Microphysiological systems for studying interactions between the liver, gut and immune system

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INTRODUCTION

Microphysiological systems (MPS), also known as organ-on-chips, are small scale in vitro cell cultures which mimic facets of tissue or organ level function (1). MPS frequently utilize primary human cells, often cultured in 3D, to obtain highly functional, physiologically relevant models. MPS can be utilised alone, but can also be connected through fluidic circuits to create advanced multi-MPS that can model the interactions between organ systems, allowing greater analysis of molecular pathways and disease mechanisms (2).

Several liver MPS systems have been developed that allow the culture of highly metabolically active primary hepatocytes. However, most current models are simple monocultures of hepatocytes and do not closely resemble the highly heterogeneous primary liver cell types and determine how these interactions drive specific pathologies. We have developed a novel system for the in vitro culture of hepatocytes in a perfused three-dimensional format, with a separate co-culture allowing interactions to be studied with a second MPS. To demonstrate the utility of this model we have generated two liver multi-MPS models.

AIM

We aimed to establish MPS for the study of liver interactions with other organ cell types. The systems utilize a transwell which was used to culture either mixed immune cell populations or Caco-2 gut epithelia, alongside cultures of functional primary human hepatocytes.

METHOD

Cryopreserved human hepatocytes (PHH) were obtained from Life Technologies (USA) and cultured in Ad-DMEM medium containing supplements. 2 x 10^5 PHH were seeded onto collagen-coated plastic dishes in static conditions, after 24 h dishes were transferred into T18 microfluidic plates and cultured with Ad-DMEM medium containing 10% fetal calf serum and 1% penicillin/streptomycin. PHH were combined with PHH in T18 wells in Ad-DMEM medium +/- 100 IU/ml interferon gamma (IFN-γ) for 24 h. A) Production of IFN-γ by PHH in the T18 system. B) IFN-γ production by PHH in T18 MPS. C) Production of IFN-γ by PHH in T18 MPS. D) IFN-γ production by PHH in T18 MPS. E) IFN-γ production by PHH in T18 MPS. F) IFN-γ production by PHH in T18 MPS. G) IFN-γ production by PHH in T18 MPS. H) IFN-γ production by PHH in T18 MPS. I) IFN-γ production by PHH in T18 MPS. J) IFN-γ production by PHH in T18 MPS. K) IFN-γ production by PHH in T18 MPS. L) IFN-γ production by PHH in T18 MPS. M) IFN-γ production by PHH in T18 MPS. N) IFN-γ production by PHH in T18 MPS. O) IFN-γ production by PHH in T18 MPS. P) IFN-γ production by PHH in T18 MPS. Q) IFN-γ production by PHH in T18 MPS. R) IFN-γ production by PHH in T18 MPS. S) IFN-γ production by PHH in T18 MPS. T) IFN-γ production by PHH in T18 MPS. U) IFN-γ production by PHH in T18 MPS. V) IFN-γ production by PHH in T18 MPS. W) IFN-γ production by PHH in T18 MPS. X) IFN-γ production by PHH in T18 MPS. Y) IFN-γ production by PHH in T18 MPS. Z) IFN-γ production by PHH in T18 MPS.