Non-Invasive Monitoring of Inflammation in a Genetically-Modified, Tissue Engineered Vascular Model

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Across the world, the leading cause of death is cardiovascular disease. An underlying cause of many cardiovascular diseases is atherosclerosis, which occurs when plaque builds up in the vascular wall and prevents the steady flow of blood. Currently, medicines targeting atherosclerosis undergo the same laborious process as all drugs. This research aims to improve the efficiency of this process by creating a tissue-engineered model of an atherosclerotic artery to serve as a preclinical tool for screening anti-atherosclerosis drugs. Cyclooxygenase-2 (COX-2) regulates cellular inflammatory processes and mediates atherogenic events. The goal of this work was to develop a method to non-invasively monitor COX-2 expression within the tissue-engineered vascular endothelium as a real-time measure of inflammation. To measure COX-2 expression, rat brain endothelial cells (RBECs) were transfected with Ad-COX2-Luc – an adenoviral vector with a COX-2 controlled luciferase reporter. Transfected RBECs were then seeded into 3 poly-dimethylsiloxane tubes stimulated with interleukin 1-beta (IL-1β), a pro-inflammatory mediator that induces COX-2 expression. Luciferin was added to the cells to initiate a bioluminescent-response. The Xenogen-IVIS Imaging System was used to detect and quantify luciferase activity within each tube. The results obtained indicated that luciferase expression correlated with the level of IL-1β. The tissue-engineered vascular model created in this research demonstrated a COX-2 inflammatory response following exposure to a pro-inflammatory cytokine. This response was monitored through a luciferase reporter and bioluminescent-imaging. Conclusively, this research project resulted in a non-invasive method of monitoring inflammation in a tissue-engineered artery.