Comparative Analysis of Cytotoxic Effects of Bisphenol A and Bisphenol S on Human Renal *HEK293* Cells

Podlich S[1], Plum C[1], Bohme K[1], Kreutz R[1], Leppert U[2] and Eisenreich A[1*]

[1]Charite-Universitatsmedizin Berlin, Institut fur Klinische Pharmakologie und Toxikologie, Berlin, Germany
[2]Charite-Universitatsmedizin Berlin, Institut fur Physiologie, Berlin, Germany

[*]**Corresponding author:** Andreas Eisenreich, Charite-Universitatsmedizin Berlin, Institut fur Klinische Pharmakologie und Toxikologie, Chariteplatz 1, 10117 Berlin, Germany, Tel: 004930450525237; E-mail: andreas.eisenreich@gmx.de

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CFX96TM Real-Time System (Bio-Rad Laboratories GmbH, Munich, Germany) was used. real-time PCR conditions: 50°C, 2 min; 95°C, 20 sec; 45 cycles 95°C, 3 sec; 60°C, 30 sec. For analyses of the mRNA expression of Bcl-2 and BAD, "TaqMan® Gene Expression Assays" Fisher Waltham, MA, USA) were used following the manufacturer's protocol.

Western blot analyses: Sodium dodecyl sulfate polyacrylamide gel electrophoresis and Western blot analyses of protein expression were performed as described previously [15,16]. Expression was determined in cell lysates of *HEK293* using antibodies against RelA (Aviva Systems Biology, Corp., San Diego, CA, USA), Akt (Merck Chemicals GmbH, Schwalbach, Germany), PDPN (Sigma-Aldrich Chemie GmbH, Munich, Germany), and GAPDH (Calbiochem, Darmstadt, Germany). of Western blot results was performed by Gel-Pro AnalyzerTM version 4.0.00.001 (Media Cybernetics, Bethesda, MD, USA) as described earlier [17,18].

Calcein AM cell viability assay (Trevigen Inc. Gaithersburg, MD, USA) was performed as described earlier [9,19] and following manufacturer's protocol. In brief, 1 x 10^4 *HEK293*

a f ects

Compared to ethanol-treated controls (EtOH), pharmacological inhibition of Akt via triciribine (10 µM) had no inhibitory on cell viability of resting cells or *HEK293* stimulated with 10 µM BPA or BPS, respectively (Figure 3). In contrast to triciribine, incubation of cells with 10 µM BAY 11-7082 led to a substantial reduction of *HEK293* cell viability post 24 h (Figure 3). Additional application of 10 µM BPA or

doses of BPA (100 µM-300 µM) concentration-dependently decreased cell viability [27]. In contrast to BPA, no cytotoxic were found in hepatocytes treated with 0 µM-300 µM BPS [27].

Renal cell viability is orchestrated via an interplay of various factors modulating the balance of pro-survival *vs.* pro-apoptotic processes, such as Akt, PDPN or members of the Bcl-2 family [9,32]. On the one hand, Akt and PDPN plays an important role in regulating pro-survival signaling and structural integrity in renal cells [9,19,33]. On the other hand, NFκB-including its subunit RelA is of major importance for cell viability and apoptosis control, amongst others via modulating gene expression of pro-survival and pro-apoptotic Bcl-2 family members [7,32,34,35].

We found that low doses of BPA (0.1 µM-10 µM) had no whereas 1000 µM BPA led to a nearly complete inhibition of Akt, PDPN, and RelA protein expression in *HEK293* post 24 hrs. In line with our Zhao and colleagues also depicted that low amounts of BPA (0 µM to 10 µM) had no impact on Akt expression in primary isolated murine ovaries *ex vivo* [36]. Further substantiating our data, Vahdati Hassani et al. showed in 2017 that treatment of Wistar rats with a high dose of BPA of 0.5 mg/kg for 30 d led to a reduced Akt protein expression in the liver of these animals [26].

Conflict

authors declare that there are no of interest.

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