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Commentary Open Access

# Effects of Biological Drugs on Human Immunocompetent

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## Commentary

Organ-on-chip (OoC) technology allows building complex in vitro models tailored specifically to the tissue/organ needs. OoC models mimic the microphysiological environment cells experience in a tissue including the vasculature-like perfusion. They are developed to potentiate several functional readouts using very low cell numbers. Over the past years, the technology has emerged as a powerful tool to support drug discovery and development with a potential for pharmaceutical R&D cost reduction1. The rise of complex treatment modalities, increasing attrition rates and low of predictively of current model systems created an urgent need for human-relevant and well-characterized in vitro models to support drug development (i) in efficacy testing by building in vitro disease models and (ii) in toxicity testing by providing a unique tool for mechanistic studies. Of particular interest for both efficacy and toxicity testing, is the human eye. Millions of people worldwide are affected by ocular disorders leading to visual impairment. Hence, to develop ophthalmic drugs and study ocular toxicity, novel human-relevant ocular tissue models are urgently needed.

To mimic the tissue complexity of the human choroid, we designed a 3-channel microfluidic platform that allows for the perfusion of circulating immune cells. The Choroid-on-Chip (CoC) comprises three main cellular components. The epithelium consists of a monolayer of human induced pluripotent stem cell (iPSC)-derived RPE in the top channel. The endothelium consists of two confluent monolayers of human primary MVECs seeded in the central channel facing on the upper side the RPE and on the lower side the melanocyte compartment. This channel is perfused using a syringe pump at a flow rate of 40 µL/h. The stromal component in the bottom channel features a cell-laden hydrogel incorporating melanocytes at defined cell densities in a 3D arrangement, orthogonal. All the epithelial, endothelial and stromal components together form a robust, viable 3D tissue [1]. The cells are homogenously seeded and distributed in a pigmented tissue throughout the entire length of the chip. The dimensions of the chip were chosen to match in vivo tissue dimensions: The total height of the 3D tissue on chip is 300 µm; the human choroidal thickness was estimated to be 266.8 ± 78.0 µm [2].

To mimic the outer blood-retina barrier (oBRB), RPE and MVECs were cultured on the two sides of the upper membrane, top and bottom respectively. The membranes were coated with Laminin, Collagen and Fibronectin, as described in detail in the Methods section, to mimic the Bruchs´ Membrane composition. The RPE formed a pigmented monolayer throughout the entire chip expressing tight junction protein zonula occludens 1 (ZO-1) and tyrosinase-related protein 1 (TYRP1), involved in the generation of melanin. MVECs formed confluent and CD31 positive monolayers throughout the entire length of the endothelial channel, endothelial layers were negative for ZO-1 in the CoC. To further assess how our model mimics the oBRB, we evaluated the permeability of the endothelial layer towards the RPE side (oBRB) and towards the stromal side of the tissue. Our data showed retention of both Carboxyfluorescein (0.377 kDa) and Dextran Texas Red (70 kDa) in the presence of the cell monolayers in all conditions. The retention was higher for the oBRB than for the endothelial-stromal barrier (twofold) and for the larger molecular weight molecule compared to the lower one [3].

The data presented here sustain the relevance of using an advanced cell culture system integrating several cell types involved in the immune response of a specific tissue to support pharmaceutical compound ranking and decision making [4]. The immune response in the CoC was shown to be sensitive to the mechanisms of T cell activation and suppression, key aspects for a human-relevant healthy and diseased in vitro model. Furthermore, the processes established for building the CoC model can potentially be translated to other tissues where the stromal, endothelial and epithelial cells are key elements of mechanisms of disease and/or toxicity and/or expanded to test multiple donors for exploratory mechanistic studies on patient-specific idiosyncrasies. This could help building a toolbox of in vitro models recapitulating aspects of the immune system to study immune-oncology therapies such as checkpoint inhibitors, TCBs and CAR-T cells [5].

### References

1. Marx U, Akabane T, Andersson TB, Baker E, Beilmann M, et al. (2020). Biology-inspired microphysiological systems to advance medicines for patient benefit and animal welfare. ALTEX 37:365-394.

2. Cipriano M, Schlünder K, Probst C, Linke K, Weiss M, et al. (2022). Human immunocompetent choroid-on-chip: a novel tool for studying ocular effects of biological drugs. Commun Biol 5:52.

3. Kanerud L, Engström GN, Tarkowski A (1995). Evidence for differential effects of sulphasalazine on systemic and mucosal immunity in rheumatoid arthritis. Ann Rheum Dis 54: 256-62.

4. NA Gillett, C Chan (2000). Applications of immunohistochemistry in the evaluation of immunosuppressive agents. Hum Exp Toxicol 19: 251-254.

5. Moreland LW, Bucy RP, Weinblatt ME, Mohler KM, Spencer-Green GT, Chatham WW (2002). Immune function in patients with rheumatoid arthritis treated with etanercept. Clin Immunol 103: 13-21.

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