Propositions associated with the thesis

Separate & Analyze: Improved mass spectrometry-based clinical proteomics by fractionation

1. The key to substantial and valid proteomic analysis of heterogeneous tissue samples is to sample the different cell populations individually and analyze them separately. *(This thesis.)*

2. Parallel reaction monitoring technology allows for the absolute quantification of multiple protein targets in small amounts of cerebrospinal fluid at and below the ng/mL level in a manner that is fast, flexible, and independent of the availability of appropriate binders, such as antibodies. *(This thesis.)*

3. In bottom-up proteomics, the uniqueness of a peptide with respect to its precursor protein is a key requirement. In the case of antibodies, it is generally not possible to determine the uniqueness due to the high sequence diversity of otherwise largely homologous sequences. However, uniqueness can be estimated and a rational selection of these peptides can be made using computational methods and large sequence repertoires. *(This thesis.)*

4. Peptides that carry specific epitope sequences including phosphorylation motifs or other modifications can be utilized to screen for the presence of corresponding (auto)antibodies without *a priori* knowledge of the antigen. *(This thesis.)*

5. Fitting acquired chromatographic data to expected chromatographic peak models is a powerful approach to objective and reproducible quantitative analysis of multiplex targeted parallel reaction monitoring data from large cohorts. *(This thesis.)*

6. In the analysis of the circulating antibody repertoire, mass spectrometry is the most evolved technique for protein sequencing. However, further advances are needed to confidently analyze individual clonotypes of the polyclonal antibody proteome/repertoire. (*Guy et al., biorxiv preprint, 2023*)

7. To warrant both, data protection & privacy and the possibility to share research data between academic institutes, solutions are needed to avoid conflicts between public access of proteomics data following common proteomics community guidelines and data protection regulations. *(Mundt, F., Open Res. Eur., 2023)*

8. Scientific publishing would benefit from, among others, dismantling access barriers, investing in robust metadata that provide the required findability of research content, and move from peer-review to peer-validation. *(Ahmed et al., Nat. Hum. Behav. 2023)*

9. Although no one likes uncertainty, transparent communication of scientific uncertainty about contested facts does not necessarily undermine public trust in science. (*Van der Bles et al., PNAS, 2020*)

10. The scientific attitude is the idea that scientists care about evidence and are willing to use evidence to change their theories (or hypotheses). This search for that one piece of data that will prove them wrong is a noble endeavor and brings many virtuous qualities of reasoning. (*Lee McIntyre, 2020*)

11. Science may be described as the art of systematic oversimplification. (*K. Popper*)