

Connexins in cardiovascular disease

Brenda R. Kwak

Associate professor

University of Geneva

Dept. of Pathology and Immunology

Dept. of Internal Medicine- Division of Cardiology

Coronary heart disease is the leading cause of morbidity and mortality in Europe. Atherosclerosis, an inflammatory disease of large and medium-sized arteries, is the most important underlying cause of coronary heart disease. Atherosclerosis involves the formation of intimal lesions that are characterized by a dysfunctional endothelium, inflammation, lipid accumulation, cell death and fibrosis. The distribution of atherosclerotic plaques is highly characteristic in human; the lesions develop predominantly near side branches of arteries, where blood flow is disturbed. The most severe clinical events follow the rupture of a plaque and sudden thrombotic occlusion of the affected artery. Then, treatment consists of procedures that allow the rapid return of blood flow to the ischemic myocardium to rescue heart muscle. Reperfusion, however, may paradoxically lead to further complications resulting from an inappropriate inflammatory response in the microcirculation.

The work in our laboratory is focused primarily on the role of connexins in atherosclerotic disease. Connexins form gap junctions, clusters of intercellular channels synchronizing responses in multi-cellular organisms through the direct exchange of ions, small metabolites and second messengers between adjacent cells. We have previously shown beneficial effects on both progression and composition of the atherosclerotic lesions in mice with reduced levels of Cx43. In contrast to the atherogenic role of Cx43, Cx37 hemichannels in macrophages and endothelial Cx40 gap junction channels are atheroprotective. Our current work concentrates on the shear stress-dependent regulation of Cx37 and Cx40 in healthy endothelium and atherosclerotic vessels as well as on the role of connexins in atherosclerosis-derived complications, such as arterial thrombosis and reperfusion injury. Finally, we like to understand the role of connexins in the development of lymphatic vasculature as well as the role that these vessels may play in the development of atherosclerotic plaques.