

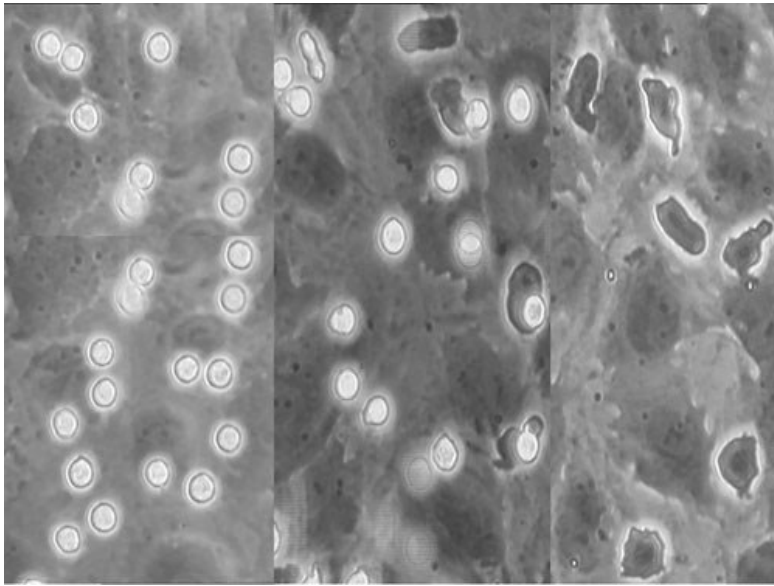
Dynamics of white cell adhesion in microvessels

Circulating white blood cells must adhere to the endothelium which lines blood vessels and migrate through it, in order to carry out their protective functions. Direct microscopic observations of the different stages in this process have given us key insights into how it is regulated.

Adhesion of flowing white cells can be observed directly in microvessels of animals using intravital microscopy, or it can be observed in model capillaries lined with cultured endothelial cells or purified adhesion receptors. We have specialised in developing in vitro models using human tissue, where blood or isolated white cells are perfused across chosen substrates. Video microscopy is used to track the flowing cells before they adhere (using fluorescence labelling when opaque whole blood is used) and to quantify their adhesion and their subsequent behaviour. A particular challenge is to analyse the rate and direction in which they actively migrate. These technologies are used to define the specific molecules used for adhesion or which stimulate the white cells to migrate, and to dissect guidance systems which direct migration. Our studies aim to understand how protective immune responses are mounted, and what goes wrong, e.g., when pathogenic substances are added to the blood, or patterns of blood flow become disturbed.

A specific example has been in analysing the velocities and paths of white cells in blood as it flows in straight tubes or in "vessels" with discontinuities in the wall, how these motions are affected by changing the contents of the blood, and how these parameters in turn affect the patterns of adhesion to the wall. Solving such complex problems require a mixture of cell biological, engineering and mathematical techniques. A recent award supporting collaboration between the Centre for Cardiovascular Science and Chemical Engineering will enable us to use more sophisticated particle tracking technologies, allied with mathematical modelling to understand fundamental factors regulating adhesion in different regions of the vasculature.

Flowing neutrophils adhering and then migrating on endothelial cells in vitro



Contact

Professor Gerard Nash, Centre for Cardiovascular Studies, The Medical School

Email: g.nash@bham.ac.uk (<mailto:g.nash@bham.ac.uk>)

Tel: 0121 414 3670