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EDITORIAL

Highlight report: the need of 'fit-for-purpose' controls for cell lines used in toxicity assays

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Recently, Simon Gutbier and colleagues from Konstanz University published an interesting article about the genomic drift of cell lines used for toxicity assays (Gutbier et al. 2018). Cell lines for toxicity testing are difficult to standardize (Nims and Reid 2017; Gore et al. 2011; Laurent et al. 2011). Therefore, journals often ask for authentification of cell line identity. This is usually achieved by short tandem repeat (STR) profiling, using multiplex PCR to simultaneously amplify several STR loci; thereby, for each cell line a unique pattern of repeating DNA is obtained. However, Gutbier and colleagues demonstrated that these standard techniques may not be sufficient. They identified a problem comparing two subpopulations of LUHMES cells maintained at the American Type Culture Collection (ATCC) or by University of Konstanz, the original provider (Gutbier et al. 2018). LUHMES cells are a cell line frequently used in in vitro neurotoxicity testing. They were obtained from an 8-week-old human fetus from precursor cells of the mesencephalon. Interestingly, LUHMES cells banked by ATCC tolerated up to 60 µM of the neurotoxic compound MPP^+ (1-methyl-4-phenylpyridinium). In contrast, cells maintained in the laboratory of the original provider at Konstanz University showed cytotoxic effects already at 3 µM (Gutbier et al. 2018). In the present study, both LUHMES sublines showed normal chromosome structures. Sequencing and genome comparison revealed approximately 70 differences that cause changes of the amino acid sequence. These changes did not lead to a straightforward explanation of the difference in susceptibility. However, the subline from ATCC downregulated tyrosine hydroxylase and dopamine transporters after differentiation, a problem not seen in the cells maintained in Konstanz (Gutbier et al. 2018).

Currently, numerous laboratories depend on the functionality of cell lines for testing of neurotoxicity (Colaianna et al. 2017; Sisnaiske et al. 2014; Micheli et al. 2018; Meléndez et al. 2018) and developmental neurotoxicity (Shinde et al. 2015, 2016, 2017; Waldmann et al. 2014, 2017; Palloca et al. 2016; Balmer et al. 2014; Weng et al. 2014). Similar problems are faced, when cell lines are used in nephrotoxicity (Cheng et al. 2018; Su et al. 2016; Gong et al. 2016), hepatotoxicity (Hammad et al. 2014; Ghallab 2017; Ghallab et al. 2016; Gu et al. 2018) and cardiotoxicity (Chaudhari et al. 2016a, b) testing. Only when primary cell is isolated the challenge of genetic drifts in vitro is avoided (Godoy et al. 2013; Arbo et al. 2016; Grinberg et al. 2014). The authors of the present study recommend a 'fit-for-purpose test' specifically chosen for the required purpose. In the case of LUHMES cells in neurotoxicity testing, a cytotoxicity test with MPP^+ seems be adequate to guarantee that cytotoxicity is already observed at concentrations of 3 µM. The study of Gutbier and colleagues illustrates that conventional methods, e.g. STR profiling, may not be sufficient to guarantee functionality of cell lines in toxicity assays.

Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

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