P-1.53

Atcun Peptides for Ultrasensitive Automated Nanopore-based Detection of Copper Ions as Disease Biomarkers and for Antimicrobial Therapy

Ivan Unksov [1], Shitanshu Devrani [1], Priyanka Mehra [1], Lena K. Müller [2], Hanna Zdhannova [1], Daniel Tietze [1], Alesia A. Tietze [1]

[1] Department of Chemistry and Molecular Biology, Wallenberg Centre for Molecular and Translational Medicine, University of Gothenburg, Gothenburg, Sweden

[2] Clemens Schöpf Institute for Organic Chemistry and Biochemistry, Darmstadt University of Technology, Darmstadt, Germany

Peptides with amino-terminal Cu(II)- and Ni(II)-binding (ATCUN) motif are promising for several applications. An elevated level of free copper in human body fluids indicates Wilson and Alzheimer's diseases, and the peptides can be used to detect these ions. Furthermore, binding of the ATCUN peptides to DNA promotes its oxidative cleavage, which can be used in antimicrobial therapies, to combat antibiotic resistance. Here we develop these two applications. We present a high-throughput microfluidic platform based on polymer nanopores (Müller et al. 2020), which automates detection of copper for enhanced sensitivity and selectivity. The system integrates a robotic sampler, electrochemical and fluorescence measurements, and data analysis enhanced by machine learning. A nanopore membrane functionalized with an ATCUN peptide demonstrated selective Cu(II) detection, with detection limits being at micromolar concentrations when fluorescence is used and at femtomolar concentrations via electrochemical measurements (Devrani et al. 2025). We show the potential of this sensor for clinical samples. In the second study, we designed ATCUN-like peptides to linearize plasmids resistant to different antibiotics (Müller et al. 2024). We show that histidine, previously believed to be mandatory for the ATCUN motif, is not essential for copper binding and sequence-specific DNA linearization.