Free Communication

LEUKOCYTE ROLLING AND RECRUITMENT BY ENDOTHELIAL CELLS: HEMORHEOLOGICAL EXPERIMENTS AND NUMERICAL SIMULATIONS

A.M. Artoli[1], A. Sequeira[1], A.S. Silva-Herdade[2], C. Saldanha[2]

ABSTRACT

The recruitment of leukocytes from the blood stream and their subsequent adhesion to endothelial walls are essential stages to the immune response system during inflammation. The precise dynamic mechanisms by which molecular mediators facilitate leukocyte arrest are still unknown. In this study combined experimental results and computer simulations are used to investigate localized hydrodynamics of individual and collective behaviour of clusters of leukocytes. Leukocyte-endothelial cell interactions in post-capillary venules of Wistar rats' cremaster muscle were monitorized by intravital microscopy. From these experiments the haemorheologic and haemodynamical measured parameters were used in time dependent three-dimensional computer simulations, using a mesoscopic lattice Boltzmann solver for shear thinning fluids. The dynamics of leukocyte clusters under non-Newtonian blood flow with shear thinning viscosity was computed and discussed. In this paper we present quantified distributions of velocity and shear stress on the surface of leukocytes and near vessel wall attachment points. We have also observed one region of maximum shear stress and two regions of minimum shear stress on the surface of leukocytes close to the endothelial wall. We verified that the collective hydrodynamic behaviour of the cluster of recruited leukocytes establishes a strong motive for additional leukocyte recruitment. It was found that the lattice Boltzmann solver used here is fully adaptive to the measured experimental parameters. This study suggests that the influence of the leukocytes rolling on the increase of the endothelial wall shear stress may support the activation of more signalling mediators during inflammation.

Key-words: *Leukocyte dynamics, intravital microscopy, computational hemorheology, wall shear stress*

[1] CEMAT, Instituto Superior Técnico, Universidade de Técnica de Lisboa, Portugal.
[2] Instituto de Biopatologia Química, Faculdade de Medicina de Lisboa – Unidade de Biopatologia Vascular, Instituto de Medicina Molecular, Portugal.

Poster

NEUTROPHIL ACTIVATION: FIBRINOGEN DEPENDENCY

Vanda Vitorino de Almeida, Henrique S.do Rosário, Carlota Saldanha
Instituto de Biopatologia Química, Faculdade de Medicina de Lisboa – Unidade de Biopatologia Vascular, Instituto de Medicina Molecular, Portugal.

Fibrinogen is a soluble plasma glycoprotein, multifunctional, that participates in haemostasis and has adhesive and inflammatory functions through specific interactions with other cells.

The concentration of this glycoprotein increase in inflammatory conditions.

A fundamental paradigm involved in the acute inflammatory response is neutrophil migration to the affected tissues to mount an initial innate response to the aggression.

The objective of this study is to characterize how fibrinogen modulates the pattern of neutrophil activation.

Neutrophils from healthy donors were isolated from peripheral venous blood and loaded with the fluorescent probe dihydrorhodamine 123 (1μM) to detect oxygen free radical production. The cells (1,0x 10^6 cell/mL) were then incubated with a range of concentrations of fibrinogen (0-400mg/dL) for 15 minutes.

Our results show that fibrinogen leads to an increase in neutrophil activation as measured by free radical production.

This effect becomes evident at borderline-high concentrations (300-400mg/dL), and in some of the individuals it was possible to differentiate two subpopulations of low-responsive and high responsive neutrophils to activation by fibrinogen.

We hypothesize that, in this regard, the concentrations of fibrinogen identified as a risk factor might promote the setting of an inflammatory microenvironment in the circulation and facilitate **cardiovascular disease progression.**