Increased Throughput in GPCR Screening using Impedance Assays: Inspiration from Organ Studies

J.A. Stolwijk; C. Kade; M. Skiba and J. Wegener
Universität Regensburg, Regensburg (Germany)
judith.stolwijk@chemie.uni-regensburg.de

G-Protein Coupled Receptors (GPCRs) belong to the most promising drug targets, as they are involved in a multitude of human diseases. In screenings for novel, effective GPCR ligands, studies on human cell cultures have nowadays largely replaced classical organ pharmacology.
Especially, label-free impedance-based assays have evolved as a valuable tool to quantify the efficiency and potency of GPCR ligands, as the method is sensitive to all signaling pathways activated that evoke changes in cell morphology [1, 2]. This so-called holistic detection of the integrated response to receptor activation has many parallels to functional measurements on organ and tissue preparations.
Impedance assays are capable of quantifying GPCR activation in cellular systems with endogenous receptor expression non-invasively with a time resolution down to several milliseconds.
However, when considering the screening of large substance libraries, the costs for the disposable electrode arrays may become limiting. Moreover, with an increasing number of samples to be studied the available time resolution is reduced.

Inspired by protocols from organ pharmacology, we investigated a simple serial agonist addition assay that circumvents the above described limitations. We report on the possibility to establish a full concentration-response curve for a GPCR agonist using a single cell layer in an impedance assay. This significantly increases throughput and reduces the costs per assay, while the time resolution, necessary to detect fast and transient cell responses, is retained.

References:

[1] C.W. Scott and M.F. Peters, *Drug Discovery Today* 15 (2010) 704 – 716
[2] J.A. Stolwijk, K. Matrougui, C.W. Renken, M. Trebak, Pflügers Archiv 467 (2015) 2193 – 2218