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## Development of an all-Human Vascularized Model of Pancreatic Islets on-Chip: Towards Personalized Medicine for Type 1 Diabetes

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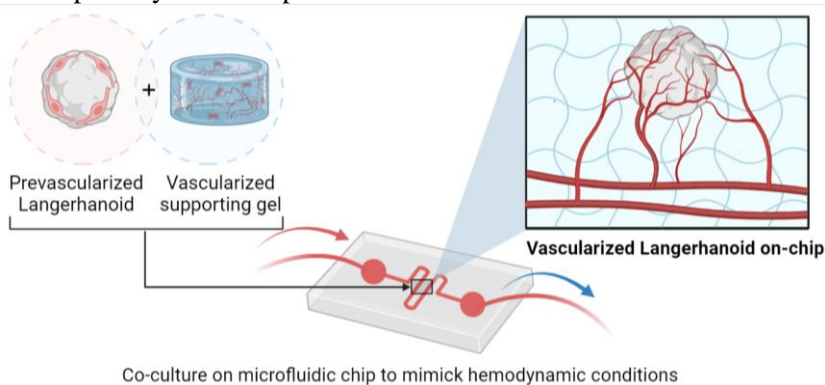
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Diabetes is a chronic disease characterized by a persistent elevation of blood glucose levels, resulting from either insulin deficiency (Type 1 diabetes) or insulin resistance (Type 2 diabetes). In 2021, diabetes affected one in eleven people globally and was responsible for nearly 2 million deaths, primarily due to long-term complications.

In recent years, diabetes research and treatments have focused on insulin restoration and maintaining normal blood glucose levels. While significant progress has been made in treating Type 1 diabetes (T1D) with exogenous insulin, cell replacement therapy, also known as pancreatic islet of Langerhans' transplantation offers a promising treatment strategy. However, several challenges, such as a shortage of donors, graft oxygenation issues, and lifelong immunosuppression currently limit the widespread application of this therapy.

Advances in T1D research and the growing emphasis on personalized medicine call for innovative experimental models that accurately replicate the complex dynamics of the patient's microenvironment. Our work presents an approach using a microfluidic chip [1], designed to mimic the physiological conditions characteristic of patients and especially to develop the vascularization.



**Figure 1** : A schematic overview of our Vascularized Langerhanoid on-chip

Central to our approach, is the incorporation of pre-vascularized human pancreatic islet organoids on-chip also referred to as Langerhanoid on-chip (Figure 1). This model is composed of three distinct auto-organised human cell types to mimic the biological functions of human islets of Langerhans. The innovative serpentine microfluidic chip previously developed [1;2] enables first: to capture pre-vascularized organoids; and second: to integrate endothelial cells, thereby replicating the structural and functional attributes of blood vessels within the microenvironment. Through the integration of essential human components, including human hydrogel matrix, medium, physiological flow rates, and endothelial cells, we aim at developing a microenvironment representative of the patient's unique biological context.

In this way, we aim at replicating the in vivo response observed during islet transplantation, providing a platform for investigating the complex interactions between the donor's transplanted islets and the recipient patient's environment. Our long-term vision involves the development of an all-human vascularized pancreatic islet-on-a-chip model that could transcend its role as an experimental platform. This innovative experimental model will not only contribute to our understanding of T1D but also holds promise for advancing personalized medicine strategies tailored to individual patient profiles

### References

- [1] Quintard C, Tubbs E, Achard JL, Navarro F, Gidrol X, Fouillet Y. *Microfluidic device integrating a network of hyper-elastic valves for automated glucose stimulation and insulin secretion collection from a single pancreatic islet*. Biosens Bioelectron. 2022 Apr 15;202:113967.
- [2] Quintard C, Tubbs E, Jonsson G, Jiao J, Wang J, Werschler N, Laporte C, Pitaval A, Bah T, Pomeranz G, Bissardon C, Kaal J, Leopoldi A, Long D, Blandin P, Achard J.-L, Battail C, Hagelkruys A, Navarro F, Fouillet Y, Penninger J, Gidrol X. *A microfluidic platform integrating functional vascularized*

