MATHEMATICAL MODELLING OF SMOOTH MUSCLE CELL MIGRATION REVEALS MECHANISMS OF EARLY FIBROUS CAP FORMATION IN ATHEROSCLEROSIS

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The fibrous cap is a ubiquitous feature of mature atherosclerotic lesions that is formed by directed migration of collagen-synthesising smooth muscle cells (SMCs) within the vessel wall. By stabilising the plaque and sequestering thrombogenic plaque content from the bloodstream, the fibrous cap provides crucial protection against clinical sequelae such as heart attack and stroke. The mechanisms of cap formation, however, remain poorly understood. In particular, it is unclear why certain plaques remain stable and robust, while others become fragile and vulnerable to rupture.

We present a differential equation model that studies the spatio-temporal dynamics of the SMC population in the vessel wall during early fibrous cap formation. Platelet-derived growth factor (PDGF) is assumed to diffuse into the plaque from the injured endothelium and the model SMCs respond by migrating from the media and proliferating in the intimal tissue. Model simulations indicate that formation of a stable cap requires a critical balance between the relative rates of cell supply from the media, chemotactic migration in the intima and cell loss by apoptosis (or phenotype change). Moreover, we identify a number of disease-associated parameters that may be linked to variations in cap stability. The model represents the first detailed *in silico* study of fibrous cap formation in atherosclerosis and establishes a framework that can be readily extended to investigate other aspects of plaque development.