Monitoring the Toxicity of Bisphenol A using Multiple Impedance-Based Cellular Assays

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Bisphenol A (BPA) is a synthetic organic chemical, that is heavily applied as an additive to produce clear and robust plastics and resins. It belongs to the mostly synthesized chemicals worldwide. Epoxy resins containing BPA are used to line water pipes and as coatings on the inside of many food and beverage cans. Because of its presence in food containers (even for baby food) concerns about its harmfulness have accumulated recently and led to new legislature in some European countries limiting its use. It has been included in the list of REACH chemicals which are monitored in detail for their harmfulness.

It was our intention to study the impact of BPA on cultured cells with a whole set of impedance-based assays focusing on different cell phenotypes like (i) cellular micromotion, (ii) cell migration, (iii) cell proliferation, (iv) toxicity in equilibrated cell layers. These studies were accompanied by well-established metabolic assays that report on metabolic activity (PrestoBlue) and the cells' oxygen consumption rate. These assays were used to test the hypothesis that BPA may affect cellular physiology differently dependent on the cellular state and that detailed toxicity profiles are more appropriate to describe a compound's toxic potential than just a single biochemical assay. Normal Rat Kidney (NRK) cells were used as model cell in all assays.

All impedance-based assays were performed according to state-of-the-art protocols taking advantage of different time resolutions and monitoring frequencies dependent on the details of the assay. Metabolic activity was studied by the commercial PrestoBlue assay that reports on the availability of the redox coenzymes NADH and NADPH, central products of catabolism. Oxygen consumption rates (OCR) were determined by monitoring the oxygen concentration beneath the cells using oxygen sensitive sensor foils and an imaging system provided by PreSens®. After dose-dependent experiments were performed, data analysis returned the EC_{50} values for each assay that are summarized in the radar plot below (Fig. 1).

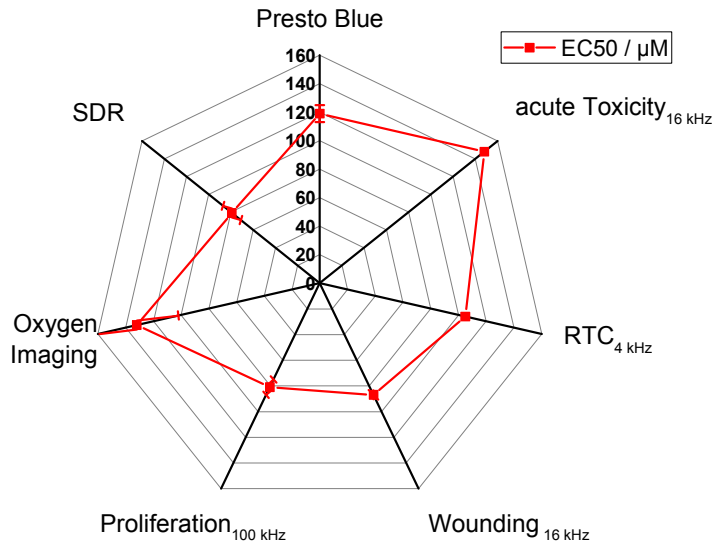

Fig. 1: Comparison of EC50 values, reporting on the impact of Bisphenol A on different cell phenotypes.