THE ENDOTHELIAL GLYCOCALIX

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As surprising as it may seem, all of us—even the coldest and toughest—carry within us an eternal romantic who tirelessly caresses and protects even the tiniest, most intimate corners of our being, day and night. This mysterious companion, unknown to most but essential to life, is the endothelial glycocalyx.

Behind these two words lies an structure whose existence in mammals was confirmed shortly before humans landed on the Moon. In an adult human, this system weighs about the same as the brain: approximately 1.4 kilograms. If fully unfolded, it would cover the area of three basketball courts. What sets it apart from other organs is that it isn't located in any specific part of the body. On the contrary, it is everywhere, in direct contact with the blood. It resembles a soft layer of velvet that internally lines all the arteries and veins in the body, from the largest to the tiniest microcapillaries (the smallest blood vessels). The thickness of this inner velvet coat ranges between 0.1 and 1.0 micrometers—that is, between a thousandth and a ten-thousandth of a millimeter.

But don't be fooled by its tiny size. Although it might seem too small to be considered a vital organ, the endothelial glycocalyx performs several critically important functions. First, it acts as a selective barrier, allowing only certain molecules to pass from the blood into the rest of the body, while also protecting against fluid loss (edema). It also serves as a lubricating layer to help transport red blood cells. In the case of microcapillaries, this is especially important, since their diameter can be smaller than the red blood cell itself. It also prevents erosion of blood vessel walls and largely stops other particles in the bloodstream from sticking to them and forming clots or blockages. Furthermore, by capturing certain molecules, it helps regulate thrombosis, inflammation, and oxidative stress. Another key role of the glycocalyx is to send signals to the outer parts of the endothelial cells (the cells lining blood vessels), guiding them to change their shape, size, and properties in response to shear forces exerted by blood flow. This ensures that blood transport remains optimal at all times and under all conditions. It also contributes to regulating the growth and migration of these endothelial cells throughout the body.

The vital importance of the glycocalyx becomes evident when it is partially or entirely lost. When this happens, atherosclerosis (accumulation of fats, cholesterol, and other substances inside and on artery walls) develops quickly, and atheromatous plaques rapidly block blood flow.

Its degradation has also been linked to strokes, hypertension, preeclampsia, and severe bacterial infections. Some bacteria produce toxins that deliberately damage the glycocalyx, giving them free rein to spread through every corner of the body. Studies conducted in 2019 showed that in cases of malaria, patients whose glycocalyx is damaged have a drastically lower survival rate. Recent research also indicates the glycocalyx plays a key role in the growth and spread of tumor cells (metastasis).

Strong evidence suggests that many complications from diabetes stem from the disease's damage to the glycocalyx in microcapillaries. This includes: Eye damage that can lead to blindness, Kidney damage, Nerve damage, and Small-vessel damage that may result in diabetic foot and gangrene.

Because of all this, the glycocalyx has become a promising therapeutic target in research aimed at treating or alleviating certain chronic and severe diseases. But despite growing interest, more than fifty years after its discovery in mammals, much about the glycocalyx remains unknown. Initial underestimation of its importance, its fragility, its tiny size, and the difficulty of observing it in live studies have all contributed to major gaps in our understanding. We also still lack knowledge about how its dysfunction causes systemic disruptions in the body. These knowledge gaps mean that medical progress in this area relies more on slow, trial-and-error approaches than on research guided by a solid understanding of how this complex organ works. Understanding the glycocalyx more deeply would undoubtedly accelerate medical advances significantly.

At the University of the Balearic Islands (UIB), our research group is working to improve understanding of the glycocalyx and its related diseases. Given how hard it is to study the glycocalyx in vivo, we've turned to numerical simulations. These models let us reproduce in fine detail how the glycocalyx behaves under fluid flow similar to blood. To do this, we first had to develop new algorithms capable of simulating such large and complex systems efficiently—detailed enough to produce reliable, quantitative results. This was the first goal of our project, GLICOSIM. We've developed the necessary computational tools, which will soon be available to other research groups. Using these tools, we are now studying two fundamental but poorly understood phenomena:

1. How the glycocalyx alters the properties of blood and red blood cells inside microcapillaries.
2. How it contributes to the initial formation of obstructive deposits in microcapillaries.

These are just a few small steps toward fully understanding the glycocalyx—but they are firm steps that bring us all closer to that final goal.