

## **Biology and Pathology**

### **Cardiovascular Disease**

#### **Introduction to Biology and Treatments – Atherosclerosis**

**Michael V. McConnell**

Stanford, California, USA

Learning Objectives:

- Understand the key biological processes involved in atherosclerosis
- Learn about promising approaches for targeted molecular imaging of atherosclerosis
- Understand the main treatments for atherosclerosis – from statins to stents

Atherosclerosis is the primary underlying cause of cardiovascular disease (heart attacks, strokes, and peripheral vascular disease) and involves multiple cell types and biological processes. It typically begins in early adulthood and progresses silently over decades, but can present suddenly with high morbidity and mortality. A multitude of risk factors (high cholesterol, cigarette smoking, hypertension, diabetes) contribute to injury and inflammation in the blood vessel wall, resulting in endothelial dysfunction, lipid deposition, macrophage accumulation, and smooth muscle cell proliferation. This atherosclerotic plaque formation can progress, initially with preservation of the vessel lumen due to outward vascular remodeling. More advanced plaques can develop necrotic cores, neovascularization, intraplaque hemorrhage, and calcification. More biologically active (so-called “vulnerable”) plaques are prone to disruption of the fibrous cap separating the lumen from the necrotic core, resulting in thrombosis/occlusion of the vessel lumen, inducing downstream ischemia and organ cell death (infarction).

Molecular imaging approaches have aimed at detecting these biological processes, including early endothelial activation, macrophage infiltration, proteolytic activity, angiogenesis, and thrombosis. The primary treatment is prevention through regular physical activity and a heart-healthy diet. In patients at increased risk and with elevated cholesterol, statin therapy has been shown to regress atherosclerosis (modestly) and prevent heart attacks and strokes (substantially). Aspirin and other platelet inhibitors are used in high-risk patients to reduce thrombosis and thus reduce heart attacks and strokes. In patients with advanced plaques that narrow the lumen enough to cause symptoms, stents can be placed to restore normal blood flow or surgery can be performed to bypass the narrowing (coronaries) or remove plaque (carotids).

The ongoing challenge in atherosclerosis has been to identify more precisely the patients (and their plaques) that are at high risk for near-term clinical events in order to optimize preventive therapy. Additionally, molecular imaging could provide crucial feedback that the therapeutic interventions chosen for a specific patient have converted their atherosclerotic plaques to a more “benign” phenotype.