinase inhibitor 2A
- RASSF1A, Ras association domain-containing protein 1
- SOCS1, Suppressor of cytokin signaling 1
- and others

Additional assays are available for relevant **cancer genotyping**:

- K-RAS
- N/H-RAS
- JAK2
- BRAF
- EGFR
- C-KIT
- IDH1/2
- MSI

More assays are part of our product pipeline and are scheduled to be launched in 2010.

Quality: varionostic participates in interlaboratory tests launched by scientific societies, e.g. EGFR, KRAS.

Our customers are scientists in the fields of epigenetics and oncology based in research institutes or companies worldwide. Among our customers are:

- German Cancer Research Centre Heidelberg (DKFZ)
- Karolinska Institutet Stockholm
- University Hospital Brussels
- Swiss Federal Institute of Technology Zurich (ETH)
- Charité Universitätsmedizin Berlin

Also we serve physician (oncology, molecular pathology) with complete analytical workflows to enable fast and reliable diagnostics to their patients.

References available on request.

## Predesigned assays

## References

## Press releases / Media information (selected)

### **varionostic launches new and innovative DNA methylation assays to be used in molecular oncology**

11/28/2008

*varionostic GmbH today announced the launch of seven innovative and ready-to-use DNA methylation assays in the field of molecular oncology (so-called predesigned assays).*

*These seven tumor markers are the first ones of a wide variety varionostic provides to enhance research on cancer. The developed epigenetical biomarkers and assay systems are CDH1, GSTP1, PTEN, MGMT, p16, RASSF1 and SOCS1.*

Europe's leading service provider for DNA methylation analysis succeed with the first assays brought onto the market as a result of an ambitious R&D collaboration with the Institutes of Pathology and Forensic Medicine of the University Hospital of Ulm (Germany). This cooperation is funded by the Federal Ministry of Economics and Technology within the ProInnoII programme.

„It's just great and we're pleased that we and our colleagues from academia were able to launch these functional and reliable assays for DNA methylation today. Together we finalized the research and developmental work in a very short turnaround time,“ said varionostic's CEO, Uwe Gerstenmaier.

The mentioned markers are of relevant genes involved in tumorigenic processes. „In addition to other biomarkers which we are running on the basis of genotyping, e.g. the K-RAS testing for metastatic colorectal cancer, we enlarged our portfolio for oncological research topics.“

More validated and high-performance methylation assays will follow within the first quarter of 2009 to support epigenetical research and to raise the understanding of tumorigenesis.

varionostic's pipeline also includes determining testing systems to apply in emerging regenerative medicine and stem cell biology.

### **varionostic detects mutations of K-RAS oncogene to support reliable therapy options in colorectal cancer**

08/26/2008

*varionostic GmbH has developed a reliable test system for detecting K-RAS mutations in co-operation with the Institute for Pathology of the University Hospital Ulm (director Prof. Dr. Peter Möller).*

*These tests could be an additional tool for targeted therapies of patients with colorectal cancer. Patients could benefit from newly developed cancer therapies depending on the genotype of the K-RAS oncogene.*

On the basis of Pyrosequencing® technology varionostic developed and launched a detection system to identify all relevant mutations of both codons 12 and 13 definitely. This developmental work was done together with experienced scientists of the Institut of Pathology.

„We're proud that we and our partners of pathology identified all testing samples of the latest trial of the German Society of Pathology (Deutsche Gesellschaft für Pathologie) correct and that we achieved the highest possible score“ said Uwe Gerstenmaier, CEO of varionostic.

In co-operation with Prof. Dr. Peter Möller of University Hospital of Ulm varionostic established the complete testing process starting with tissue sections and resulting in well-defined results of mutation analysis. Now for the first time there is a well-priced testing system available for all possible mutations. The assay system of the co-operation of the two partners detects not only the common 7 mutations but also additional rare ones (together 12 mutations), an assay for codon 61 is also available.

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