

Development of a Lab-on-Chip device to test myelotoxic effect of drugs and chemicals

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In 2006 the European Centre for the Validation of Alternative Methods (EVCAM) has approved the Colony Forming Unit-Granulocytes-Macrophages (CFU-GM) test, which is the first and currently unique test applied to evaluate the myelotoxicity of xenobiotics in vitro[1]. The test is a clonogenic assay consisting on seeding bone marrow progenitors in a methylcellulose semi-solid medium and counting the colonies of cells formed by the surviving progenitors which are still able to demonstrate clonogenic activity after toxicant exposure. In this context, our objective was to miniaturize and optimize the current state-of-art in vitro myelotoxicity test by developing a Lab-on-Chip (LoC) platform consisting of two functional elements: a culture region and a linear dilution generator. The culture region is organized in six units, each composed by three lines of 10 culture chambers. The second element delivers six linear dilutions of xenobiotic agents (concentrations ranging from 1 to 0, step 0.2) from two input ports to the culture units. Chamber dimensions and number have been chosen to host at least three progenitor cells in each culture unit, being i) 10 the target number of cells seeded in each chamber, and ii) 1% the population clonogenicity factor. The LoC platform was validated both in terms of cell seeding uniformity and biocompatibility using cord blood mononuclear cells (CB MNCs). Upon 4 days of culture, a significant increase in the number of cells was recorded, suggesting early colonies formation. In this study, a LoC device integrating high-throughput screening capabilities was presented. The proposed platform could represent a powerful tool in the hematotoxicity test field, offering high reproducibility and experimental costs, related to amount of drugs required and quantification of colony forming unit cells.

[1] A. Pessina, B. Albella, M. Bayo, J. Bueren, P. Brantom, S. Casati, et al. *Toxicol Sci*, **75** (2003), p. 355-67.