Vessel –on-a-chip: advanced in vitro model for cardiovascular research

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INTRODUCTION

Atherosclerosis is a chronic inflammatory disease of the arterial vessels that is behind of the main vascular pathologies as myocardial infarction and stroke. Atherosclerosis is a complex multifactorial process, but the physical factors such as **flow-induced shear stress** have an important role both in the onset and the progression of **endothelial dysfunction**. Traditional 2D endothelial models were useful to understand the biological factors that lead to atherosclerosis, but new *in vitro* models are needed to study the flow effects into the atherosclerosis mechanisms and the underlying therapeutic targets. Bflow models include relevant features such as circular section and a wide range of channels sizes

In this work we present three models which are designed to study the following features:

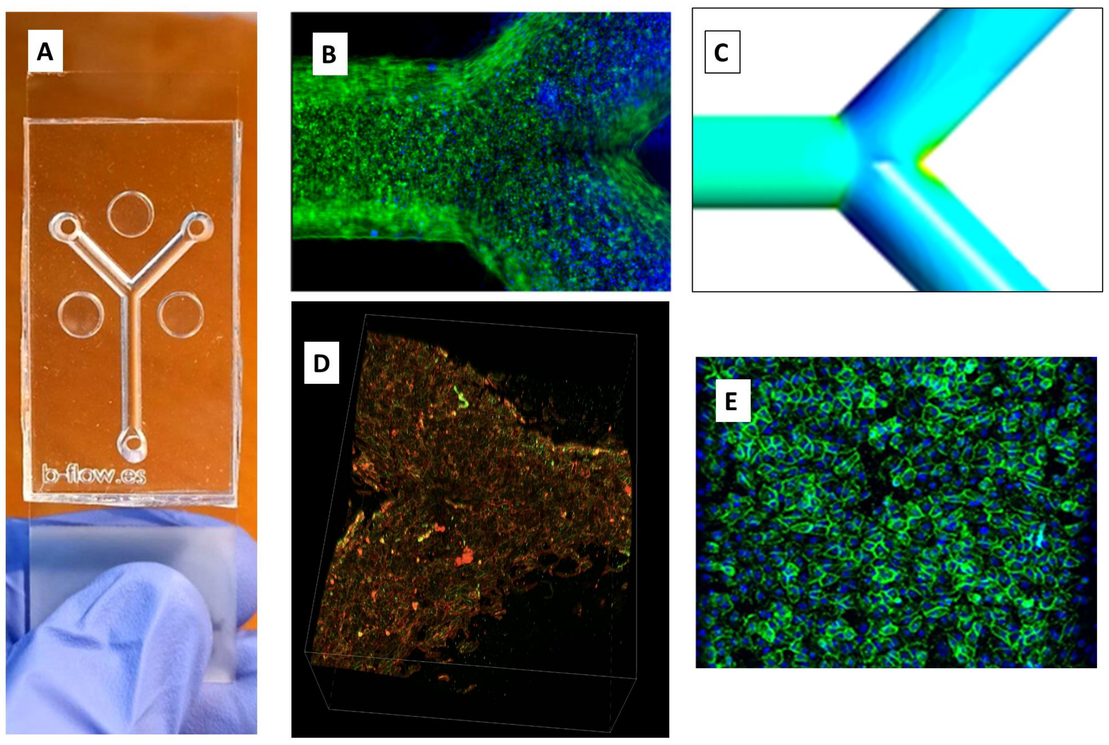
- **Vessel-on-a-chip** with a bifurcation to characterize the local flow effects on the endothelial layer, including a model to functionalize with extracellular matrix (ECM).
- **Atherosclerosis-on-a-chip** with a bifurcation with an atherosclerotic plaque in one branch.
- **Microvascular & Barrier chip** with a region to stablish an extracellular matrix to perform assays of microvessels, angiogenesis and/or endothelial barrier.

METHODS

Vessel-on-a-chip devices from BFlow were cultured with human umbilical vein endothelial cells. Different flow conditions were stablished with an external peristaltic pump. Different stainings were performed into the chips including live staining with AM-calcein, hoescht 33342, phalloidin and VE-cadherin immunostaining. Numerical simulations were performed to evaluate the precise flow effects into the chip.

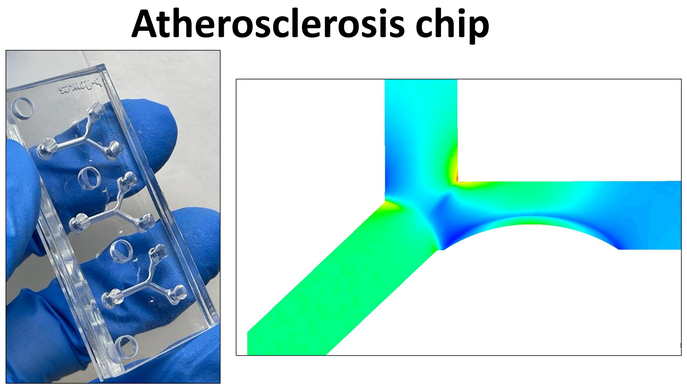
RESULTS

Bifurcated Vessel-on-a-chip



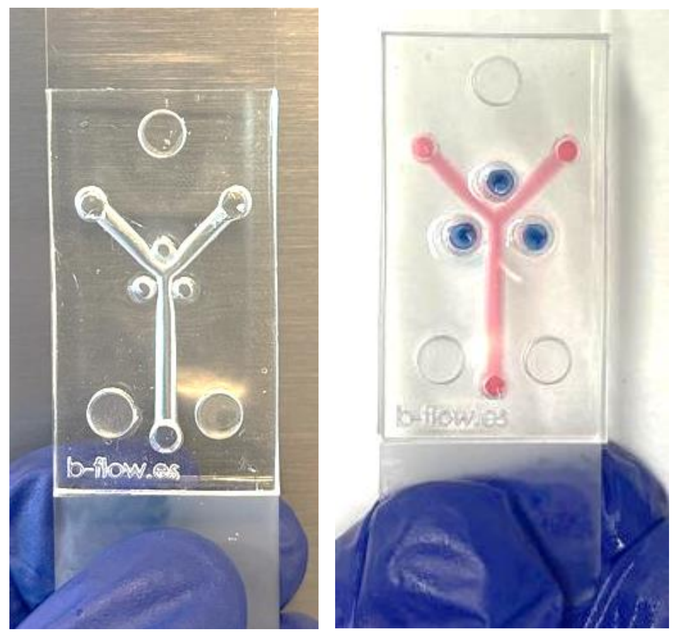
A) Image of the chip before the experimental setup. **B)** Epifluorescence microscopy image of HUVEC stained with AM-calcein and hoescht 33342 covering the walls of the chip. **C)** Numerical simulation of the bifurcation showing the differential shear stress. **D)** 3D bifurcation reconstruction using confocal microscopy of HUVEC stained with phalloidin and VE-cadherin**. E)** HUVEC immunostained with VE-Cadherin antibody and secondary antibody Alexa 488.

Atherosclerosis chip



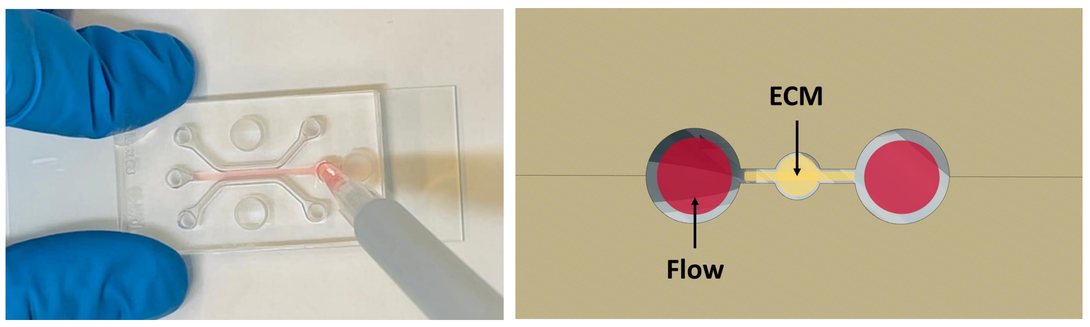
On the **left**, image of the chip before the experimental setup. On the **right**, wall shear stress numerical simulation of the atherosclerosis model, with one healthy branch and the flow alterations by the atherosclerosis plaque in the other branch.

ECM Vessel-on-a-chip



On the **left**, image of a ECM Vessel-on-a-chip before the experimental setup. On the **right**, image of the loaded chip where the ECM is confined (blue) and the cell culture medium is filling the bifurcation (pink).

Microvascular & Barrier chip



On the **left**, image of the extracelular matrix loading into the chip. On the **right**, schematic image of the sagital section of the chip indicating where the extracelullar matrix is confined and the complete circular section of the lateral channels.

CONCLUSIONS

Bifurcated Vessel-on-a-chip reproduces the local flow effects into big arteries, being possible to functionalize these regions with ECM. Atherosclerosis chip reproduce the strong flow effects induced by the plaque. Microvascular & Barrier chip is a relevant model to study both microvascular formation and endothelial barrier function. In this work we presented four new models which will allow to improve our knowledge in endothelial biology, the cardiovascular pathophysiology and to design new therapies.

BIBLIOGRAPHY

Check the related papers here

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CONFLICT OF INTEREST

Laura Vázquez-Vázquez, Lois Rivas-Meizoso, Bastián Carnero, Elias Ferreiro-Vila, Sylvana V. Varela-Ballesta and Bruno K, Rodiño-Janeiro are employees of BFlow S.L.. M. Teresa Flores-Arias and Ezequiel Álvarez are founders and partners of BFlow S.L.