In vitro micro-physiological models for predictive toxicology & disease modelling

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Organotypic culture of human tissue has a great potential to bridge the existing gap between in vivo and in vitro studies and to enable in-depth study of disease pathogenesis and therapy with low cost. Recent advances in microfluidic-based co-cell culture have enabled the realization of physiologically relevant in vitro models of specific human tissues. These systems have been used to study the contribution of micro-environmental factors to cellular morphogenesis in health and disease states, therefore, can be used to answer fundamental biological questions and develop a reliable alternative to animal models, and enable screening of potential new drug compounds. In this paper, we will discuss three immune competent micro-physiological models, namely the human gastrointestinal tract[1], the human epidermis[2] and the adipose tissue[3], the interaction of immune cells with these tissues and their role in inflammation. We will emphasis on the interaction between the adipocytes and immune cells to highlight the role of immune cell infiltration in the adipose tissue in the pathogenesis of diabetes type 2. A three-dimensional perfusion-based microfluidic system has been realized and utilized to host the three biological models. It enables co-culturing of two different types of cells that are physically separated but fluidically and chemically connected which enables the exchange of paracrine signals between the two cell types. The co-culture was maintained viable for more than three weeks during which cells were differentiated such that their phenotypes, morphologically and functionally, resemble the corresponding cells in the human tissue. Inflammation was induced in the biological system, and the response of the co-culture was detected. The biological models have been characterized in both health and disease states. Various commercial drugs are being tested to evaluate the in vitro system response.

References

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