Elaboration of an in vitro test for the carcinogenesis evaluation of chemical and natural compounds used in the cosmetic industry.

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Abstract:

Toxicological tests for cosmetic products are classically performed on animal models. Prohibitive costs and evolution of the perception about animal experimentation in the general public have encouraged the development of in vitro tests capable of predicting the toxicity of compounds potentially classifiable as “CMR” (Carcinogenic, Mutagenic and/or Reprotoxic).

In this work, we establish relevant transcriptomic signatures of CMR compounds on lung epithelia using 2D (such as the normal human bronchial epithelium cells, BEA-2B) and 3D cultures.

3D cultures defined as “air liquid interface” (ALI) reconstitute a differentiated epithelium composed of different types of cells (ciliated cells, goblet cells, etc.).

Two known CMR toxicants (cadmium chloride ($CdCl_2$), hydroquinone (HQ)) were selected according to previous literature.

ALI and BEAS-2B cultures were first analysed by microarray gene expression profiling upon incubation with the two toxicants. This transcriptomic analysis performed on bulk cells revealed a comparable response based on a 200 genes signature between the two culture systems used and a better reproducibility when using the BEAS-2B model.

Next, we performed single cell analysis to identify potential bias linked to the ALI culture systems and differences in the biological response to the treatment at the cell subpopulations level.

We identified cell-type specific responses that allowed us to establish a transcriptomic signature for each cell type composing the ALI system in response to the toxicants and a hierarchy of “responding cell types”.

Overall, our results show that the ALI system associated with a Single cell analysis can be successful used as an alternative to in vivo inhalation toxicology studies.