Precision Medicine
by DNA and RNA Profiling

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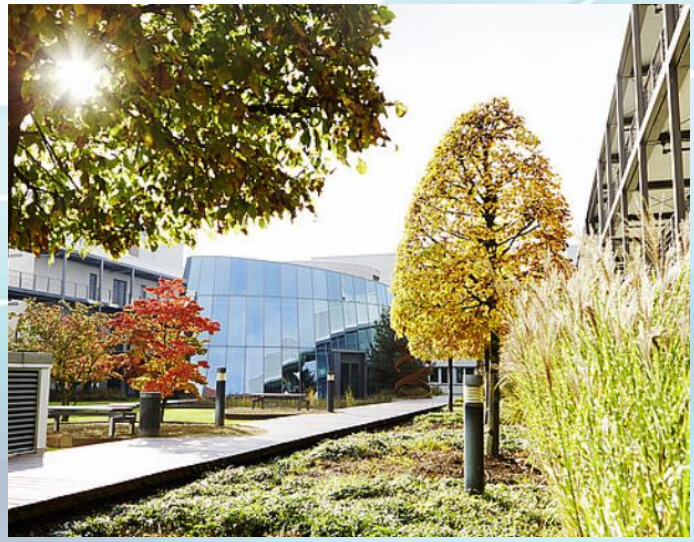
Founded	**December 2005**
Staff	**14**
Competence	**NGS-based Solutions for Precision Medicine and other fields of life science**
	Bioinformatics



GenXPro`s
“TrueQuant” Technique, Patent Approved 2016

Bundesrepublik Deutschland

Urkunde

über die Erteilung des
Patents Nr. 10 2008 025 656

Bezeichnung:
Verfahren zur quantitativen Analyse von Nukleinsäuren, Marker dafür und deren Verwendung

IPC:
C12Q 1/68

Inhaber/Inhaberin:
GenXPro GmbH, 60438 Frankfurt, DE

Erfinder/Erfinderin:
Rotter, Björn, Dr., 60320 Frankfurt, DE

Tag der Anmeldung:
28.05.2008

Tag der Veröffentlichung der Patenterteilung:
28.07.2016

Die Präsidentin des Deutschen Patent- und Markenamts

Cornelia Rudloff-Schäffer

München, 28.07.2016

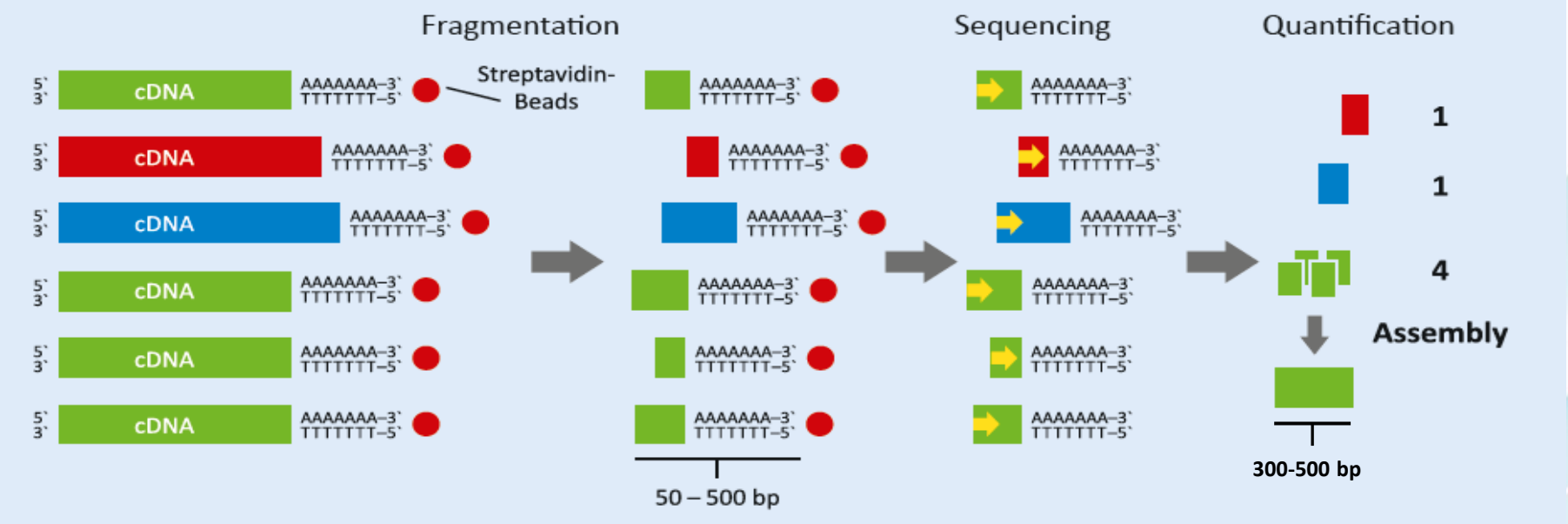
Den aktuellen Rechtsstand und Schutzumfang entnehmen Sie bitte dem DPMAregister unter www.dpma.de

Significantly improves sensitivity and accuracy of NGS data.

Applied in

- Mutation detection
- Non Invasive Prenatal Testing
- Liquid Biopsies
- Gene Expression Analyses
- Epigenetic Analyses
- Companion Diagnostics

USP:
Massive Analyses of cDNA Ends (MACE) for "Clinical RNA-Seq"

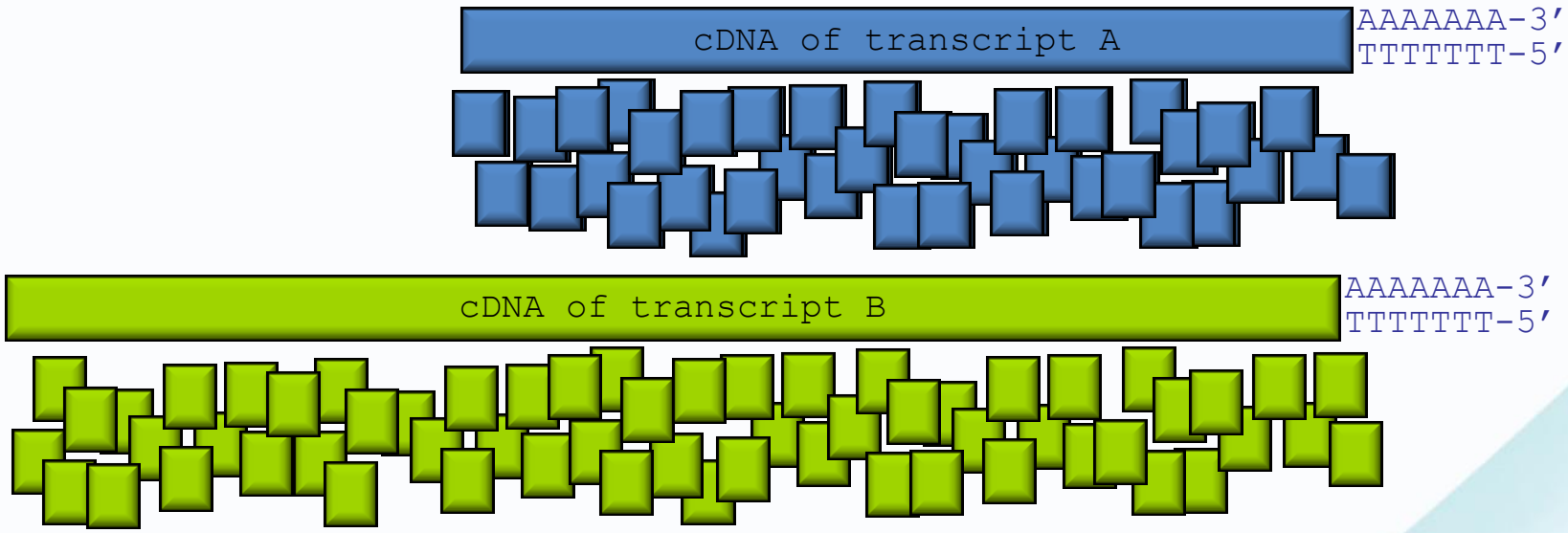


Advantages

- only 10% sequencing depth required compared to RNA-Seq
- Amount of unnecessary data reduced by 90%
- More robust : degradation of the RNA is less influencing than for RNASeq
- Very accurate quantification
- Works also on MiSeq

RNA-Seq vs. MACE-Seq

RNA-Seq



Many reads per transcript, the longer, the more fragments...

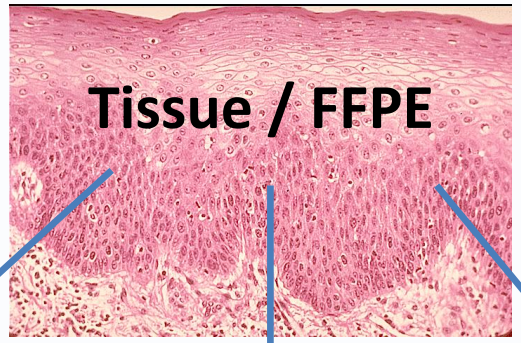
MACE-Seq

one read = one transcript

For the same depth of analysis, RNA-Seq requires about 10-30 times more sequencing*

*Asmann et. al 2009

GenXPro Portfolio



DNA

RNA

smallRNA

Next Generation Sequencing

- Mutations
- CNVs
- Methylation

- Gene Expression
- Biological Pathways
- Fusion Genes

- Expression
- Biological Pathways

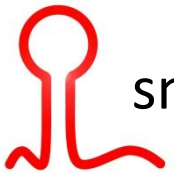
Biomarkers, Disease Mechanisms, Drug Targets

GenXPro Portfolio

Liquid Biopsies

Blood or Urine

DNA



smallRNA

Next Generation Sequencing

- Mutations
- CNVs
- Methylation

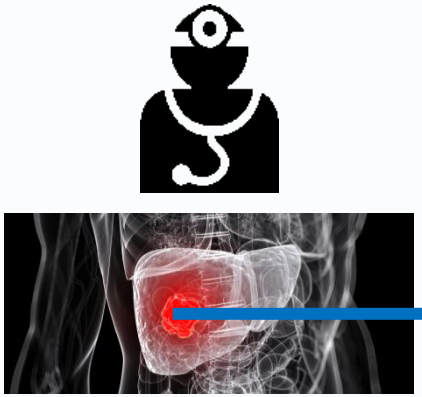
- Expression
- Biological Pathways

Biomarkers, Disease Mechanisms, Drug Targets

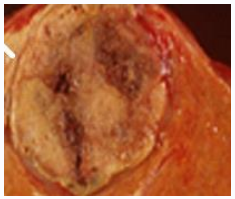
Applications

- Patient stratification
- Companion Diagnostics
- Drug Repurposing
- Treatment Success Monitoring

Precision Medicine workflow
“Molecular Pattern Diagnostics”



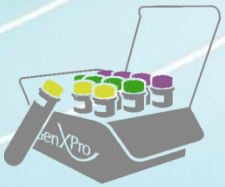
Tumor Resection



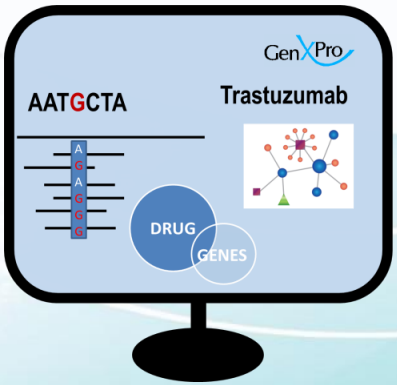
Histopathology: identification of tumor and normal tissue (FFPE)

DNA & RNA

GenXPro NGS-Kits



NG-Sequencing



Drug

GenXPro
Molecular Tumor Board Software
Molecular Pathways & Mutations

GenXPro‘s Molecular Pattern Diagnostics is the Next Step in Personalized Medicine

OPEN

Citation: Cell Death and Disease (2017) 8, e2867; doi:10.1038/cddis.2017.229
Official journal of the Cell Death Differentiation Association
www.nature.com/cddis

Precision medicine for hepatocelluar carcinoma using molecular pattern diagnostics: results from a preclinical pilot study

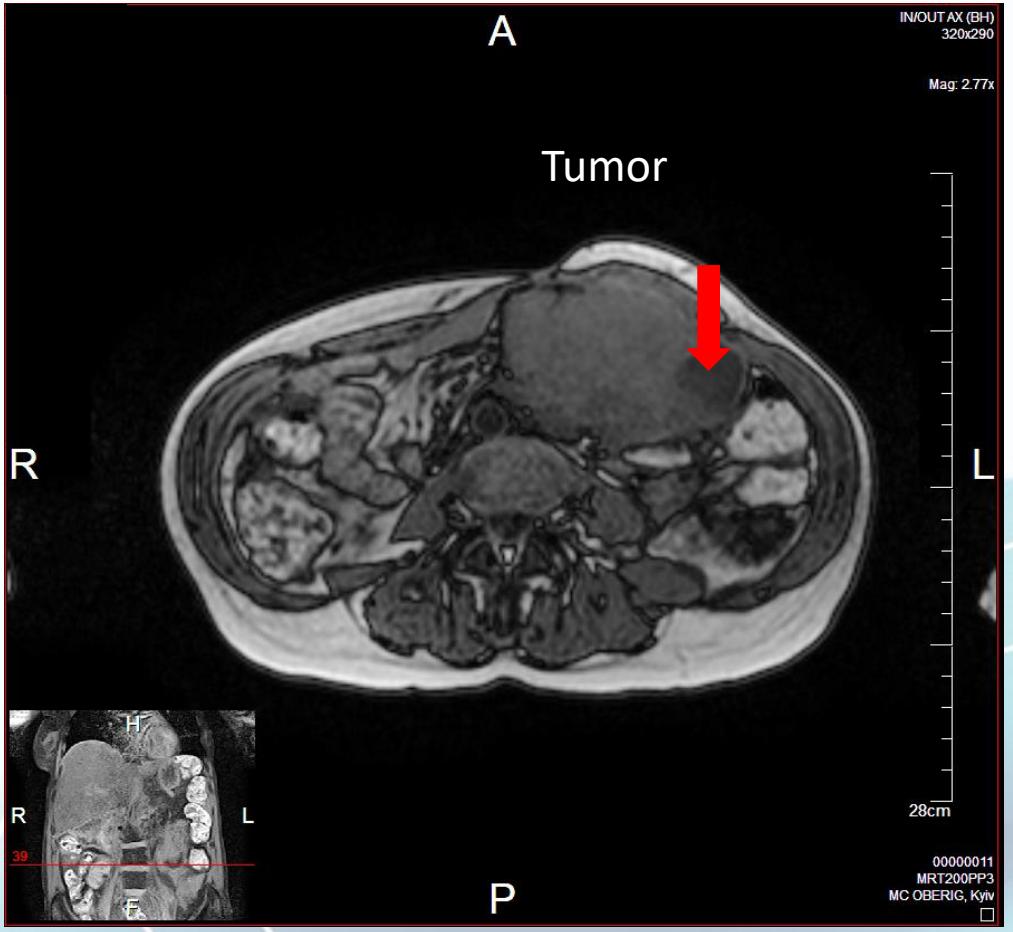
Rahul Agarwal[1], Yuan Cao[2], Klaus Hoffmeier[1], Nicolas Krezdorn[1], Lukas Jost[1], Alejandro Rodriguez Meisel[1], Ruth Jüngling[1], Francesco Dituri[2], Serena Mancarella[2], Björn Rotter[1], Peter Winter[1] and Gianluigi Giannelli*[,2]

The aim of this study was to design a road map for personalizing cancer therapy in hepatocellular carcinoma (HCC) by using molecular pattern diagnostics. As an exploratory study, we investigated molecular patterns of tissues of two tumors from individual HCC patients, which in previous experiments had shown contrasting reactions to the phase 2 transforming growth factor beta receptor 1 inhibitor galunisertib. Cancer-driving molecular patterns encompass – *inter alias* – altered transcription profiles and somatic mutations in coding regions differentiating tumors from their respective peritumoral tissues and from each other. Massive analysis of cDNA ends and all-exome sequencing demonstrate a highly divergent transcriptional and mutational landscape, respectively, for the two tumors, that offers potential explanations for the tumors contrasting responses to galunisertib. Molecular pattern diagnostics (MPDs) suggest alternative, individual-tumor-specific therapies, which in both cases deviate from the standard sorafenib treatment and from each other. Suggested personalized therapies use kinase inhibitors and immune-focused drugs as well as low-toxicity natural compounds identified using an advanced bioinformatics routine included in the MPD protocol. The MPD pipeline we describe here for the prediction of suitable drugs for treatment of two contrasting HCCs may serve as a blueprint for the design of therapies for various types of cancer.

Cell Death and Disease (2017) **8,** e2867; doi:10.1038/cddis.2017.229; published online 8 June 2017

Example
Therapeutic decision based on RNA

Dedifferentiated liposarcoma patient, female, 60 years



Results of DNA Analysis

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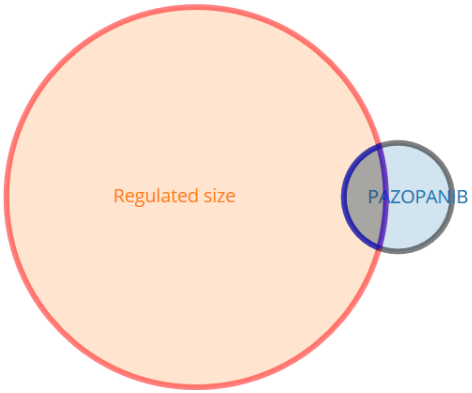
No actionable mutation for targeted therapy identified

Results MACE-Seq (RNA)

Therapeutic Targets upregulated for therapeutic decision support

Drug shown to be effective for this liposarcoma: **Pazopanib**

Results of molecular tumor board software:



Overlapping genes

PDGFRB
nml_GXP62: 143.893
nml_GXP61: 5.557
log2FC: 4.69454636011

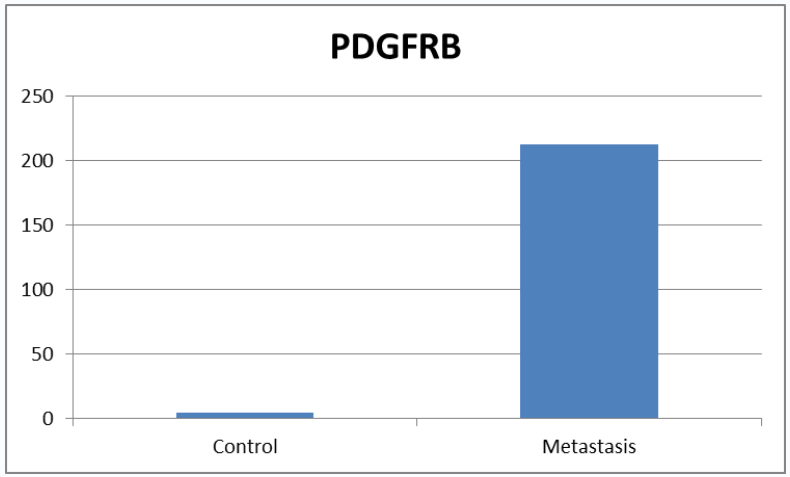
PDGFRA
nml_GXP62: 212.247
nml_GXP61: 4.874
log2FC: 5.4444941009

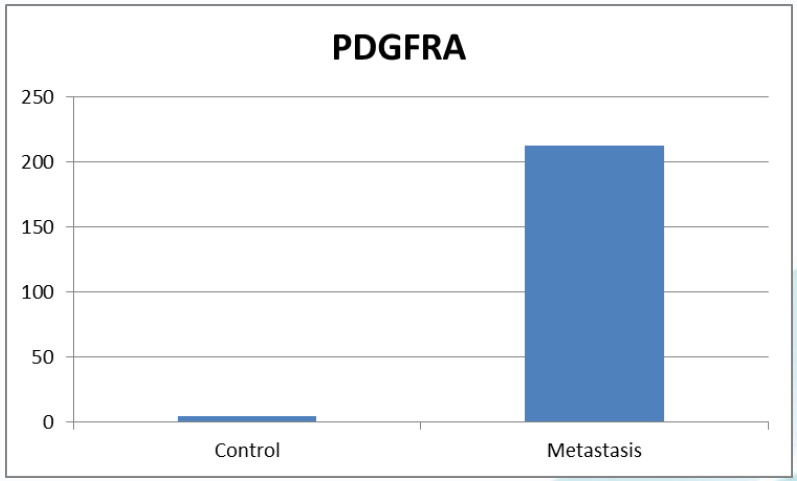
FGF1
nml_GXP62: 1.165
nml_GXP61: 0.195
log2FC: 2.57878392579

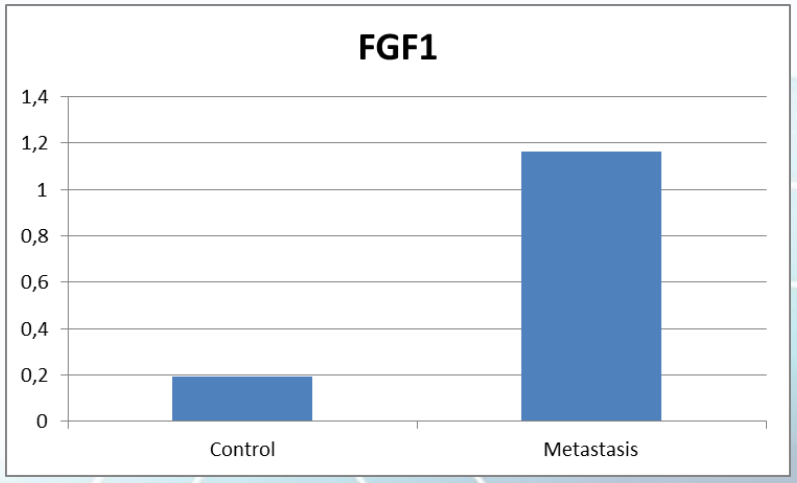
KIT
nml_GXP62: 3.107
nml_GXP61: 0.195
log2FC: 3.99397621237

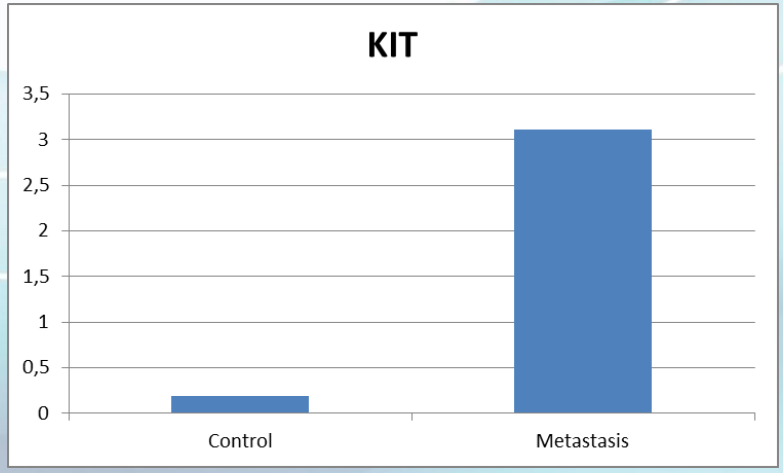
Expression of Drug Targets for Pazopanib

(Transcripts per Million)



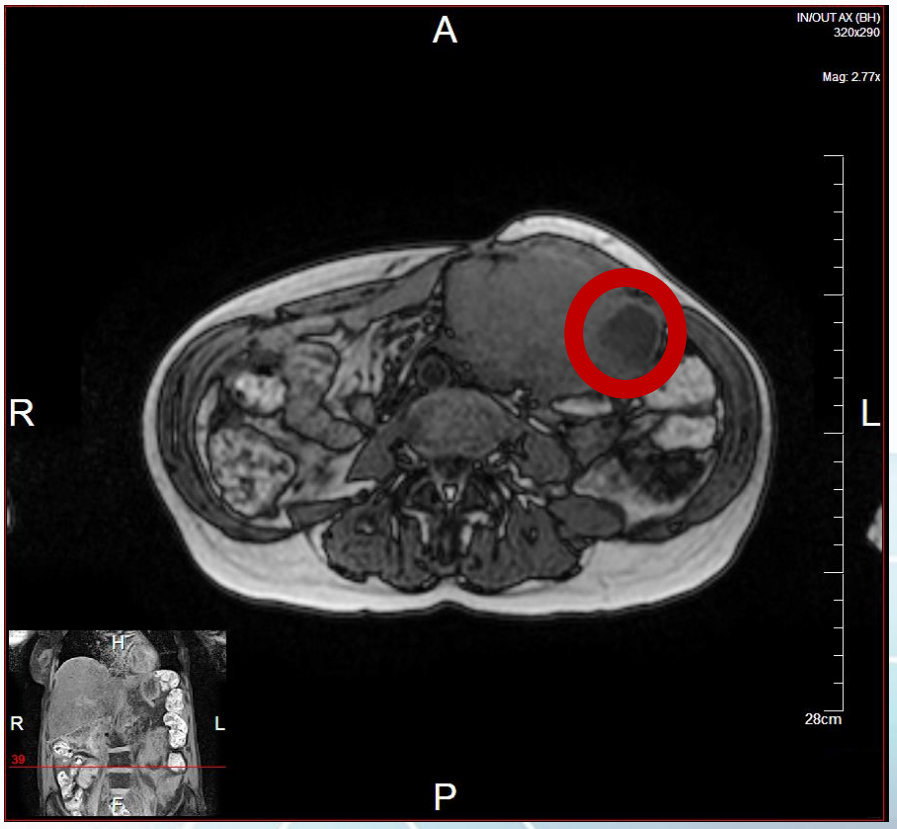


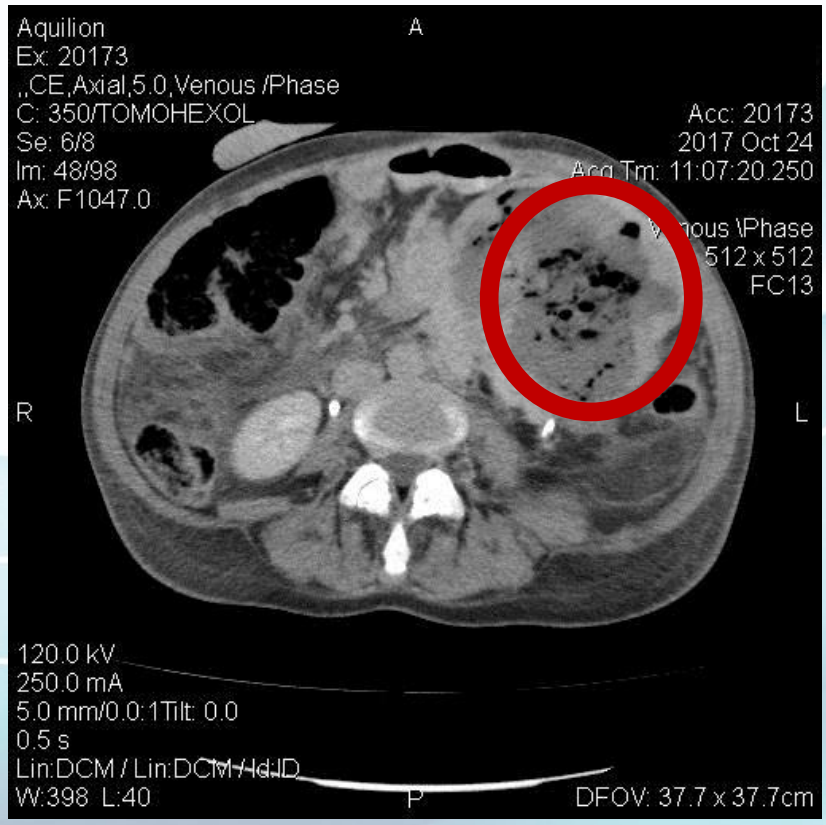




Treatment decision: Pazopanib

Strong increase of necrosis in tumor after 3 weeks of treatment
-> therapeutic effect





Biomarkers

Biomarkers: Epigenetic DNA markers in circulating DNA (cfDNA) for Pancreatic cancers

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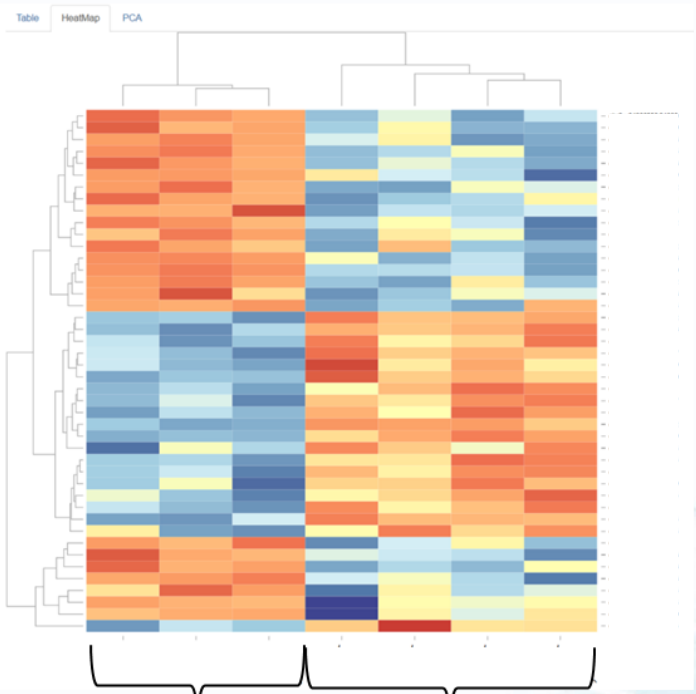
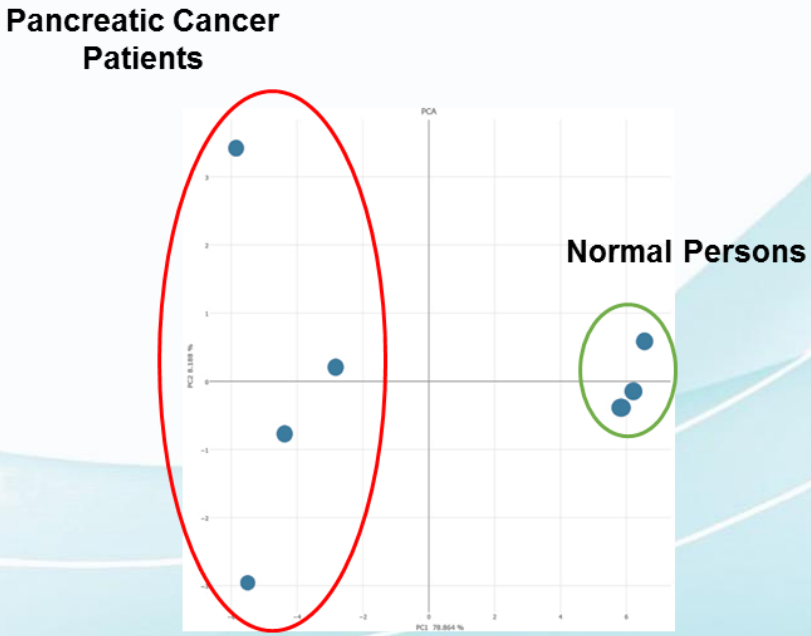
Unsupervised clustered heatmap



Principle component analysis



Biomarkers: MACE-Seq and RNA-Seq derived

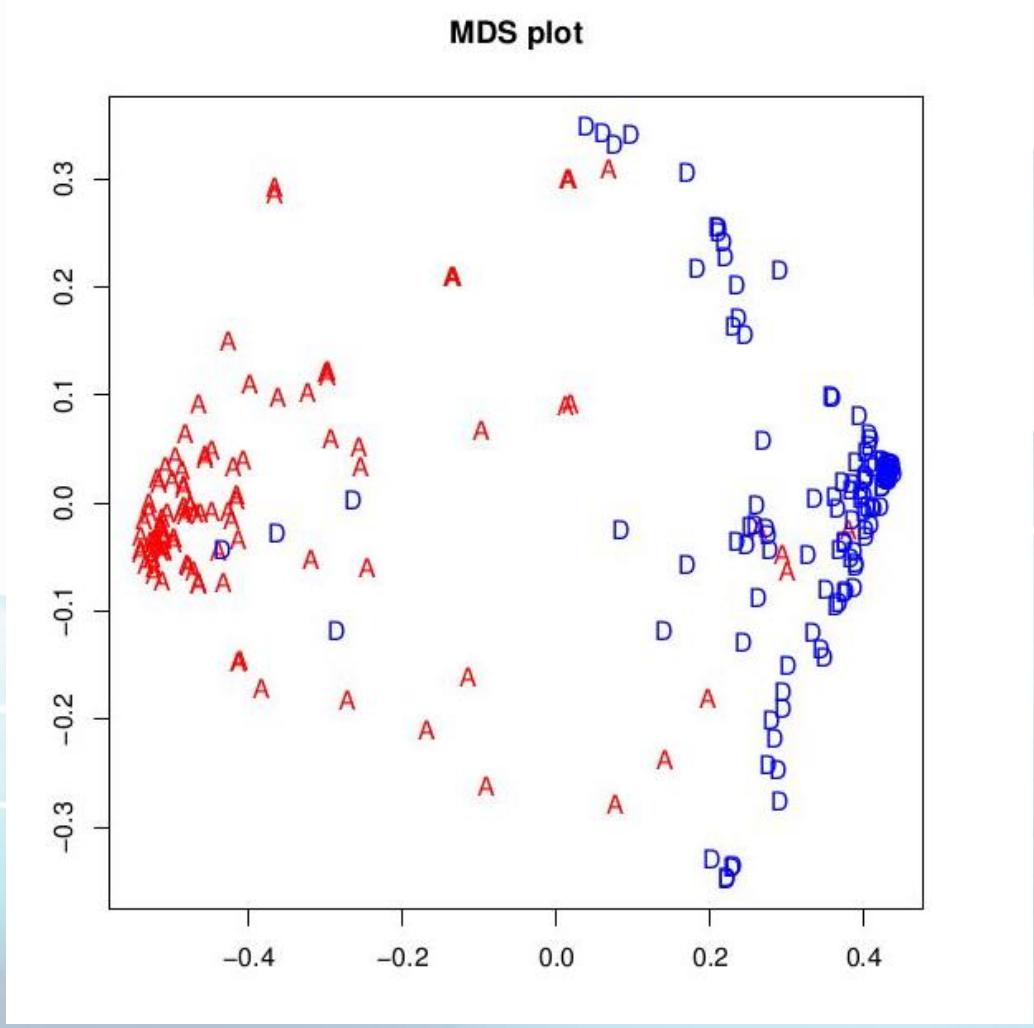
Based on machine learning algorithms, Kidney Cancer

Predicting survival according to patient transcription profiles

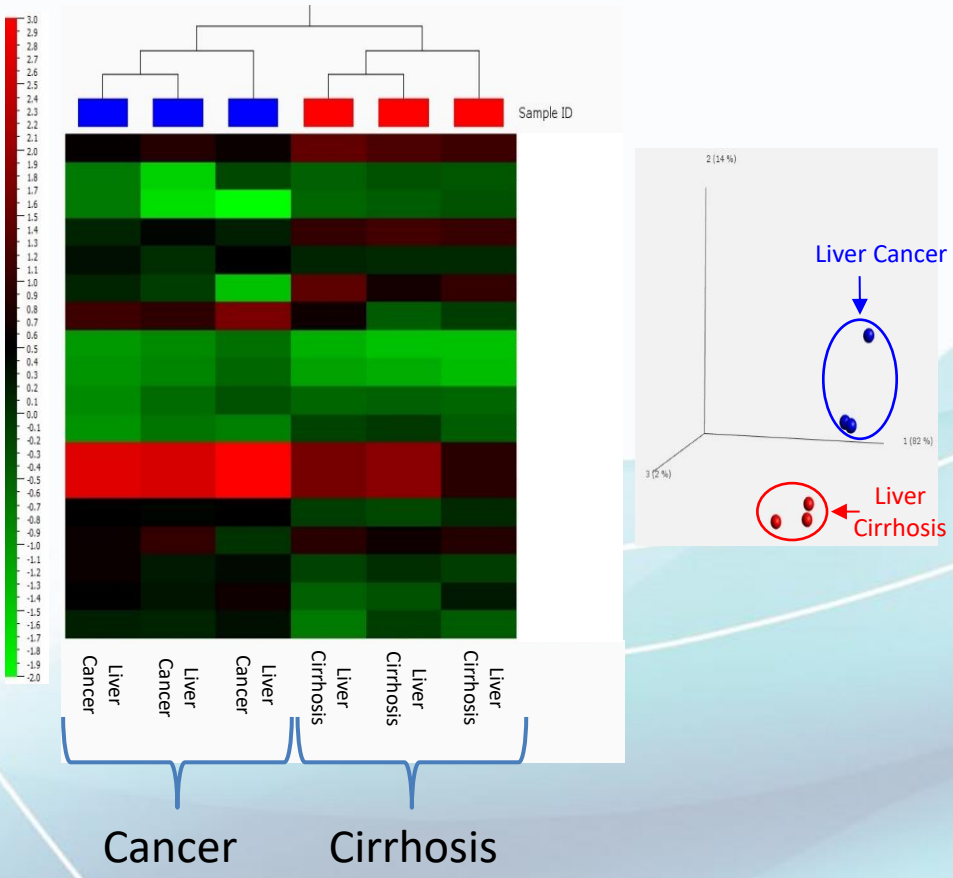
Set of Predictor Genes sorts patients into groups with high and low probability of survival

A: Alive

D: Deceased



Biomarkers: small RNA markers in Blood distinguish between liver cancer and cirrhosis



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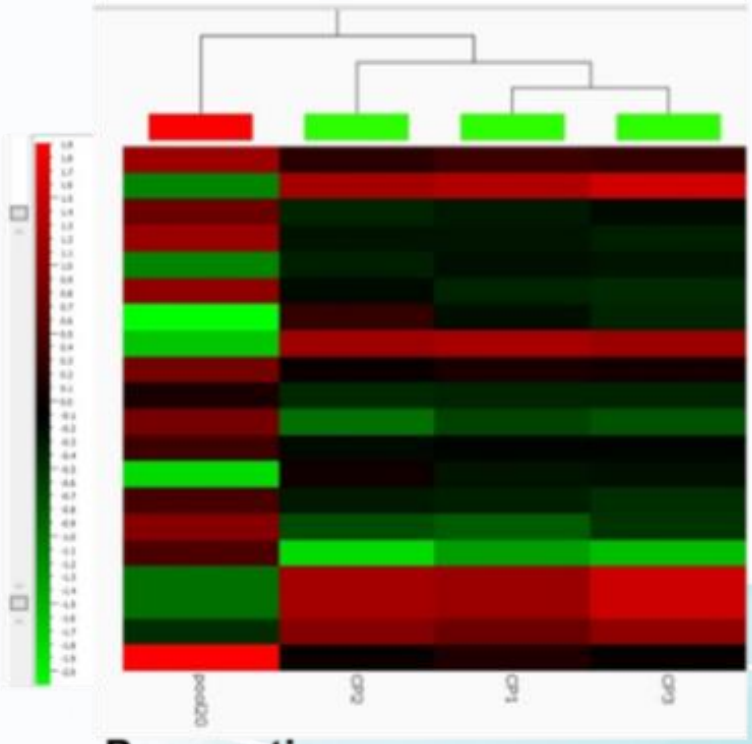
microRNAs in exosomes from plasma of pancreatic cancer and liver cirrhosis patients discriminate between the diseases



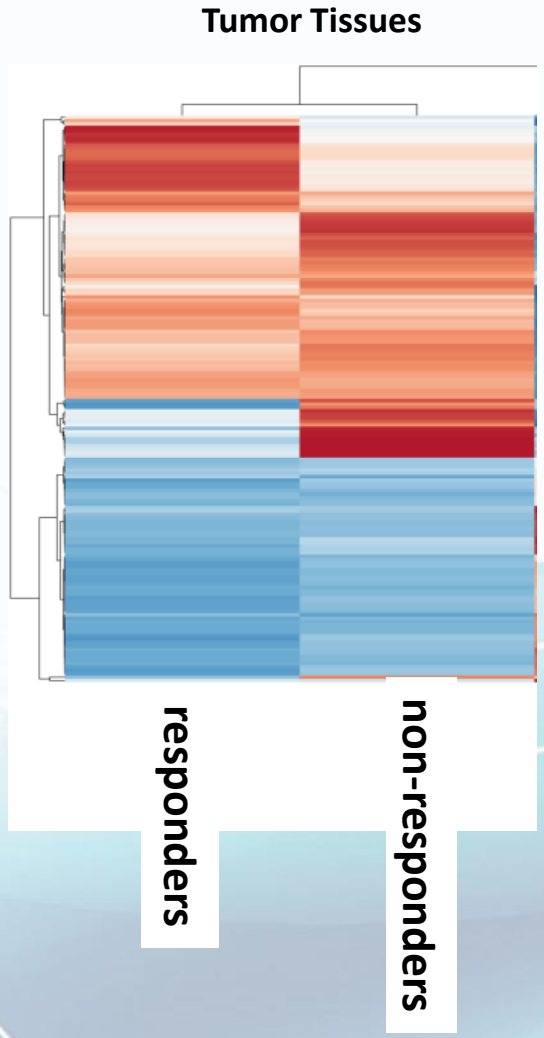
20 of approx. 400 microRNAs

Pancreatic cancer

Liver cirrhosis

Biomarkers: MACE-SEQ

Distinguish between the tissues of responders and non-responders to the phase II trial of TGF-ß blocker Galunisertib in liver cancer



Price for innovative Precision Medicine Concept

THANK YOU FOR ATTENTION

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