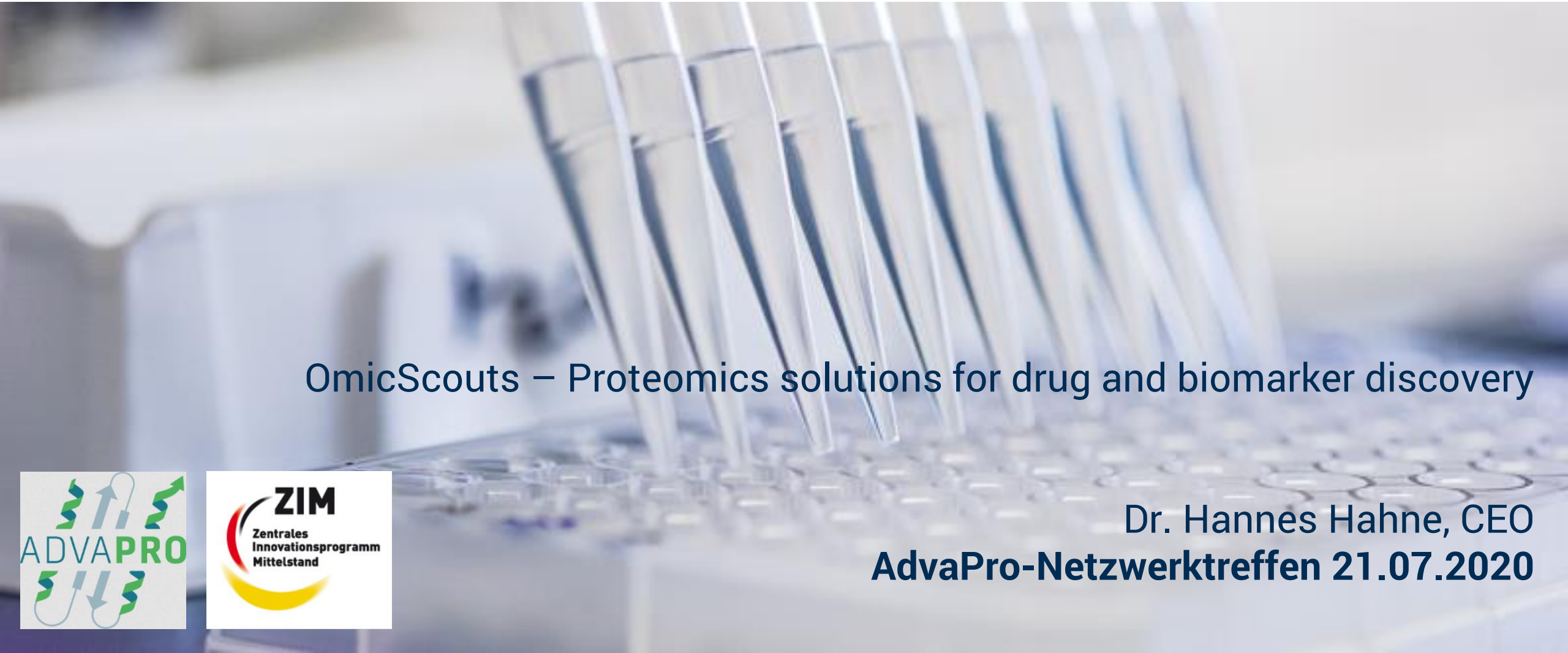


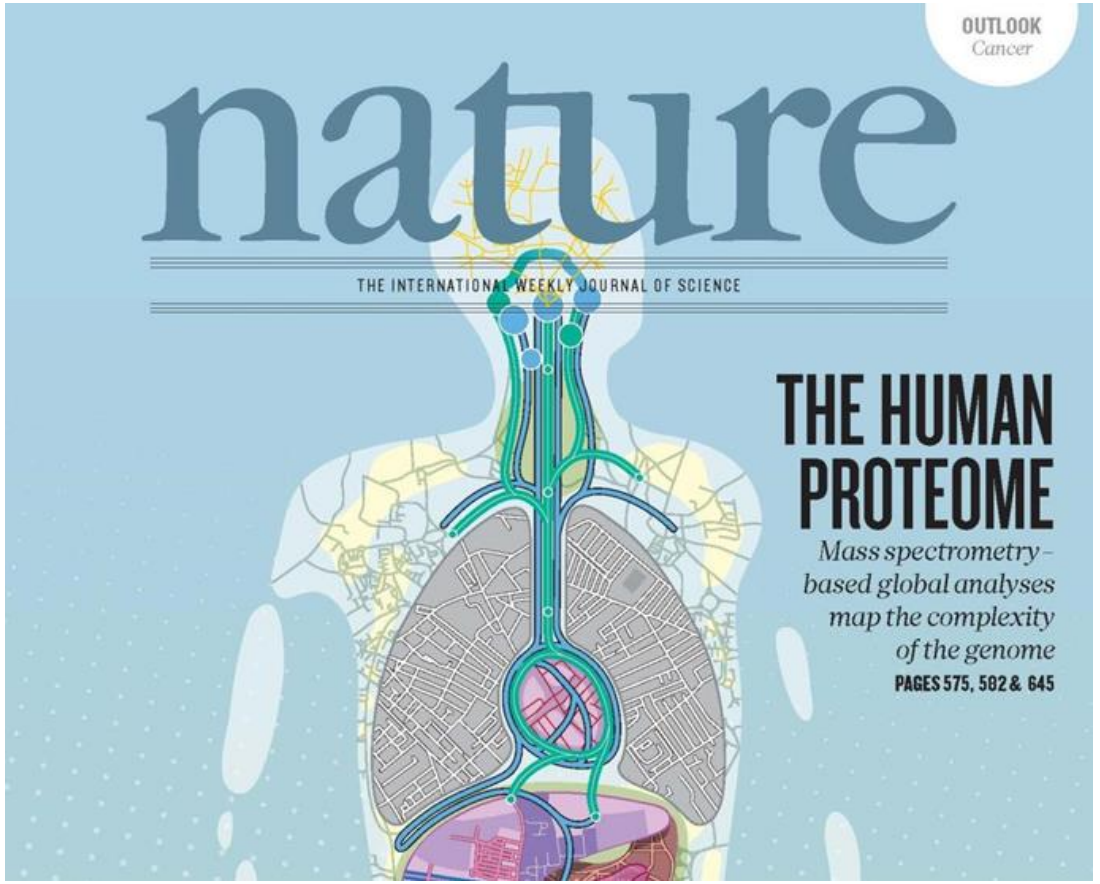
OmicScouts – Proteomics solutions for drug and biomarker discovery

Dr. Hannes Hahne, CEO

AdvaPro-Netzwerktreffen 21.07.2020

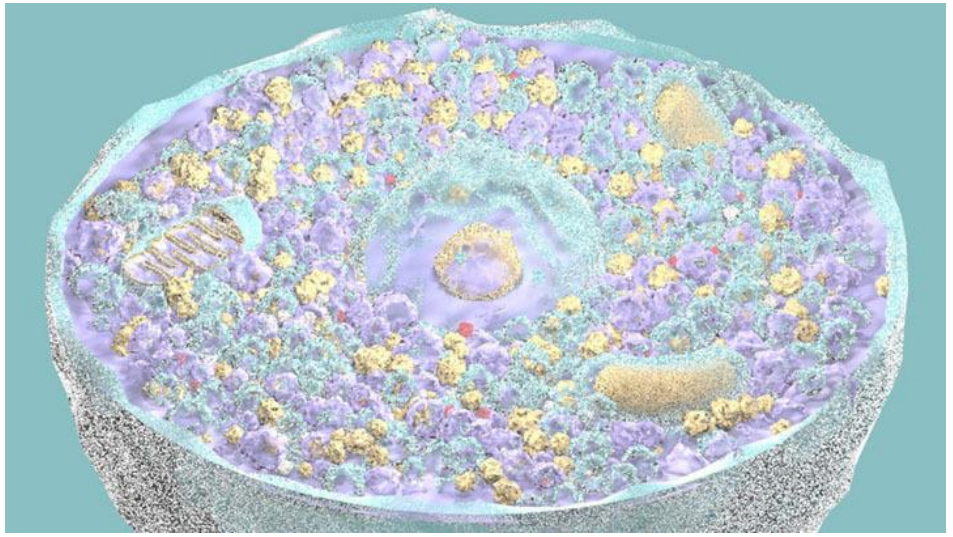
OmicScouts - Excellence in (chemical) proteomics

- OmicScouts was founded 2014 and is a spin-off of **Bernhard Kuster's lab at the Technical University of Munich**, a world-wide leading proteomics laboratory
- OmicScouts' founders and team (co-)authored **more than 150 original publications**, including in **Nature, Science, Cell, Nature Biotechnology, and Nature Methods**
- OmicScouts maintains and further develops a comprehensive portfolio of proteomics technologies, **focussed on drug discovery**
- OmicScouts provides **customized solutions** to support drug discovery and development needs of 10 out of top20 pharma and crop science companies



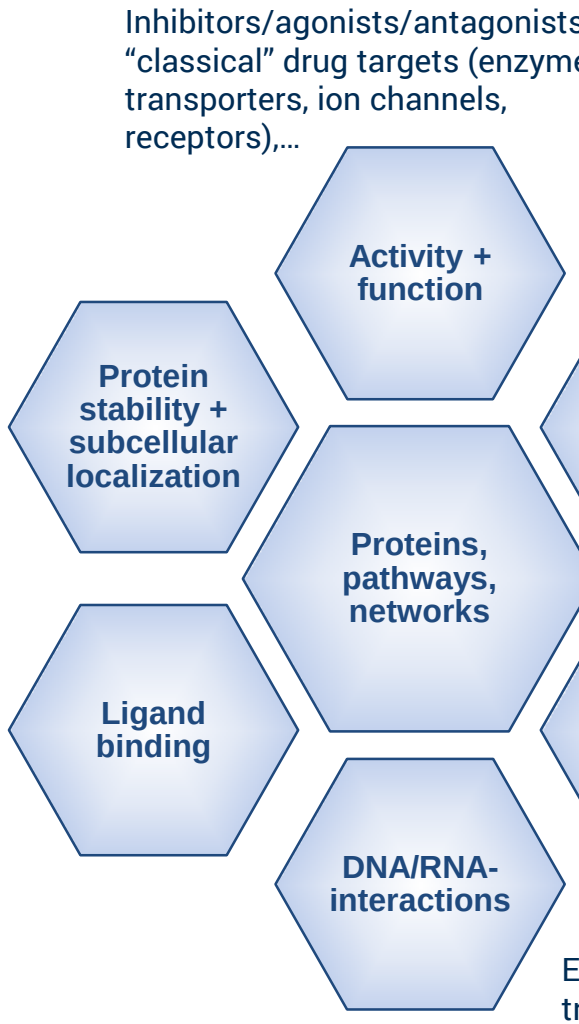
Some broad areas where proteomics can be applied

- **Characterizing (disease) biology, identifying targets**
  - Protein expression
  - Repertoire of post-translational modifications
- **Characterizing drug interactions**
  - Target deconvolution
  - Selectivity profiling, polypharmacology
- **Characterizing drug MoA**
  - Protein expression and PTM profiling
  - Target validation
- **Identifying (PD) biomarkers**
  - Target/pathway modulation/engagement
  - Prediction of therapeutic response
- **Understanding drug resistance mechanisms**
  - Protein expression
  - Reprogramming of pathway activity (PTMs)



Pharmacological modulation of protein activity and function in time and space

Our mission



Inhibitors/agonists/antagonists of "classical" drug targets (enzymes, transporters, ion channels, receptors),…

PROTACs, IMiDs, nuclear receptors, nuclear pore complex inhibitors…

Ribosome inhibitors, spliceosome inhibitors, epigenetic drugs,…

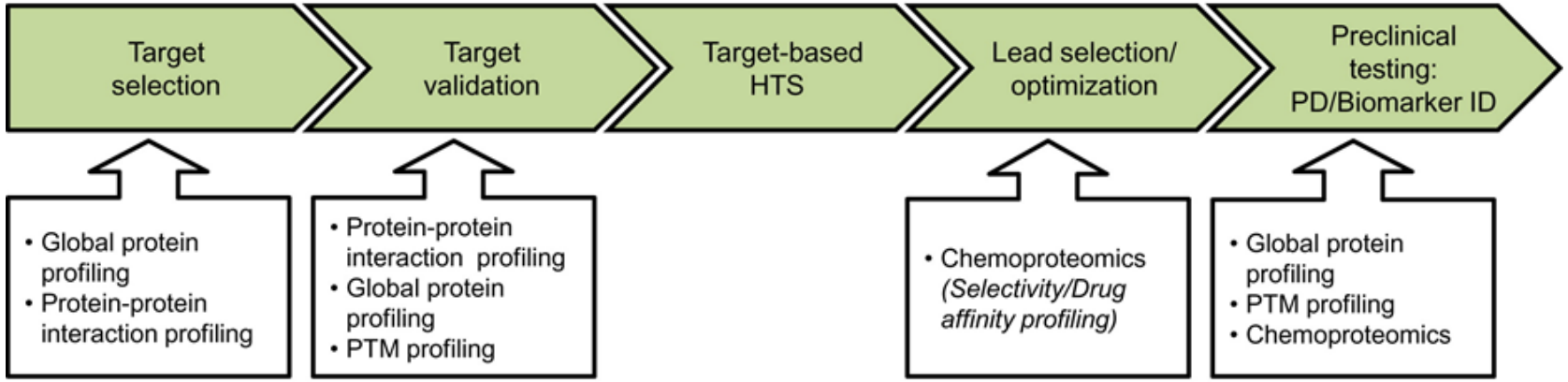
Competitive, allosteric, covalent,…

PPI inhibitors,…

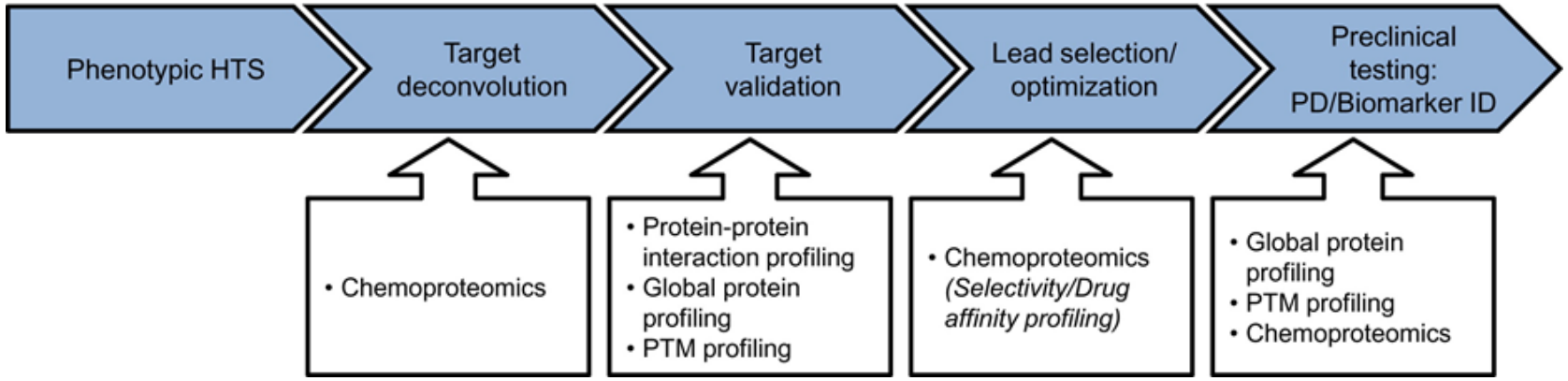
Epigenetic drugs, transcription factors, RNA modifying enzymes,…

Proteomics for (preclinical) drug discovery

Target-based drug discovery



Phenotypic drug discovery



Schematic representation of drug discovery strategies – Proteomics can support and facilitate both target-based drug discovery and phenotypic drug discovery with a variety of technologies

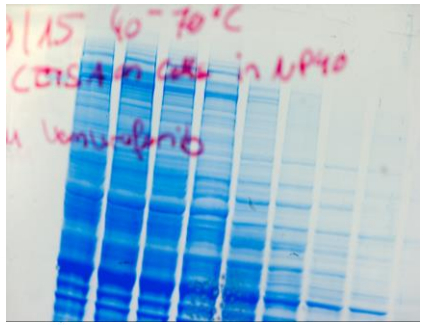
Source: Schirle, Bantscheff, Kuster, Chem Biol, 2012, 19(1):72-84

Overview of OmicScouts' services

- **ProteomeScout™**
  - Unbiased search for targets & biomarkers
- **BiomarkerScout™**
  - Highly parallel marker protein quantification by MS
- **TargetScout™**
  - Target deconvolution
  - Target selectivity studies
- **KinomeScout™**
  - Quantifying kinase inhibitor selectivity
- **TurnoverScout™**
  - Optimising PROTACs, IMiDs, etc., quantifying target degradation and synthesis in parallel
- **SignallingScout™**
  - Mapping compound-induced signalling pathways
- **Consulting**

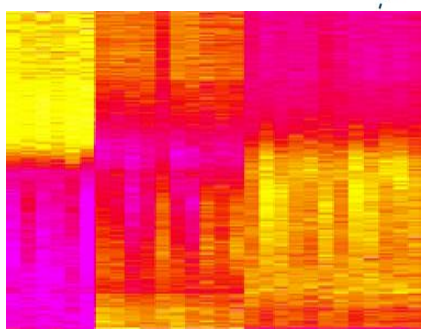
End-to-end solutions tailored to project needs

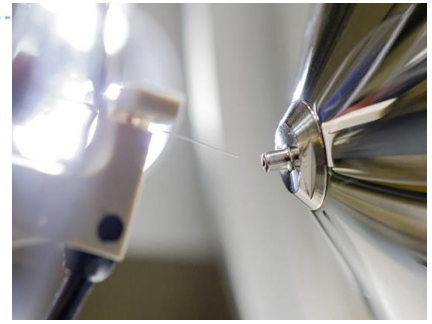
Cell culture and biology
>100 cell lines readily available
Up to BSL-2



Biochemistry
Fully equipped biochemistry lab
Basis of our broad portfolio of technologies

Bioinformatics and computational biology
Systems-wide and multi-omics analysis
Big data analytics



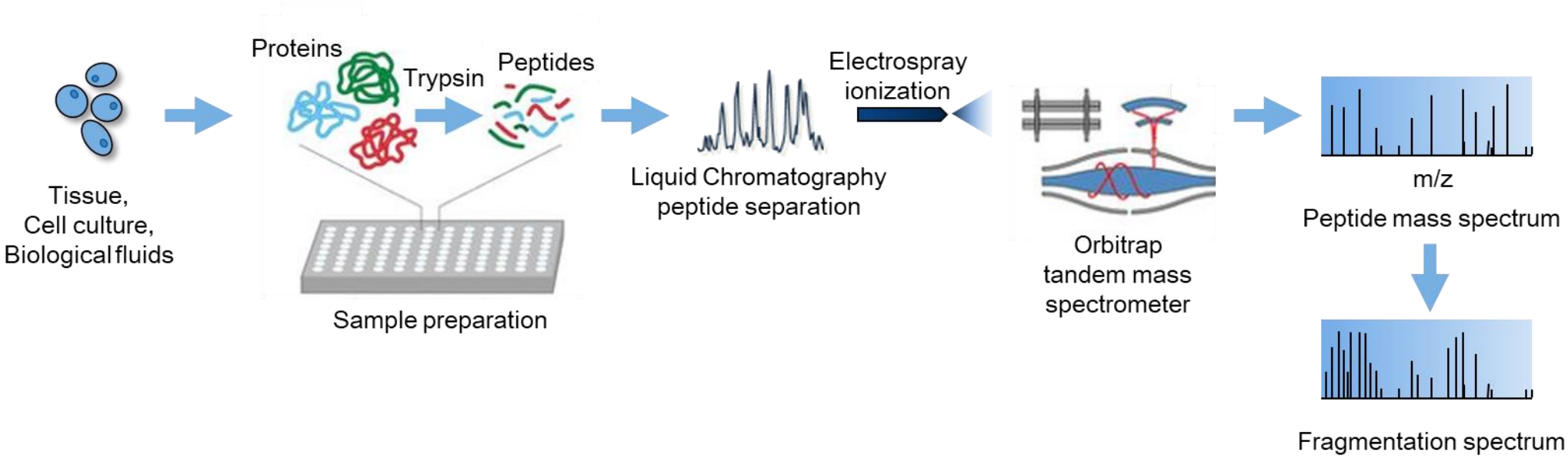


Mass spectrometry-based proteomics
Industry leading nLC-MS/MS equipment for comprehensive proteomic analyes
Automated data processing and QC

Mass spectrometry-based proteomics

An enabling technology

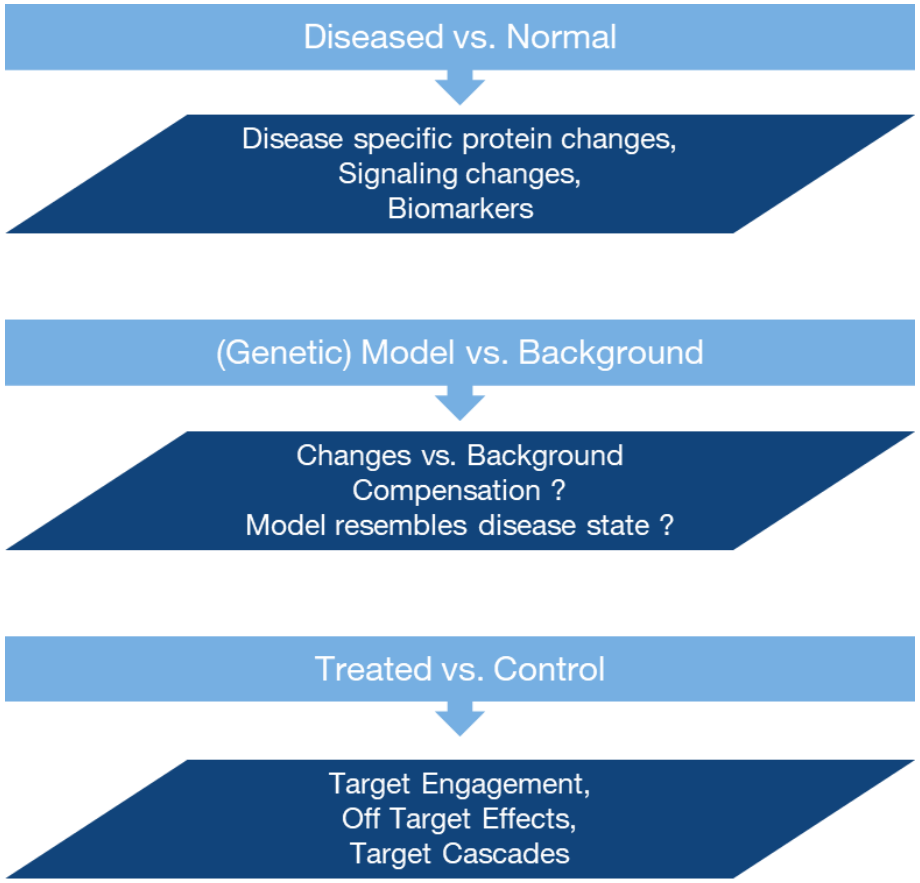
- Sample preparation: quantitative protein extraction from tissue, cell culture, and biological liquids
- Protein fractionation: ligand affinity, ligand stabilization, specific modifications (e.g. phosphorylation), cellular localization
- Proteolytic digestion: cleavage by trypsin or other specific proteases into better manageable peptides
- Peptide pre-fractionation: resulting peptide mixtures are separated by hydrophobicity, charge, or size as needed to reduce sample complexity
- Peptide fractionation & detection: LC peptide fractionation and direct elution into first mass spectrometry (MS) stage (peptide mass)
- Peptide sequencing & quantification: MS peptide ion fragmentation in second MS stage for sequence deduction and quantification



ProteomeScout™

Unbiased discovery of novel targets & biomarkers in different indications

- ProteomeScout™ enables highly parallel protein quantification, determining meaningful proteome differences between samples, resulting in target and biomarker discovery
- OmicScouts has significant experience designing adapted work flows: optimized sample preparations, peptide separation and proteome profiling up to a depth of 10,000 proteins
- Parallelisation and multiplexing are employed to safe costs and increase comparability between samples
- OmicScouts has experience with a wide range of samples:
  - fresh and frozen tissues
  - body fluids
  - formalin fixed paraffin embedded tissue
  - cellular extracts
  - bacteria
  - plants



BiomarkerScout™

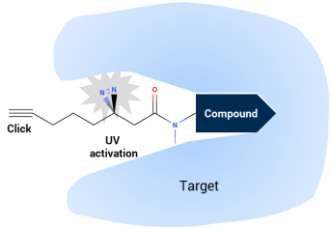
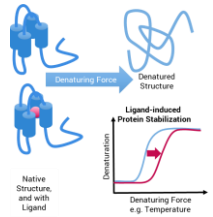
Quantification of marker proteins in large sample cohorts

- BiomarkerScout™ is an MS-based quantification of established protein markers
- Quantification is achieved by Parallel Reaction Monitoring (PRM) or non-radioactive heavy isotope labelled internal standards
- The technology enables accurate, sensitive and parallel quantification of up to 100 protein markers across hundreds of samples (e.g. patient samples, model tissues, cell line panels)
- BiomarkerScout™ facilitates the translation of pre-clinical results into the clinic by validating target engagement and signalling
- BiomarkerScout™ helps to validate predictive clinical markers

Nano-ESI interface of a mass spectrometer

Overview of target deconvolution approaches

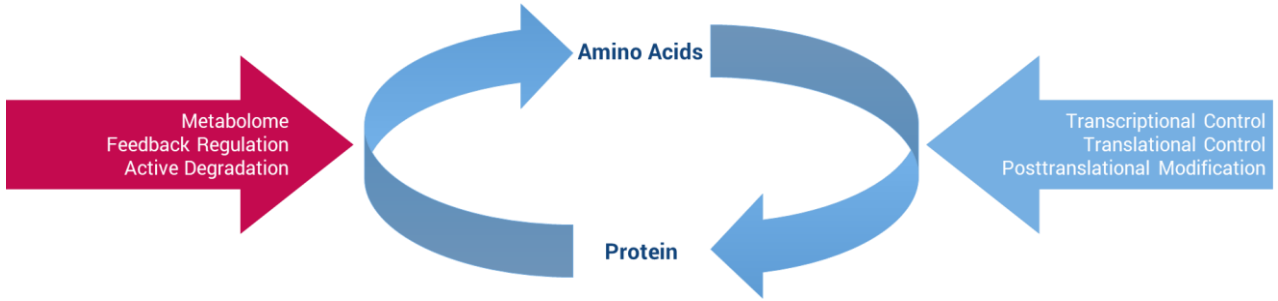
Characterization of drug:target interactions

Principle	Affinity Chromatography	Activity-based Labelling	Photo-affinity Labelling	Label-free Approaches
				
Requires…	Immobilized affinity probe	Trifunctional probe • Pharmacophore • Active-site targeting moiety • Enrichment handle	Trifunctional probe • Pharmacophore • Photo-cross-linker • Enrichment handle	Ligand, separation of native and denatured protein, but no label
Works well for…	Kinases, HDAC complexes, many traditional targets	Proteases, lipases, kinases, other enzymes	Integral membrane proteins	Abundant proteins, proteins amenable to (de-) stabilization
Does not work so well for…	Integral membrane proteins	Proteins without modifiable active sites	Targets with active site on protein surface	Low abundant proteins, membrane proteins

TurnoverScout™ - quantifying protein degradation & synthesis in parallel

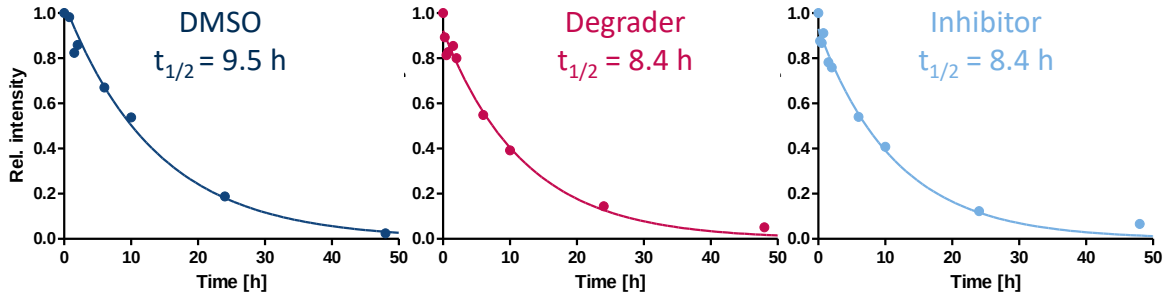
Tracking compound-induced changes in protein turnover

- Combination of pulse labelling and compound treatment enable proteome-wide determination of protein degradation and synthesis rates in parallel
- Example (→): Analysis of a non-target protein for degradation (top) and synthesis (bottom) rates after treatment of cells with: DMSO, a 'degrader' compound, and a small molecule 'inhibitor
- Consistent detection and quantification of ≈ 8,000 proteins



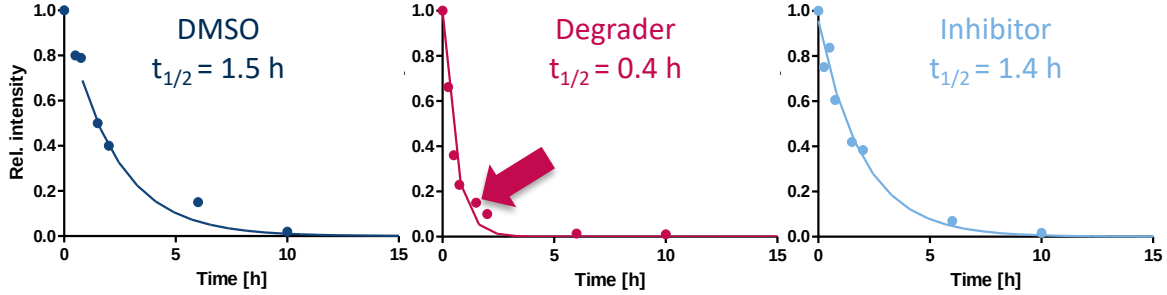
Results Non-Target Protein

Degradation:



Degradation:

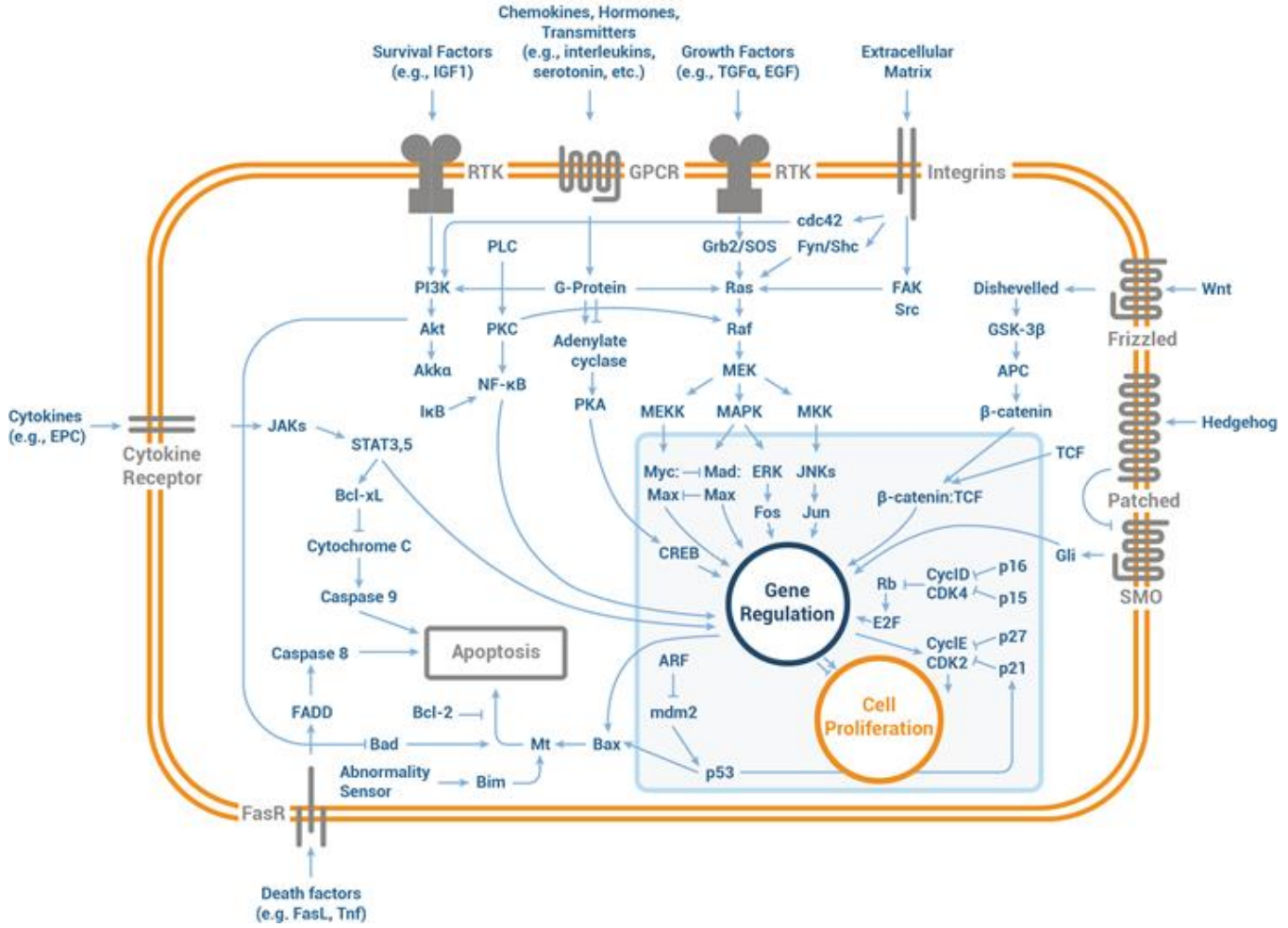
Results Target Protein



SignallingScout™

Investigating drug action on signalling pathways

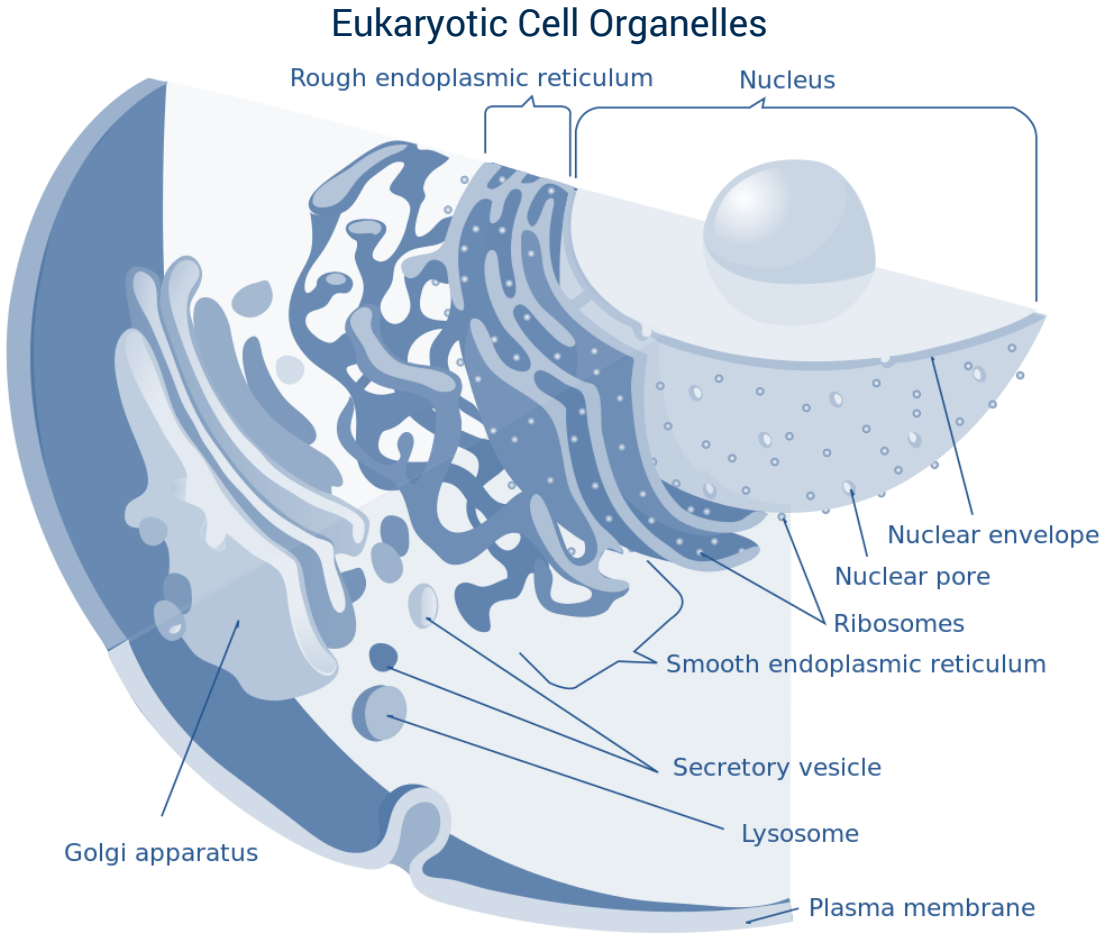
- SignallingScout™ enables profiling of phosphorylation events in hundreds of proteins concomitantly
- SignallingScout™ is used to evaluate compound action in all pathways simultaneously
- Enables selection of lead compounds, optimizing on-target effects and reducing off-target effects
- Investigation in different physiological models reveals tissue or cell-type specific drug activity



Subcellular proteomes

Investigating subcellular proteome dynamics upon drug treatment

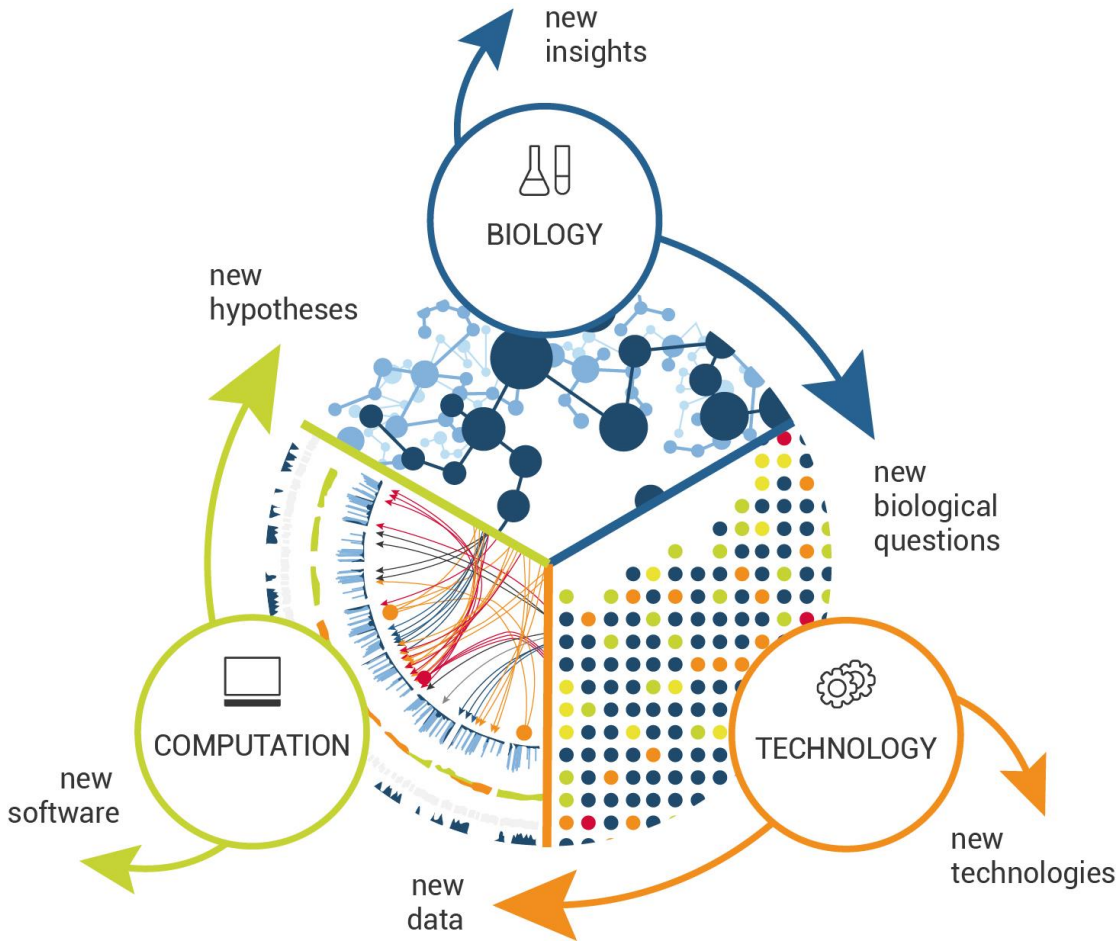
- Subcellular localization is essential to protein function and has been suggested as a means to achieve functional diversity.
- It is involved in **important regulatory processes**, like receptor internalization **and diseases** as failed processing from Golgi to cell membrane
- OmicScouts has experience in dividing the proteome into multiple subcellular fractions and analysing them independently for **quantitative protein changes**, incl. PTM differences
- Methods vary from simple membrane preparations to full subcellular fractionation
- Proteins are efficiently released from all fractions by harsh detergent treatment
- Detection of multiple peptides per protein support reliable protein quantification



Consulting and data analysis

Generating information and knowledge from data

- Omicscouts designs experimental strategies to fit customers drug discovery and lead optimization needs
- Resulting data are evaluated against background data and integrated to lead to clear results
- Drug action and target signalling can be elucidated to form a clearer picture on drug mode of action
- OmicScouts advanced bioinformatics tools extract systemic data and reveal relevant results
- Data analyses include: genomics, statistics, cluster analyses, machine learning approaches, feature selection, multivariate statistics, correlation analysis, lasso / elastic net procedures, pathway and network analyses, …



We are looking for…

… interesting new contacts and R&D projects…

Contact

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