SPHN/PHRT Driver Project:
Swiss Molecular Pathology Breakthrough Platform

Andre Kahles
Biomedical Informatics Group
(for the PIs Mark Rubin & Gunnar Rätsch)

Principle Investigators

Mark Rubin
University Hospital Bern
@MarkARubin1

Gunnar Rätsch
ETH Zurich
@gxr
Overview: Swiss Molecular Pathology Breakthrough Platform

### SPHN Driver Project

**Universität Bern / Inselspital**
- Mark A Rubin (Main Applicant)
- Tobias Grob (WP2)
- Rémy Bruggmann (WP1,3)

**Universitätspital Zürich**
- Holger Moch (Co-Applicant, WP2)

... will create a breakthrough *clinical genomics platform* to manage and *share data across Switzerland* to help our clinicians and scientists untangle the complexity of therapy-related resistance - together with the international research community.

### PHRT Project

**ETH-Zürich**
- Gunnar Rätsch (Co-Applicant, WP3,5,6)

**EPFL-Ludwig Institute**
- George Coukos (Co-Applicant, WP4,6)

... will put our *SPHN Driver* to the test and address important cancer immunology question:  
**Why do only some patients respond** to drugs blocking immune checkpoints such as the PD-1/PD-L1 pathway and what is the potential *mechanism of response and resistance*.
Some of the many people involved
Example: International Cancer Genome Consortium

Approximately 800 scientists

PCAWG Workgroup 3
Transcriptome/Genome Analysis Group
WGL: Brooks, Brazma, Rätsch

Approximately 50 papers have been or will be submitted to Nature from this effort in (2018)
Collaborative Project Principles/Goals

“It is amazing what you can accomplish if you do not care who gets the credit.”
— Harry S. Truman

- Be part of something great
- Support junior faculty and students
- Change clinical and research practices
- Have fun working together
SOCIBP Collaboration Scheme

Hospital

SPHN: Pathology
PHRT: Immuno-Oncology

ETH/University

Bioinformatics
Data Science

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SPHN Part: Main Aims & Partners

WP1. Determine optimal configuration for uniform genomics reporting to enable reliable sharing of clinical and research data. (SIB/Others)

WP2. Harmonize Swiss uniform genomics reporting format(s) for clinical and research interoperability. (Pathlink SNF & Onco SPHN)

WP3. Establish external SOCIBP sites and improve use/operator features for broader clinical and research connectivity (SIB/SAKK/Intern’l)
Goal: Integrated clinical report with detailed interpretation

Better treatment for patients
Harmonized across hospitals
Observational data collection of thousands of patients to enable biomedical research
Visualizations & Analyses of Swiss Cancer Cohorts
PHRT Part: Main Question & Aims

Why do only some patients respond to drugs blocking immune checkpoints such as the PD-1/PD-L1 pathway and what is the potential mechanism of response and resistance?

Work Packages:

WP4. Sample Collection and Processing
WP5. Integrative Genomics Analysis
WP6. Validation with Immune landscaping of tumors and prediction of treatment success from genomic/transcriptomic data

Data:

- Detailed clinical data (via SPHN)
- RNA-seq and Whole genome sequencing (via Swiss Genome Center/PHRT platform)
- Mass Spectrometry (via Swiss Proteome Center/PHRT platform)
- Deep Immuno profiling, T-Cell receptor sequencing (via Ludwig Cancer Center Lausanne)
Analysis of Aberrant Splicing in Cancer in 8,705 tumors

Summary: Swiss Molecular Pathology Breakthrough Platform

SPHN Driver Project

... will create a breakthrough genomics platform to manage and share data across Switzerland to help our clinicians and scientists untangle the complexity of therapy-related resistance.

- Optimize & harmonize molecular pathology reports
- Build on SPHN/BiomedIT infrastructure for data sharing and analysis
- Enables novel research & brings breakthroughs

PHRT Project

... will put our SPHN Driver to the test and address important cancer immunology question:
Why do only some patients respond to drugs blocking immune checkpoints such as the PD-1/PD-L1 pathway and what is the potential mechanism of response and resistance.

- Understand the effect of alternative splicing in cancer and immunotherapy
- Identify & combine molecular markers
- predict immunotherapy success with Machine Learning
- Translate findings back to clinical practice
Synergies with other projects

Observation: Many projects face similar challenges and have closely related requirements.

Suggestion: Use possibilities for knowledge exchange and harmonization.

Opportunities for harmonization:
- semantic harmonization on pathology data (via Patholink project; Holger Moch)
- semantic harmonization on clinical data (via SPHN semantics working group)
- semantic harmonization on genomics data (currently unaddressed)
- harmonization of variant calling and annotation procedures (currently unaddressed)
Thank You!

Questions?