

Cardiovascular diseases are one of the leading causes of death worldwide, accounting for approximately 18 million fatalities each year. Particularly dangerous are conditions caused by the blockage of blood flow in vessels, resulting from the accumulation of lipids, primarily cholesterol, and the formation of thrombi. These conditions often require urgent cardiological intervention, most commonly the implantation of a stent to widen the vessel and restore normal blood flow. Unfortunately, in many cases, stent implantation is associated with serious complications. One of these is mechanical damage to the vessel wall, which can trigger an inflammatory response, platelet aggregation, and thrombus formation. This cascade of events may lead to restenosis, defined as the re-narrowing of the vessel lumen by as much as 50–75%.

A key role in maintaining proper vessel function is played by cell signaling – the way cells communicate with each other using signaling molecules. One of the essential mechanisms involved is purinergic signaling, based on the interaction of purine nucleotides (such as Ado, AMP, ADP, and ATP), their specific receptors, and enzymes that hydrolyze or transform these molecules. This mechanism regulates critical processes such as vascular tone, inflammation, and tissue regeneration. Disruptions in this signaling system can contribute to the development and progression of cardiovascular diseases.

The aim of this project is to investigate the protective, regenerative, and remodeling properties of the AK-GO bioconstruct, in which adenylate kinase (AK) is immobilized on the surface of graphene oxide (GO). Unlike typical enzymes that catalyze hydrolysis reactions, AK facilitates phosphate group transfer between purines ($ATP + AMP \rightleftharpoons 2 ADP$), helping to maintain the extracellular balance of purine nucleotides. In this way, AK supports vascular homeostasis by reducing inflammatory and aggregatory processes.

The research will include the synthesis and purification of the AK-GO bioconstruct and its application in a series of in vitro experiments using commercial cell lines of endothelial cells (HUVEC) and vascular smooth muscle cells (HUVSMC). Under physiological conditions, both cell types form the vessel wall and are actively involved in disease processes, making them suitable models for studying cardiovascular disease development. The project will assess, among others, the proliferative and migratory potential of the cells, the activity of extracellular enzymes degrading purine transmitters, and the concentration of extracellular purine nucleotides. We will also measure levels of pro- and anti-inflammatory cytokines, assess membrane permeability, and perform HUVEC-HUVSMC co-cultures to better understand cellular interactions.

We expect that AK-GO will exhibit anti-inflammatory, anti-aggregatory, and anti-restenotic properties, while also providing protection to damaged vascular wall cells. In the future, this bioconstruct may serve as an innovative stent coating that not only restores blood flow but also significantly reduces the risk of complications and supports tissue regeneration.