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Heart/Liver-on-a-chip as a Model for the Evaluation of Cardiotoxicity Induced by Chemotherapies †

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Abstract: Drug discovery faces challenges due to the absence of suitable preclinical tests, including conventional cell cultures and animal studies. Organ-on-a-chip devices can simulate the whole-body response to therapeutics by fluidically connecting microscale cell cultures and generating a realistic model of human organs of interest. We designed and fabricated a pumpless heart/liver-on-a-chip (HLC) using the HepG2 hepatocellular carcinoma cells and H9c2 rat cardiomyocytes to reproduce the cardiotoxicity induced by doxorubicin (DOX) *in vitro*. Our cell studies proved the high viability of both cells up to 5 days of culture in HLC. The developed device demonstrated more significant damage to heart cells within the HLC than conventional static 3D culture in the case of DOX treatment, which is due to exposure of cells to both the parent drug and its cardiotoxic metabolite, Doxorubicinol (DOXOL). Our designed HLC device represents a good approach to assess the off-target toxicity of drugs and their metabolites, which is expected to improve current preclinical studies.

Keywords: organ-on-a-chip; microfabrication; drug metabolism; cardiotoxicity; doxorubicin.

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Conflicts of Interest

The authors declare no conflict of interest.