Sciomics.

Biomarker signatures and mechanism-based disease definitions for Precision Medicine

Sciomics GmbH
Karl-Landsteiner Str. 6
69151 Neckargemünd
Germany

Dr. Ronny Schmidt
Head of Contract Research
ronny.schmidt@sciomics.de
(+49) 6221 42948-33

www.sciomics.de

sciomics
enabling precision medicine

Sciomics. Enabling precision medicine through innovative protein biomarkers

- founded in April 2013 as a spin-off of German Cancer Research Centre (DKFZ)
- outstanding expertise and experience for proteomic and post-translational modification protein profiling
- located in Neckargemünd / Heidelberg (Germany)

- highly innovative research projects with pharmaceutical industry and academic consortia

Two divisions:
1. protein and post-translational modification (PTM) profiling as contract research service
2. in-house development and verification of protein biomarkers for precision medicine



Sciomics. Precision Medicine - that's how we do it

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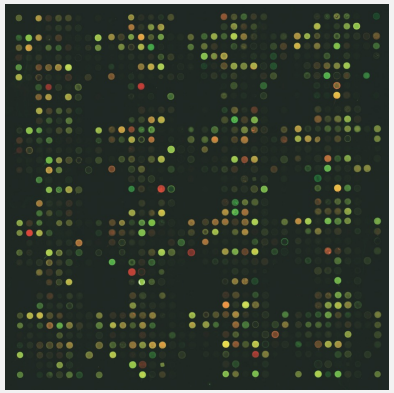
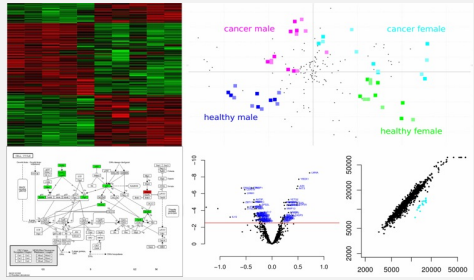
Scientific expertise
- long-standing **experience**
- **pharma/academic collaborations**
- **strong scientific focus**

Potent analysis platform
- ideal platform for selection of optimal biomarker matrix
- broad coverage of several key medical areas
- strong focus on immune system

High-throughput discovery



AI-enhanced data analysis



maximum insights into disease biology, biomarker candidates

Novel biomarkers
for further development with strategic partners

Intellectual property
patent portfolio based on data generated by our antibody microarray platform (e.g. cancer, organ failure, infectious diseases)

Knowledge

Advancing a new approach in medicine.

PRECISION MEDICINE
. mechanism-based
. objective
. fast
. precise

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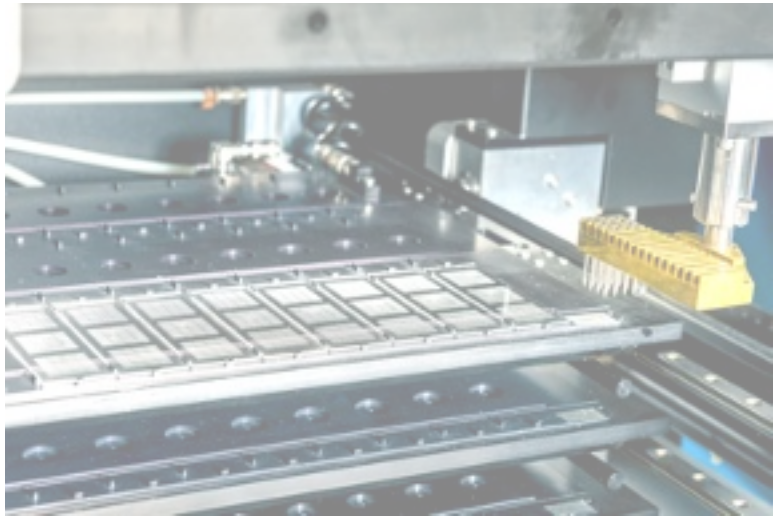
New pipeline projects

Project	Indication	Discovery	Verification
scioCOV	Covid-19		
scioAKI	Acute Kidney Injury		
scioPaca	Pancreatic Cancer		
scioEndoCar	Endometrial Cancer		
scioPD1	PD-1 treatment melanoma		
scioVesi	Bladder Cancer		
scioMCDS	MCDS		
scioBM6	Undisclosed indication		

Current development pipeline featuring 8 development projects


1. Protein and post-translational modification (PTM) profiling as a contract research service

scioDiscover platform - antibody microarray-based protein profiling
> 15+ years of development

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Based on 15+ years of development

Schröder C., *et al.* (2010)
Dual-color proteomic profiling of complex samples with a microarray of 810 cancer-related antibodies.
Mol Cell Proteomics.9:1271-80. → LINK

Schröder C., *et al.* (2013)
Plasma protein analysis of patients with different B-cell lymphomas using highcontent antibody microarrays.
Proteomics Clin Appl.7:802-812. → LINK

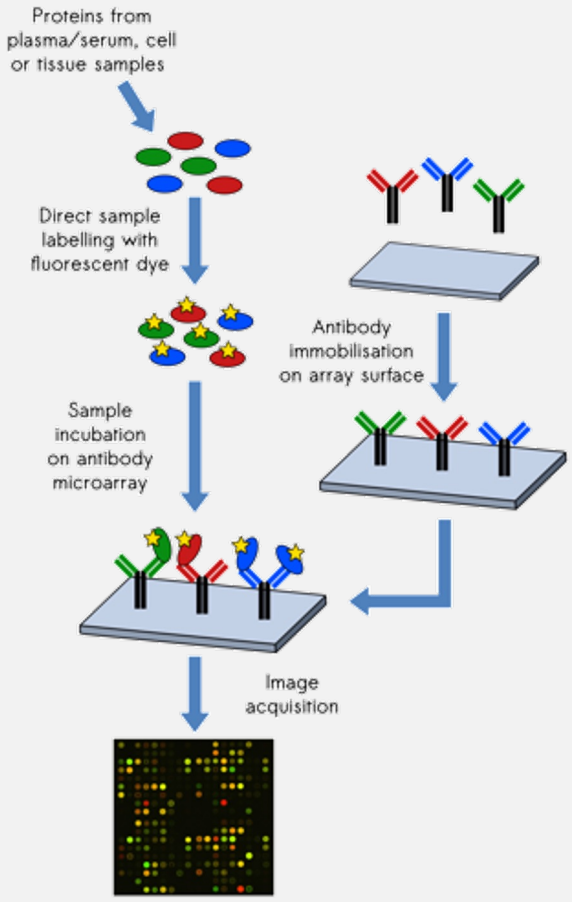
Srinivasan H, *et al.* (2014)
Prediction of recurrence of non muscleinvasive bladder cancer by means of a protein signature identified by antibody microarray analyses.
Proteomics. 14(11):1333-42. → LINK

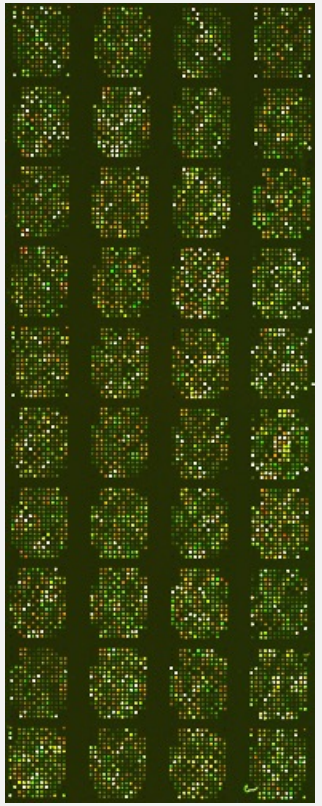
Sill M., *et al.* (2010)
Assessment and optimisation of normalisation methods for dual-colour antibody microarrays.
BMC Bioinformatics. 11:556. → LINK

Alhamdani M.S., *et al.* (2010)
Single-Step Procedure for the Isolation of Proteins at Near-Native Conditions from Mammalian Tissue for Proteomic Analysis of Antibody Microarrays.
J Prot Res. 9(2):963-971. → LINK

Kusnezow W. *et al.* (2007)
Antibody microarray-based profiling of complex specimens: systematic evaluation of labeling strategies.
Proteomics. 7(11):1786-1799. → LINK

work-flow of our scioDiscover platform





4 replicates per antibody and sample

Characteristics of scioDiscover

- parallel analysis of **1,438 proteins**
- **robust assay** that requires very **low sample volumes**

"what happens on protein level?"

- identification and verification of protein biomarkers
- drug target screening
- characterization of disease models
- analysis of pathway activity
- mode-of-action analyses

scioDiscover platform
> extensive coverage of cancer pathways

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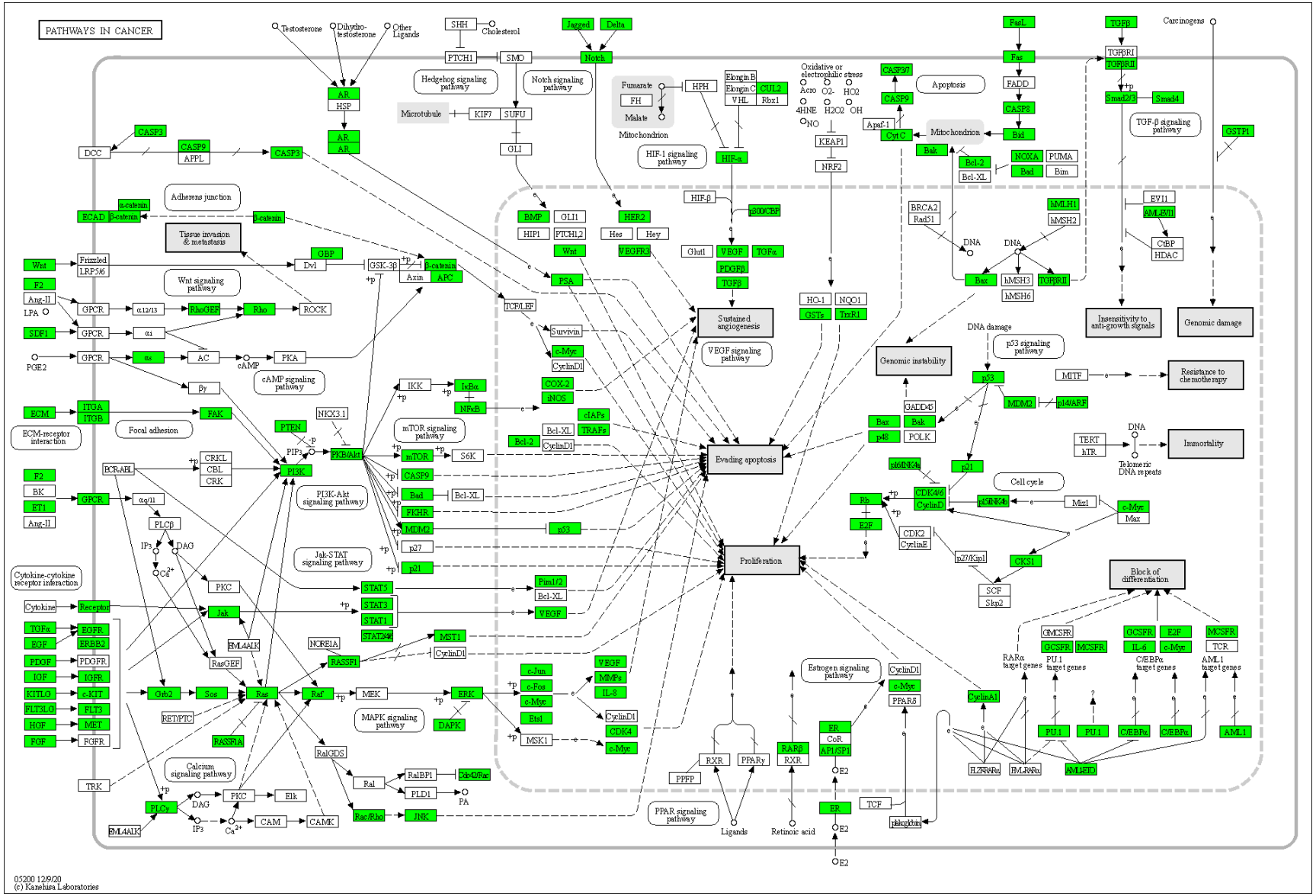

proteins covered by scioDiscover

scioDiscover platform
> application example: **biomarker discovery** project

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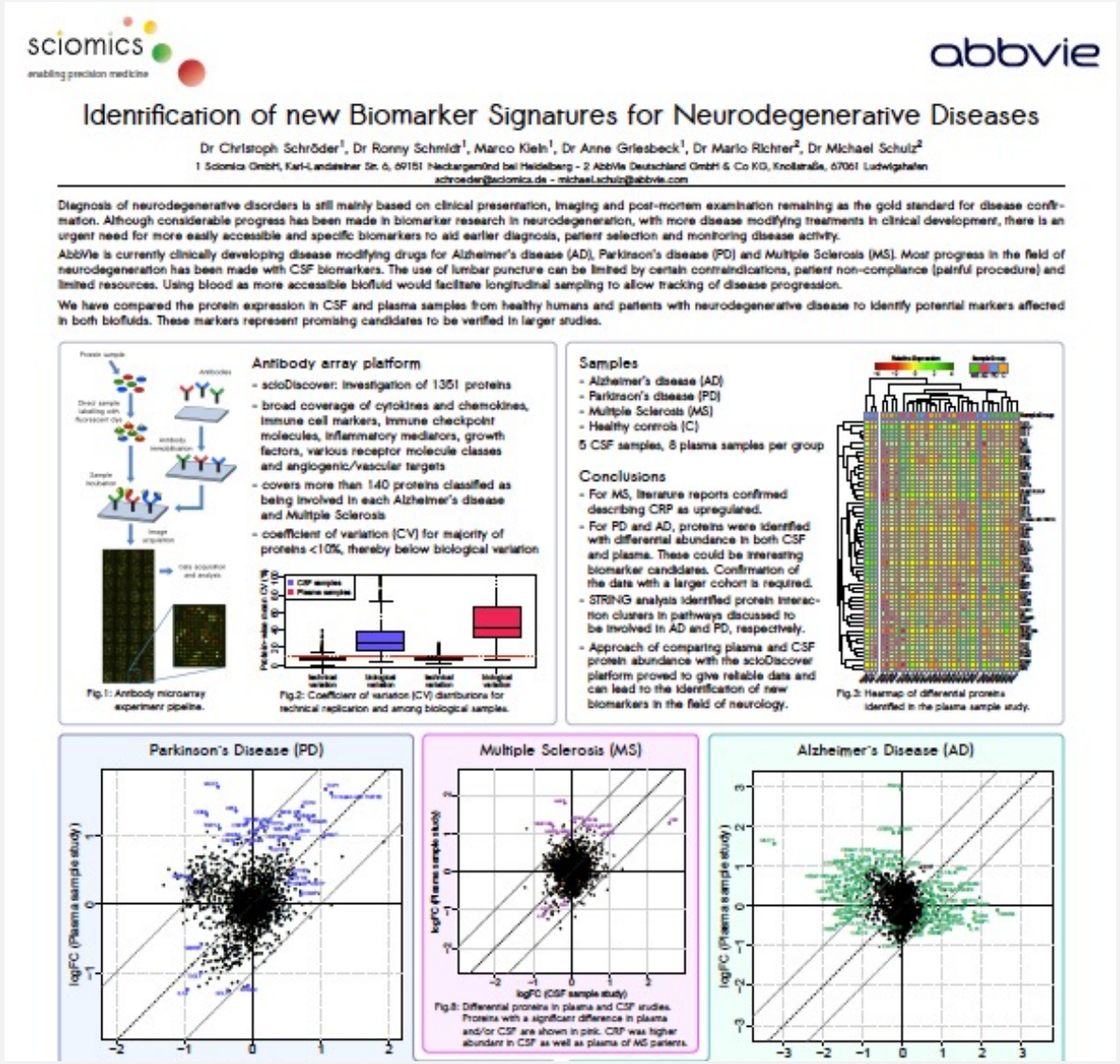
Contract research project

- support of **understanding of disease mechanism(s)** and potential drug targets for Alzheimer's disease (AD), Parkinson's disease (PD), Multiple Sclerosis (MS)
- large project → **needs collaboration**
- comparison of patient samples and healthy control samples
- PD: Parallel investigation of CSF, plasma and organoid model samples → **maximum knowledge generation**
- comparisons across various sample types and species
- time from sample arrival to final report: 3-6 weeks



scioDiscover platform
> application example: **biomarker discovery** project

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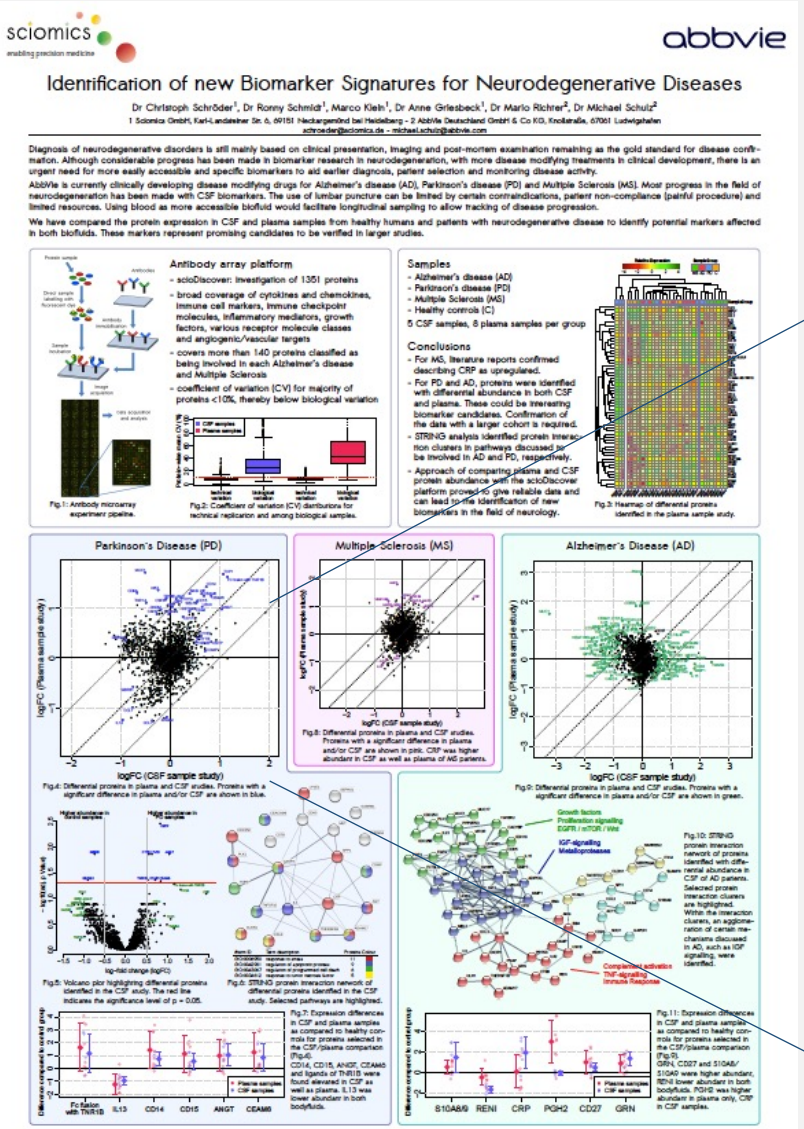
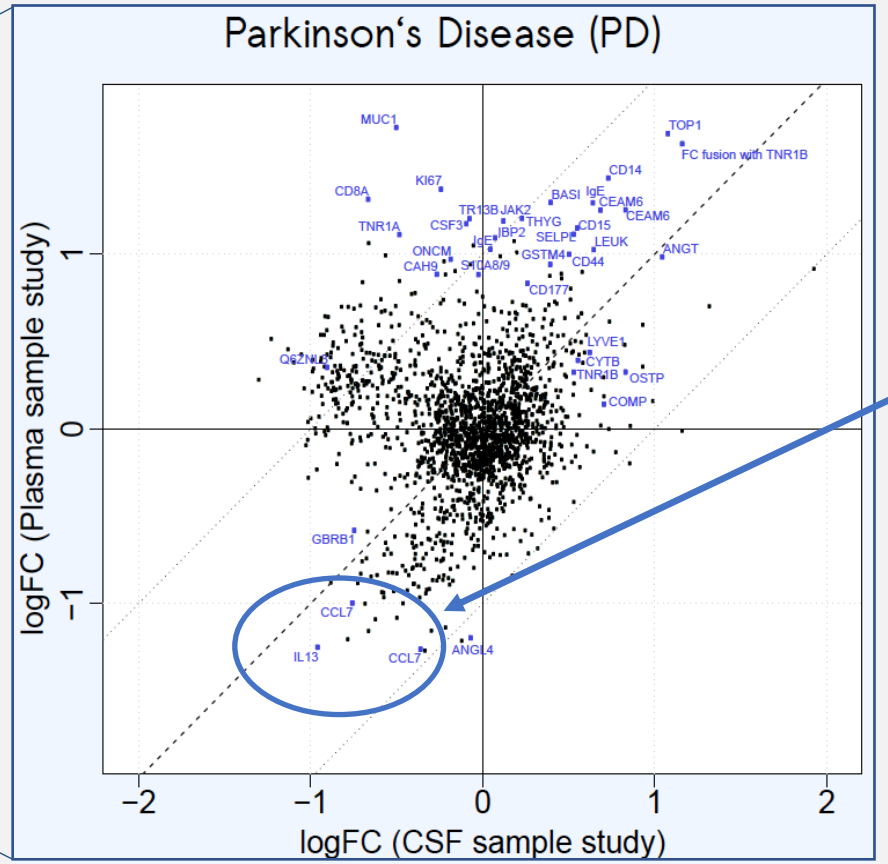


New biomarker candidates identified



- co-regulation of inflammatory markers in CSF and plasma
- goals achieved:

→ easier accessible biomarker

→ platform works across multiple sample types

scioDiscover platform
> application example: **drug target discovery** project

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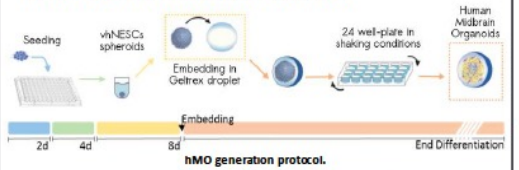
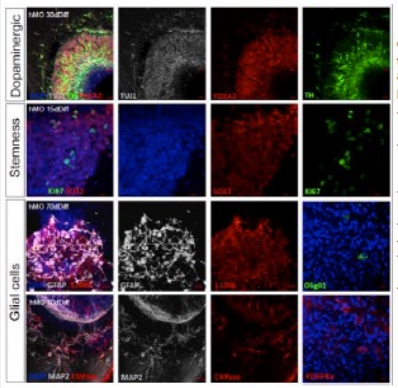
Human Midbrain Organoids (hMO)

- derived from induced pluripotent stem cells of PD patients harboring alterations of α-synuclein (SNCA)
- SNCA is a major component of Lewy neurites and Lewy bodies, intracellular aggregates that represent a pathological hallmark of synucleinopathies such as Parkinson's disease (PD)



hMO generation protocol.

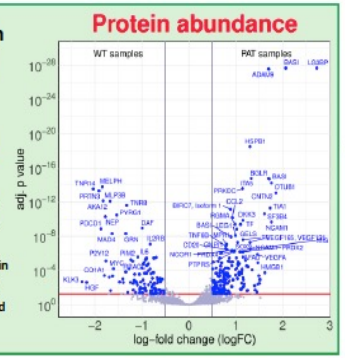


Confocal images of the hMO population at different time points
- Neurons (TUJ1, MAP2)
- Tyrosine hidroxilase positive neurons (TH)
- ventral identity (FOXA2)
- Proliferation (ki67)
- Stemness (SOX2)
- Astrocytes (GFAP & S100b)
- Oligodendrocytes (CNPase, PDGFRa, Olig1)

Profiling of brain organoid cell samples

Study comparing Parkinson's (PAT) and control (WT) organoid models

- Galectin-3-binding protein (LG3BP) promotes integrin mediated cell adhesion
- increased VEGF signalling in patient samples identified
- DKK3 identified in organoid cells and supernatants



Organo Therapeutics abbvie sciomics

In-depth Molecular Profiling of Parkinson's Disease using Advanced Midbrain Organoid Models

Ronny Schmidt(1), Javier Jarazo(3), Jens Schwamborn(3), Marco Klein(1), Mario Richter(2), Michael Schulz(2), Christoph Schröder(1)

1 Sciomics GmbH, Karl-Landsteiner Str. 6, 69151 Neckargemünd, Germany
2 AbbVie Deutschland GmbH & Co KG, Knollstraße, 67061 Ludwigshafen, Germany
3 Organo Therapeutics, 6A avenue des Hauts-Fourneaux, L-4365 Esch-sur-Alzette, Luxembourg
3 University of Luxembourg, Luxembourg Centre for Systems Biomedicine (LCSB), avenue du Swing, L-4367 Belvaux, Luxembourg

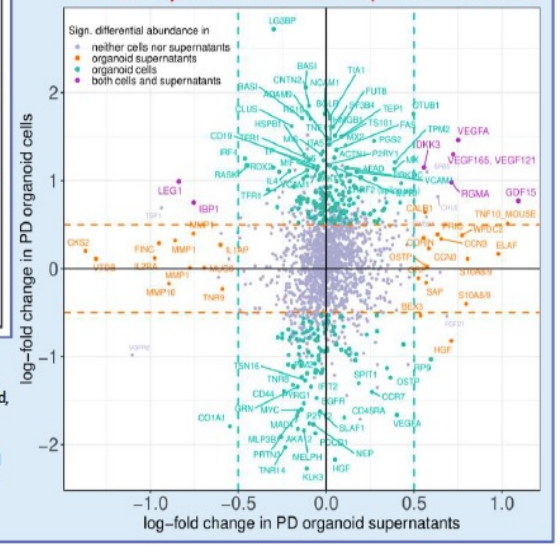
Novel models for the use in Parkinson's disease (PD) drug development are needed and midbrain organoids may fulfil these needs.
Combining patient derived midbrain organoid models with Sciomics assays enable analyses on protein, phosphorylation and ubiquitination level to identify molecular mechanisms for PD and new potential drug targets efficiently, limiting the use of animal models while being closer to the patient situation.
In the presented study PD midbrain organoids and culture supernatants from midbrain organoids were analysed on protein, phosphorylation and ubiquitination level. The results demonstrate the feasibility of such combined analysis and have yielded insights into the PD biology. Important proteins such as GDF15 and DKK3 were identified in the supernatants as well as matching phosphorylation and ubiquitination levels of TBB3 in both midbrain organoids and supernatant.

Conclusions

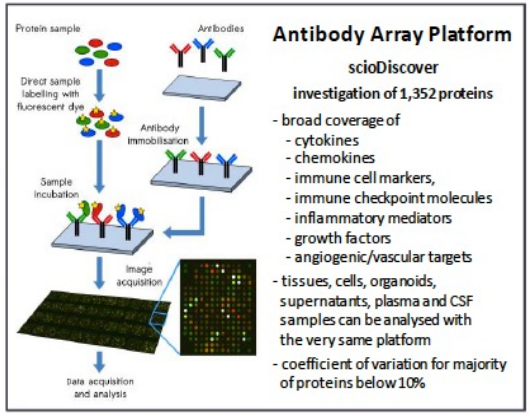
- analysis of organoid cells and supernatants on protein, phosphorylation and ubiquitination level feasible
- minimal sample amount needed
- data integration across different sample types successful
- midbrain organoid models in combination with antibody array based protein and PTM profilings enable the identification of PD biomarkers and the in-depth study of disease mechanisms without being dependent on patient samples

Integration of organoid cell and supernatant profiling

Differential protein abundance – supernatants vs cells



- Several proteins differentially abundant in both organoid cells and supernatants were identified, which are already discussed as potential biomarkers in PD.
- This indicates that an integrated protein and PTM profiling could represent a useful tool in biomarker identification.



Antibody Array Platform

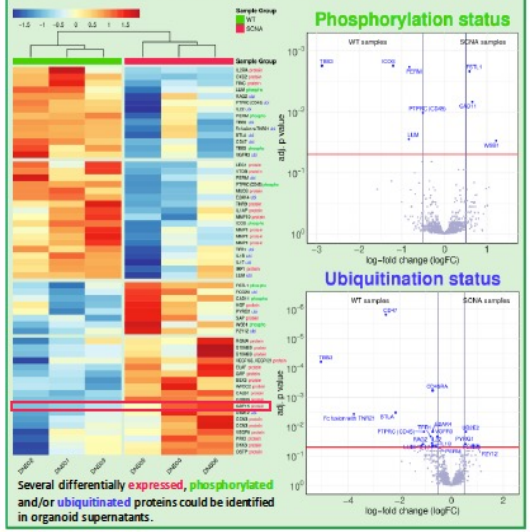
scioDiscover
investigation of 1,352 proteins

- broad coverage of
  - cytokines
  - chemokines
  - immune cell markers,
  - immune checkpoint molecules
  - inflammatory mediators
  - growth factors
  - angiogenic/vascular targets
- tissues, cells, organoids, supernatants, plasma and CSF samples can be analysed with the very same platform
- coefficient of variation for majority of proteins below 10%

Profiling of brain organoid supernatants

Pilot study comparing SCNA and control (WT) organoid models

- increased VEGF and lower MMP1 activity in SCNA organoids
- TBB3 differentially phosphorylated and ubiquitinated in organoids
- GDF15 identified up-regulated in PD, concurrent with literature reports



Several differentially expressed, phosphorylated and/or ubiquitinated proteins could be identified in organoid supernatants.

- knowledge generation across different models and sample types
- collaboration: pharma and start-up

All-in-one experiment

- biomarker candidates
- biological insights
- model characterisation
- comparison of organoids to patient samples

scioDiscover platform

> scioDiscover - enhancing key activities in pharmaceutical R&D

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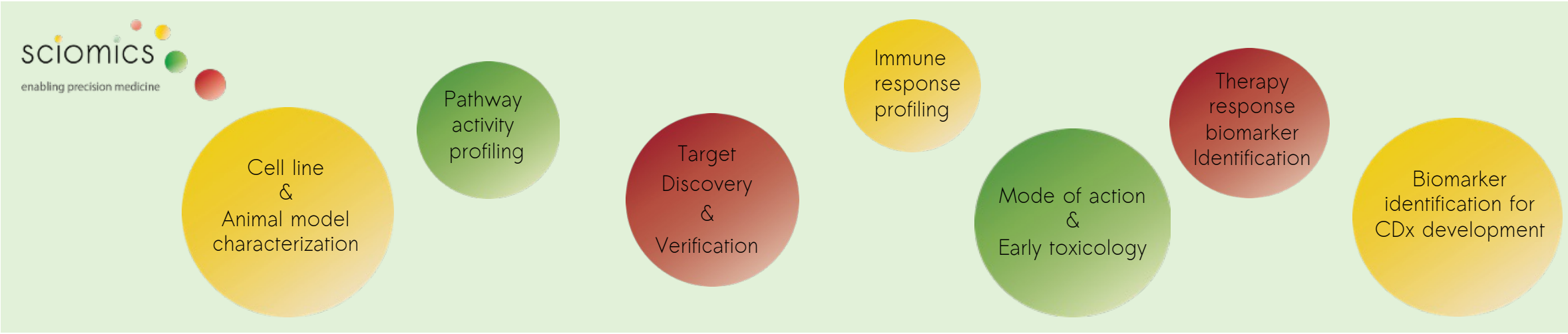

Discovery → Lead identification & validation → Pre-clinical studies → Clinical Phases

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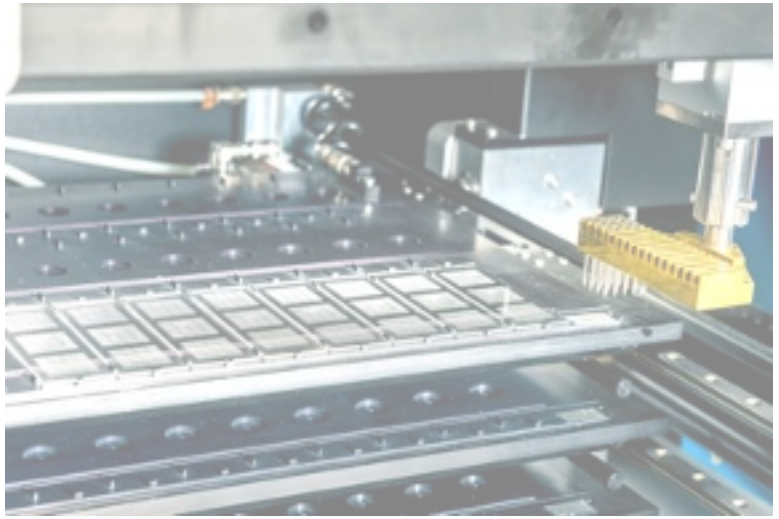
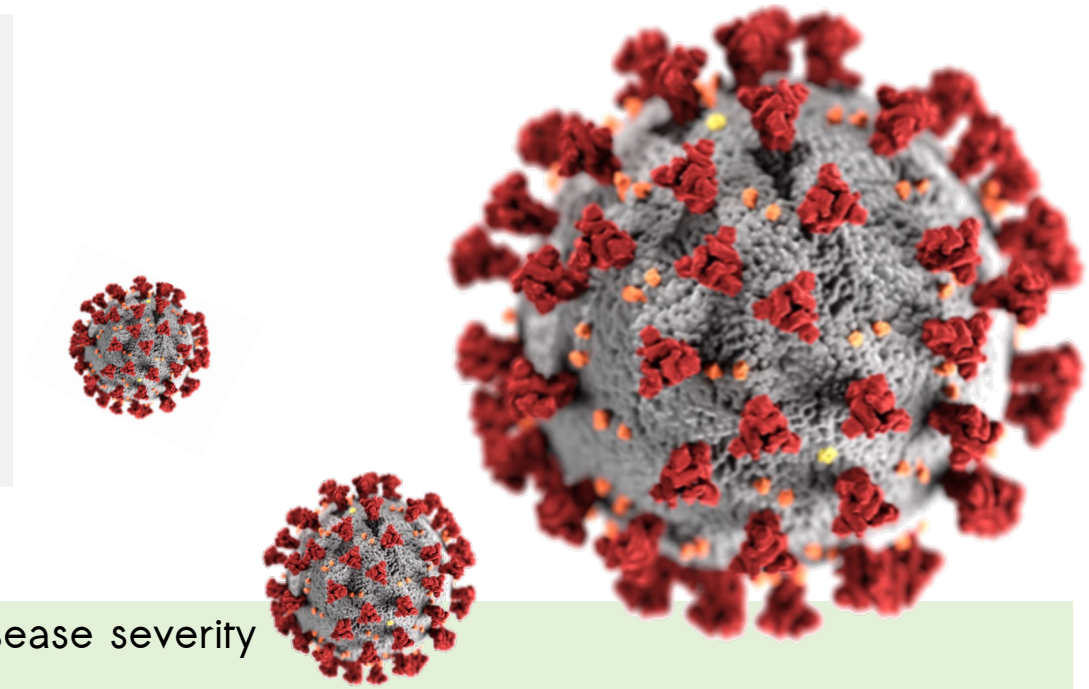


2. In-house development and verification of protein biomarkers for precision medicine

Sciomics. A biomarker discovery pipeline addressing highly relevant indications
> scioCOV

Project	Indication	Discovery	Verification
scioCOV	**Covid-19**		
scioAKI	Acute Kidney Injury		
scioPaca	Pancreatic Cancer		
scioEndoCar	Endometrial Cancer		
scioPD1	PD-1 treatment melanoma		
scioVesi	Bladder Cancer		
scioMCDS	MCDS		
scioBM6	Undisclosed indication		



scioCOV: Sciomics‘ Covid-19 biomarkers for prediction of disease severity

In two independent studies, we found a range of significantly up- or downregulated proteins that can predict the upcoming disease course for patients in an early acute phase of the infection.

Our smart, AI-enhanced biomarker panels clearly outperform single markers in regards to precision. These biomarkers have been validated, patented and combined by AI-enhanced data analysis to optimum biomarker panels.

Now we look for strategic partners to enhance Covid-19 diagnostics and therapies together.

Picture: https://www.pei.de/DE/newsroom/dossier/coronavirus/coronavirus-inhalt.html

Sciomics. A biomarker discovery pipeline addressing highly relevant indications
> scioAKI

Project	Indication	Discovery	Verification
scioCOV	Covid-19		
scioAKI	**Acute Kidney Injury**		
scioPaca	Pancreatic Cancer		
scioEndoCar	Endometrial Cancer		
scioPD1	PD-1 treatment melanoma		
scioVesi	Bladder Cancer		
scioMCDS	MCDS		
scioBM6	Undisclosed indication		

scioAKI: Biomarkers for handling the risk of peri–operative acute kidney injury

Peri-operative Acute Kidney Injury (AKI) is a problem with high unmet medical need, affecting 10-50 % of patients after severe surgery and causing high mortality or lifelong dialysis/kidney transplantation.

In our studies, we found 156 differential biomarker candidates of which we defined TOP 30 markers with predictive and diagnostic power.

Using these patented markers (EP3904883A1, WO2021204910A1), surgical procedure and medication can be individually risk-adjusted for every patient and thus significantly decrease the risk of AKI.

Picture:https://www.labiotech.eu/trends-news/am-pharma-acute-kidney-injury/

Sciomics. A biomarker discovery pipeline addressing highly relevant indications
> scioVesi

Project	Indication	Discovery	Verification
scioCOV	Covid-19		
scioAKI	Acute Kidney Injury		
scioPaca	Pancreatic Cancer		
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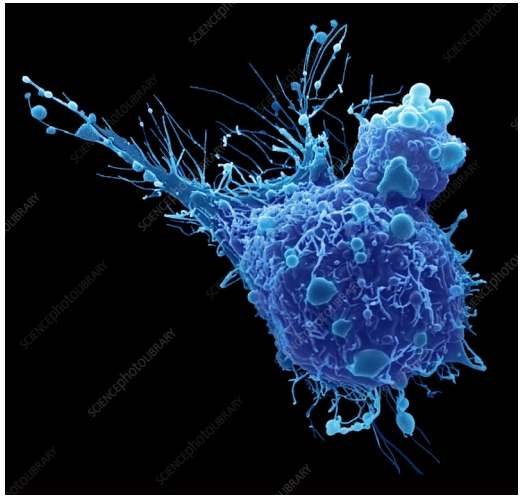
scioPD1	PD-1 treatment melanoma		
scioVesi	**Bladder Cancer**		
scioMCDS	MCDS		
scioBM6	Undisclosed indication		



scioVesi: Sciomics' bladder cancer biomarkers for predicting local recurrences after initial diagnosis / therapy

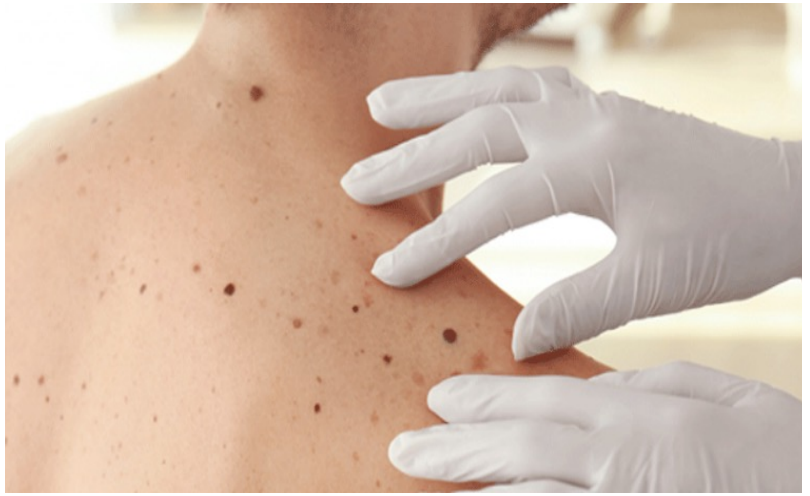
Within this collaboration project with the DKFZ, we could identify markers within the tumours that can predict recurrence in bladder cancer. These can be used for a prognostic test to improve the unfavourable and expensive situation of surveillance (cystoscopy required every 3 months, low patient compliance) significantly.

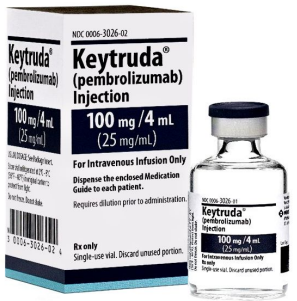
Based on our findings, the following patent applications have been filed: EP2718720B1, WO2012168421A1, US2014193927A1.

Picture: https://www.sciencephoto.com/media/783201/view/bladder-cancer-cell-sem

Sciomics. A biomarker discovery pipeline addressing highly relevant indications
> scioPD1

Project	Indication	Discovery	Verification
scioCOV	Covid-19		
scioAKI	Acute Kidney Injury		
scioPaca	Pancreatic Cancer		
scioEndoCar	Endometrial Cancer		
scioPD1	**PD-1 treatment melanoma**		
scioVesi	Bladder Cancer		
scioMCDS	MCDS		
scioBM6	Undisclosed indication		





scioPD1: Prediction of therapy response to Pembrolizumab treatment in melanoma

In this study, we could identify more than 60 differentially abundant proteins distinguishing non-responders and responders to the treatment of melanoma with Pembrolizumab.

Pembrolizumab is a very promising drug with excellent efficacy in a certain patient group. However, it can cause heavy side-effects which leads to a lack in compliance among many patients. Combining Pembrolizumab with molecular biomarkers for precise patient stratification and selection can enhance melanoma therapy significantly.

Pictures: https://www.eortc.org/blog/2020/09/28/eortc-melanoma-group-changing-daily-practice-for-cancer-patients/
https://de.thesocialmedwork.com/keytruda-pembrolizumab

Scientific publications
Customer testimonials

Dr. Ronny Schmidt
Head of Contract Research

ronny.schmidt@sciomics.de
http://www.sciomics.de

Karl-Landsteiner Str. 6
69151 Neckargemünd
Germany

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