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GEOMETRICAL EFFECTS IN CELL – PARTICLE INTERACTIONS AT THE MESOSCALE

*** Paolo Decuzzi [1,2], Mauro Ferrari [2,3]**

[1] University of Magna Graecia
p.decuzzi@unicz.it

[2] University of Texas Health Science Center Houston

[3] M.D. Anderson Cancer Center and Rice University

Mauro.Ferrari@uth.tmc.edu
Paolo.Decuzzi@uth.tmc.edu

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ABSTRACT

Systemically administered nanoparticles before reaching their final target and execute their missions, have to make their way into the circulatory system, reach the diseased microvasculature, extravasate crossing the blood vessels, diffuse through the extracellular matrix (ECM) and eventually bind to the target cell. For particles designed to target the diseased vasculature, three issues are of importance (Fig.1): the margination dynamics, the strength of adhesion and the control of cell internalization. The term margination dynamics refers to the lateral drifting of the particles towards the walls of the blood vessels, that favours the search for the diseased vasculature and allows eventually for firm adhesion, if the conditions are met. The term strength of adhesion is referred to the ability of a particle to attach firmly at the blood vessels withstanding the hemodynamic forces; and finally, the term internalization is referred to the ability of an adherent particle to control uptake by the host cell.

A broad spectrum of nanoparticles to be used as drug carriers (drug delivery systems) and contrast agents (biomedical imaging systems) have been presented in the literature with different compositions, chemico-physical properties, sizes and shapes. For instance, the Mitragotri.s group has recently reported on a method to fabricate polystyrene particles with more than 20 different shapes and characteristic sizes ranging from 60 nm up to 30 μm [1] and has addressed the importance of the particle shape in phagocytic processes; the DeSimone's group has developed an extremely versatile and flexible method for the direct fabrication of shape-specific nano-biomaterials [2]; silicon microfabricated particles with an hemispherical shape have been produced by Cohen and colleagues [3]. On the other hand, Nature provides a variety of biological corpuscles with shapes which differ substantially from spherical. For example, red blood cells have a biconcave disc shape; platelets have an oblate spheroidal shape; the shape of most proteins as BSA, Fibrinogen, IgG deviates significantly from the spherical.

The authors over the last years have developed a series of mathematical and experimental models [4-7] to investigate the effect of geometrical features, as size and

shape, on the interaction of nanoparticles with cells at the micro- and nano-scale. In this work, in-silico, in-vitro and in-vivo results are presented emphasizing the effect of particle geometry (size and shape) on the performances of systemically administered particles targeted to the diseased vasculature.

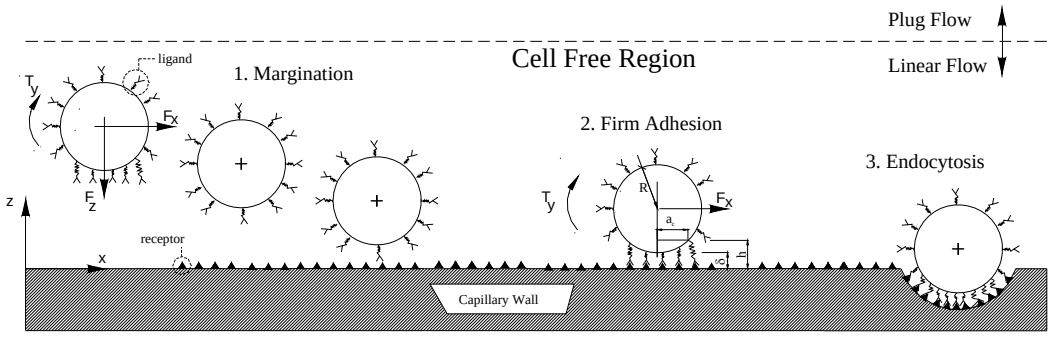

Fig.1: Margination, Adhesion and Endocytosis: three events in the interaction of a nanovector with a cell layer under a linear shear flow.

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