Reconstructed Human Epidermis (RhE) Monitoring via the IMOLA-IVD

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The gross disconnect between preclinical toxicity screening and clinical testing causes a low success rate for new drug candidates. Substantial numbers of redundant samples are prepared in order to analyze cellular reactions over an extended time course. Furthermore, protocols that investigate organ toxicity using animal testing are inaccurate at predicting in vivo toxicity and present an ethical dilemma in regards to animal welfare. The advent of more accurate 3D in vitro cultures like organs-on-a-chip (OOCs) has improved our ability to probe the potential effects of drug candidates in vivo. However, standard colorimetric assays, which are labor intensive and may affect the underlying cellular activity, are still used to assay new cultures. Cellular microphysiometry systems like the IMOLA-IVD (cellasys GmbH), a microsensor array-based assaying technique, offer a solution to these issues with the ability to noninvasively monitor biological changes in real-time. To date, the IMOLA-IVD's has been used to monitor morphology, oxygen consumption and extracellular acidification rate from a diverse array of standard cellular cultures ranging from planar cultures to biopsied tissue [1]. When combined with more complex in vitro cultures, these "biochips" can be converted into rapid, high-content, cell-based assays that are easily automated.
In the presented work, a candidate 3D in vitro culture, the reconstructed human epidermis (RhE) artificial skin, was integrated with a modified IMOLA-IVD biochip for online monitoring of extracellular acidification. RhE, grown on standard polycarbonate membrane culture inserts, mimic the structure and function of standard human epidermis. A few have already been used in Organization for Economic Cooperation and Development (OECD) validated in in vitro skin irritation and toxicity assays. Monitoring the metabolic output of an RhE in real-time can reveal time-resolved data on the toxic effect new compounds have on the epidermis. Automatic screening can also provide a new pathway that can revolutionize the process of testing new chemicals for skin irritancy. For this reason, we developed the protocol for an automated skin corrosion/irritation assay. IMOLA Biochip-D's were modified to perfuse cell culture inserts with medium while maintaining an air-liquid interface. Metabolic signals were recorded in real-time in an incubator via the IMOLA-IVD system. RhE from CellSystems GmbH (epiCS) cultured on culture inserts were perfused automatically with medium via a peristaltic pump, IMOLA fluidic modules and the DALiA control software. Future work will involve developing this method into irritancy and corrosivity assays that follow from OECD testing guideline 431 (corrosion) and 439 (irritation), by exposing the epiCS to potentially toxic agents.

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[1] D. Weiss, M. Brischwein, H. Grothe, B. Wolf, and J. Wiest, "Label-free monitoring of whole cell vitality," Conf Proc IEEE Eng Med Biol Soc, vol. 2013, pp. 1607-10, 2013.

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