



## Eurofins Pharma Services

### Pharmacogenetic and Pharmacogenomic Services

#### **Eurofins Medigenomix GmbH – Professional Partner in Pharmacogenetics and Pharmacogenomics**

#### **Pharmacogenetics and Pharmacogenomics – Our Expertise**

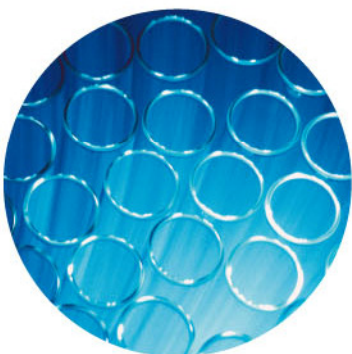
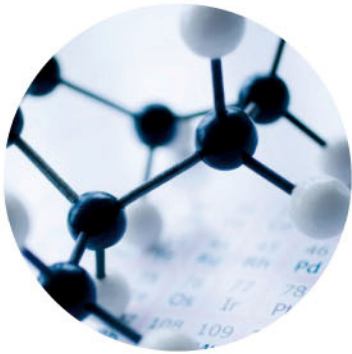
Pharmacogenetic and pharmacogenomic analysis of the effects of pharmaceutical compounds helps to realize the concept of individualized drug therapy or personalized medicine.

#### **Pharmacogenetics / Pharmacogenomics**

While **pharmacogenetics** describes genetic variations between individuals and their influence on the efficacy and side effects of drugs, **pharmacogenomics** examines interactions of drugs with the whole genome: changes of gene expression profiles which are caused by drugs are analysed

The main question is, why patients who suffer from the same disease, react completely different to an identical drug treatment: while some patients respond in the predicted way (responders), others show no response at all (non-responders). A third group of patients experience severe adverse effects under drug treatment which makes the medication process hazardous.

These differences in drug responses are largely caused by genetic polymorphisms, mostly by single nucleotide polymorphisms (SNPs) and combinations of two or more SNPs. It is the aim to discriminate responders and non-responders to certain drugs for example in the scope of clinical studies and to identify individuals at increased risk for adverse drug reactions each based on variations in relevant genes.

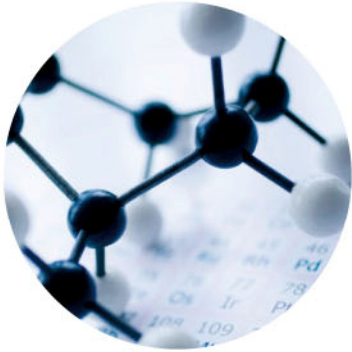




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### Pharmacogenetic and Pharmacogenomic Services

Hence, pharmacogenetics and pharmacogenomics are contributing to improve drug treatment and to enable and support the development of drugs, which are safer, more targeted and individualized.

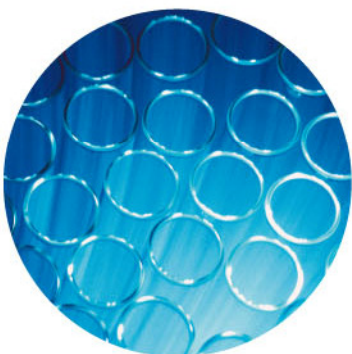


Genetic variability is seen both in the area of pharmacokinetics (absorption, distribution, metabolism and excretion, ADME) and in the area of pharmacodynamics (drug effects).

For example genetic variations can influence the activity or have an effect on the expression of the following proteins:



- **Drug metabolizing enzymes, DMEs**  
(Phase I enzymes/Cytochrome P450 enzymes, e.g. CYP2D6; Phase II enzymes, e.g. N-acetyl transferases)
- **Drug transporters**  
(Solute Carrier (SLC) – and ATP Binding Cassette (ABC) – transporters, e.g. organic cation transporters, OCTs, as members of the SLC family)
- **Drug receptors**  
(ligand controlled ion channels or class 1 receptors, e.g. glutamate receptor; G-protein coupled receptors (GPCRs) or class 2 receptors, e.g.  $\beta$ -receptor; enzymatic receptors, e.g. insulin receptor; receptors regulating gene expression, e.g. steroid hormone receptor)
- **G-proteins**  
e.g. GNAS1 or GNB3



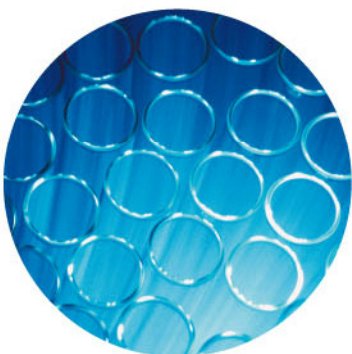
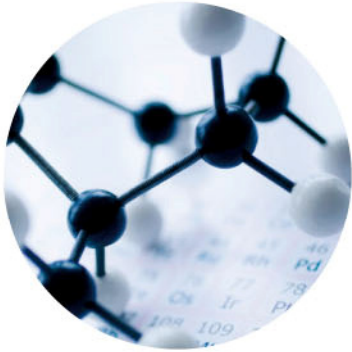
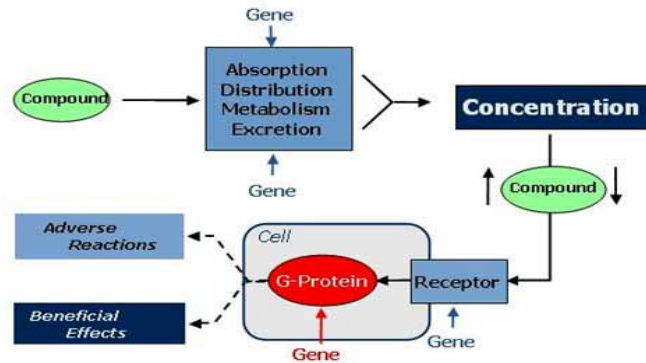


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### Pharmacogenetic and Pharmacogenomic Services

The figure below shows the pathways including positions of genes which are relevant for drug response and drug effects:

#### Genes Determine Drug Effects



Eurofins Medigenomix offers a comprehensive services portfolio for the entire drug development process, from preclinical research to clinical phase III trials. For example, we offer different genome-wide screening approaches, such as transcriptome analysis, resequencing and metagenomic analyses based on the "next generation sequencing" technology. Using state-of-the-art technologies like sequencing, TaqMan and mass spectrometry (MALDI), we offer analysis of all relevant genes, including analysis of defined SNPs within these genes or the analysis of the entire gene of interest including all exons, introns and regulatory regions, like promoters, enhancers and 5’-/3’- untranslated regions.

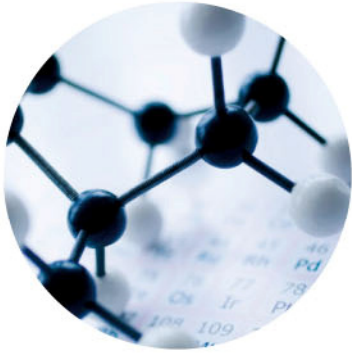
#### **One Focus: Analysis of G-Proteins**

These proteins play a major role in signal transduction from all receptors into the cell. These receptors are the main target structures of many drugs.



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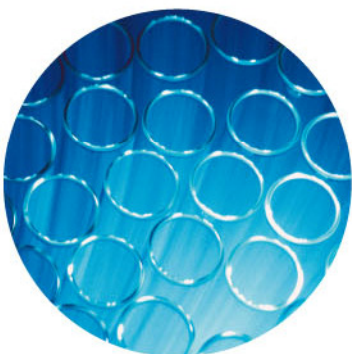
## Pharmacogenetic and Pharmacogenomic Services



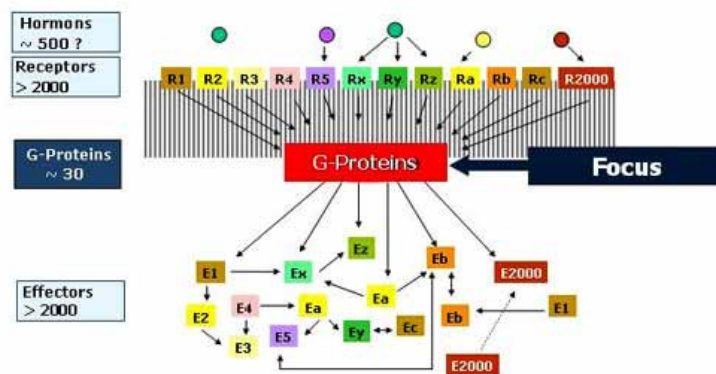
G-proteins are thus in the centre of cellular information transmission (signal transduction). Based on this approach, Professor Siffert's team at the Institute of Pharmacogenetics, University of Essen, Medical School identified patterns of genes and polymorphisms which allow prediction of drug effects on a new level of accuracy. It is now possible to predict, which patients will respond to drugs of different indications with a high probability.



The associated genetic tests have been validated in clinical trials and are the subject of patents which have been already issued and of patent applications. In addition to these genetic testing services, Eurofins Medigenomix offers with the assistance of Professor Siffert expert advice in the scope of evaluation and interpretation of results and comprehensive scientific consultancy.



### Focus on G-Protein Genes



A number of studies have shown that by using the "Drug Response Panel" (referring to analysis of polymorphisms in

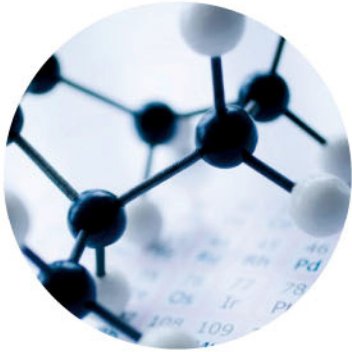


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genes coding for G proteins), drug reactions can be predicted with high precision for example for the following indications:

- Response and progress of a therapy with antidepressants
- Successful therapy of obesity treatment
- Response to anti-cancer drugs

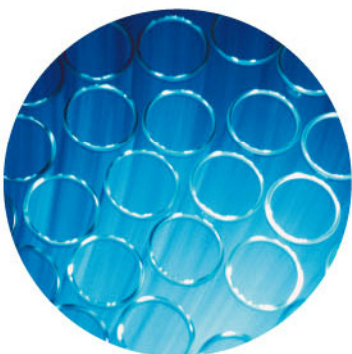


In the area of G-proteins Eurofins Medigenomix offers amongst others the analysis of G-protein-coding genes, e.g. in the scope of clinical trials or in the area of preclinical research, and exclusive / non-exclusive usage of patented genetic tests for different indications (through acquisition of license).



#### **Application of Pharmacogenetics**

Within a given indication, drugs are only effective for about 60% of all patients. Response rates in oncology are often even significantly lower (10-20%). Besides, some patients show adverse drug reactions. Precise prediction of responders to individual drugs and of patients, which show adverse drug reactions, allow individualised or personalised drug therapy. There are clear benefits for patients and doctors, but also for the pharmaceutical companies, like the following:



- Cost savings due to lower research expenses: reduced proband and patient numbers are necessary in clinical trials to reach same statistical relevance
- Possibility of re-evaluation / re-positioning of failed drugs or failed clinical trials based on pharmacogenetic aspects



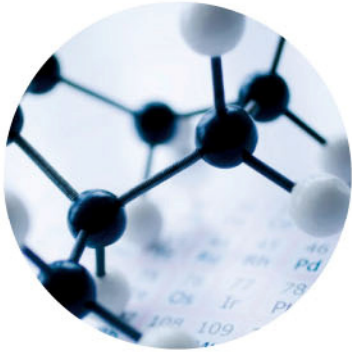
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There are several applications in the pharmaceutical industry for analysis in the area of pharmacogenetics / pharmacogenomics, like transcriptome analysis, or specific analysis of target genes.

Examples:

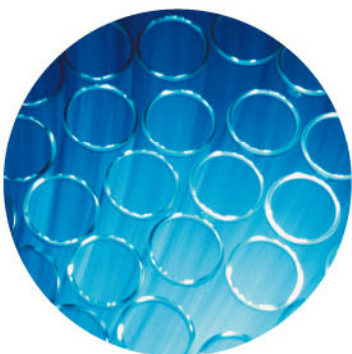
- Detection of genetic variability of drug effects on the genome level
- Analysis of drug reactions and drug toxicity on gene expression (expression profiling)
- Identification of responders / non-responders in clinical trials of phase I-IV



### Pharma Services Portfolio

Eurofins Medigenomix offers a broad spectrum of services in the areas of analysis, research and development. We offer our services for single samples as well as for batches of few to several thousand samples. We attach great importance to well-founded scientific consultancy prior to and during all projects and studies.

With our services we help you to develop agents and drugs more efficiently and economically, to use them optimally and precisely regarding their effectiveness and last, but not least, to better avoid possible adverse effects.



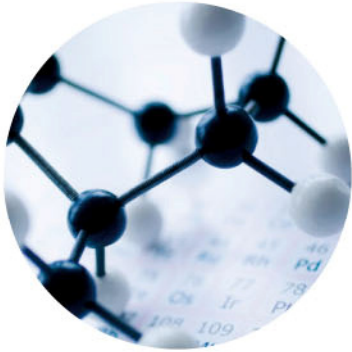
Our pharma services portfolio includes, among other things, the following services:

- Large scale DNA and RNA extraction from different sources, e.g. for Biobanking
- GLP-compliant genotyping and sequencing



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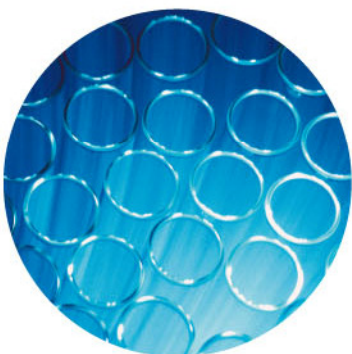
### Pharmacogenetic and Pharmacogenomic Services



- SNP, mutation and biomarker analysis
- Analysis of complete target/candidate genes
- Expression analysis
- Assay development and validation
- Scientific consultancy
- Project consultancy and project management



In addition to analysis of pharmacogenetically relevant genes (cytochrome P450, phase II enzymes, transporter, G-proteins and receptors), Eurofins Medigenomix offers likewise analysis of genes, which play an important role in clinical diagnostics, e.g. genes relevant for lactose intolerance/lactase persistence, for breast cancer or for progressive lung disease (alpha-1-antitrypsin (AAT) deficiency), and analysis of tumour markers like prostate cancer antigen 3 (ProgenSA PCA3 Assay, Gen-Probe).



Eurofins Medigenomix completes its comprehensive pharma services portfolio through addition of versatile services in the following key areas:

- Genomics: e.g. re-sequencing of individual areas of defined genes, ultra-deep sequencing on amplicon level and transcriptome-analysis/expression-profiling using "Next Generation Sequencing" platforms
- Virus and microbiological diagnostics: e.g. virus load determination, genotyping, sequencing and quantitative analyses of viruses and bacteria
- Gene synthesis

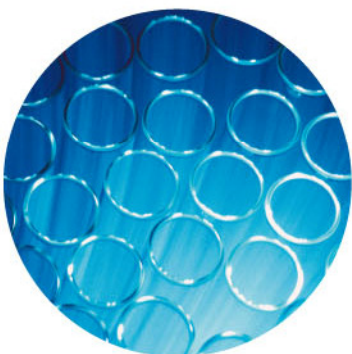
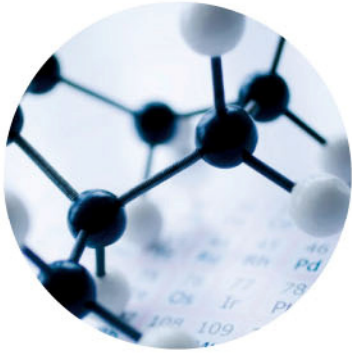


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#### **Bioinformatics**

Based on cooperation with Genomatix Software GmbH, a leading company in complex analysis and interpretation of Next Generation Sequencing (NGS) data, Eurofins Medigenomix offers state-of-the-art solutions for comprehensive genome analysis and re-sequencing projects in the scope of the drug development process. For example we offer a comprehensive service for human exome capture, targeted resequencing and data interpretation. For this service a new complete human exome array was developed, based on Roche NimbleGen sequence capture technology.



#### **Technical Equipment**



Eurofins Medigenomix is equipped with the latest technical devices for high throughput analysis allowing short turn-around times. Based on our equipment, our service portfolio and on constant investment in our competent personnel we contribute to

make drug development and therapy safer and more efficient. Amongst others we are equipped with the following devices:

ROCHE Genome Sequencers FLX  
ROCHE Genome Sequencer Junior  
ABI 3730 XL 96 Capillary Sequencers  
ABI 3100/3130xl 16 Capillary Sequencers  
Sequenom MALDI-TOF

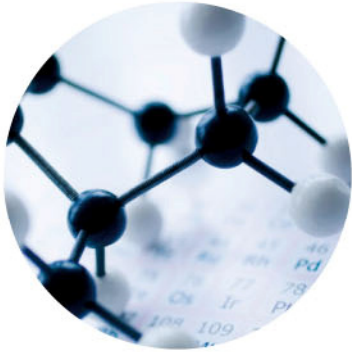




# Eurofins Pharma Services

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Real Time PCR Devices (ABI and Roche)  
Beckman Pipetting Robots  
Hamilton Robotics Systems  
Chemagen Robots, Chemagic  
Qiagen QIAcube



### Quality Management System

Eurofins Medigenomix is certified according to ISO EN 9001:2008. For the areas of Forensic Genetics, Veterinary Diagnostics and Food Authenticity Testing we are accredited according to ISO 17025:2005.

In addition, we are consistently audited by clients from the pharmaceutical industry. With a



robust quality management system in place inclusive SOPs for all workflows, validated processes and equipment, established QC and QA systems, and with our team of well-trained and highly qualified specialists, we can guarantee the highest quality of our services.



### Contact

Please feel free to discuss your project or study with us:

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