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Accurate high-throughput prediction of human organ-specific toxicities

Evaluating the toxicity of chemicals, drug candidates and other compounds requires predictive methods. There is a steeply increasing demand for alternative methods due to various problems associated with animal experiments and changes in legislation (e.g. animal bans for cosmetics testing). However, many alternative methods are of unknown predictivity, and accepted alternative methods for predicting toxicity for human internal organs are not available. This problem is addressed by our work, which was initially focused on the kidney. Recently, we have developed the first animal-free platforms for the accurate prediction of nephrotoxicity in humans. These technologies have received various international awards, including the Lush Science Prize 2016. Our methods include the only available predictive methods based on human induced pluripotent stem cell-derived renal cells and a predictive high-throughput platform. The high-throughput platform is currently applied in collaboration with the US Environmental Protection Agency to predict the human nephrotoxicity of ToxCast compounds. The test balanced accuracies of our predictive methods range between ~80% - 90%, and these methods also reveal injury mechanisms and compound-induced cellular pathways. Based on a similar methodology we are now developing high-throughput platforms for predicting toxicity for other human organ systems, including liver and vasculature. Furthermore, we are establishing predictive organ-on-chip platforms for efficient repeated dose testing and dose-response assessment.

Biography

Daniele Zink earned her PhD from the University of Heidelberg, Germany in 1995 and completed her Habilitation (2001) at the Ludwig Maximilian University of Munich. In 2001, she was awarded funding of a Junior Group from the Volkswagen-Foundation, which she led until she moved to the Institute of Bioengineering and Nanotechnology (IBN) in Singapore in 2007. Her work on predictive in vitro models has been awarded by Merck Millipore and the US Society of Toxicology. She has won the prestigious LUSH Prize (2016, Science Category). She holds 10 patents/patent applications; is Editorial Board Member of Scientific Reports; has more than 70 peer reviewed publications and is Co-Founder and Director of the spin-off company Cellbae.

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