Developing new tools for drug testing: introducing a microfluidic platform mimicking the spleen for future pharmacological trials

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Constant evolution and improvements on areas such as tissue engineering, microfluidics and nanotechnology have made it possible to partially close the gap between conventional *in vitro* cell cultures and animal model-based studies. A step forward in this field concerns organ-on-chip technologies, capable of reproducing the most relevant physiological features of an organ in a microfluidic device.

Research in microfluidic devices that represents organ models is still in its infancy, but offers a tantalizing glimpse into future of drug testing and biological hypotheses evaluation.[1]

Drug testing in animal models is time-consuming, costly, and often does not accurately predict the adverse effects in humans. Toward a more reliable output, several platforms, in the interface between nanobio and tissue engineering, have been developed in the past years[2,3] with the aim to supplement or supplant animal studies or at least try to prioritize them.

Nevertheless, no one developed before a spleen-like platform for studying the importance of this organ in differente haematological diseases.

Similar in structure to a large lymph node, the spleen is a complex three-dimensional branched vasculature exquisitely adapted to perform different functions containing closed/rapid and open/slow microcirculations, compartmentalized parenchyma and sinusoidal structure forcing erythrocytes to squeeze through interstitial slits (IES) before reaching venous circulation.[4]

Taking into account these features, we designed and developed a multilayered microfluidic device of the first ever functional human splenon-on-a-chip, mimicking the hydrodynamic behavior of the spleen's red pulp, to evaluate and simulate its activities, mechanics and physiological responses. Different physiological features have been translated into engineering elements that can be combined to integrate a biomimetic splenon model[5] (the minimal functional unit of the spleen).

This biochip-based platform should allow a deeper understanding of the underlying mechanisms of *Plasmodium* parasite infection and contribute to vaccine development and drug testing of malaria and other hematological disorders. Preliminary results showed significant statistical differences in terms of cell deformability between old vs. fresh RBCs (p=0.001) and non-parasitized vs. *P. Yoelii* parasitized reticulocytes (p=0.006) when passing through the 2 µm constrictions simulating the IES.

Still, additional challenges remain before these *in vitro* models can be used in applications such as diagnostics, but they could be the future of drug testing and biological platforms.

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