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Targeting transporters with HTS electrophysiology: The glutamate transporter EAAT3 on the SURFE²R 96SE.

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Due to the growing interest in membrane transporters as drug targets there is an increasing demand for efficient, reliable and flexible activity measuring systems. Solid Supported Membrane (SSM)-based electrophysiology has emerged as an promising technology for the biophysical and pharmacological characterization of electrogenic membrane proteins, such as transporters and ion pumps.

SSM-based electrophysiology is a label-free measuring method which allows the use of reconstituted protein or membrane samples from native tissues or cell culture. High-sensitivity and robustness allow the resolution of low turnover transport and even binding- events, which usually cannot be detected with conventional electrophysiological methods. Although invented in the 90's and more than 100 different proteins tested, the method is still under-utilized. One reason for this has been the limited throughput.

Here, we present data on the neuronal glutamate transporter EAAT3 using a novel high throughput instrument for SSM measurements, the SURFE²R 96SE. EAAT3 is involved in the neuronal re-uptake of glutamate and plays a central role in the regulation of excitatory neurotransmission, which makes it an highly interesting drug target. Implementing the SURFE²R 96SE instrument, we were able to determine substrate affinities and their interaction, and to compare the effect of six known inhibitors directly with each other. Furthermore we were able to resolve substrate binding and to show the described anion conductance of the transporter. Overall our data renders the SURFE²R 96SE a potent and flexible tool for transporter research and drug screening.