GTR seminar Quantifying proteins in single cells at high-throughput



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The fate and physiology of individual cells are controlled by networks of interacting proteins. Yet, our ability to quantitatively analyze protein networks in single cells has remained limited. To expand it, we developed SCoPE2. It combines concepts from Single-Cell ProtEomics by Mass Spectrometry (SCoPE-MS) with automated and miniaturized sample preparation that lowers cost and hands-on time. SCoPE2 uses data-driven analytics to optimize instrument parameters for sampling more ion copies per protein, thus supporting quantification with improved count statistics. Furthermore, SCoPE2 uses a principled Bayesian framework that enhances peptide sequencing. These advances enabled SCoPE2 to quantify over 2,000 proteins in 357 single monocytes and macrophages in about 85 hours. The quantified proteins enabled separating the single cells by cell-type and identifying sub-populations of macrophages. Our methodology lays the foundation for quantitative analysis of protein networks at single-cell resolution.

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