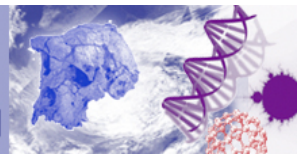
Cancer



Guest contribution by Dr Jeffrey Karp

Key words : blood vessel, cancer, cell rolling, endothelial cells, metastasis, p-selectin, selectins, tissue,

Slowing Cell Rolling in the Bloodstream

2 Nov, 2007 10:10 am

Cell rolling is an important physiological and pathological process that is used to recruit specific cells in the bloodstream to a target tissue. This process may be exploited for biomedical applications to capture and separate specific cell types. One of the most commonly studied proteins that regulate cell rolling is P-selectin. By coating surfaces with this protein, biofunctional surfaces that induce cell rolling can be prepared.

Human existence and longevity relies on the ability of cells to travel through the bloodstream to distant regions in the body to aid in tissue repair. One may question, "how can fast moving cells in blood possibly locate and stop within specific tissues?" Blood vessels contain a layer of cells called endothelial cells that are in continuous contact with flowing blood. During inflammation, the endothelial cells express certain adhesive arms, or molecules, on their surface which grab onto specific moving cells and cause them to slow down and roll. This permits the cells to further reduce their speed and sense regenerative or other signals originating from damaged or diseased tissues.

Cell rolling is of primary biological importance given its role in recruitment of blood cells to sites of inflammation, homing of stem cells during bone marrow transplantation, and it is involved in the pathology of cancer metastasis where tumor cells may break off from a tumor and travel through the blood stream to initiate tumor formation at a distant sites.

The molecules on the endothelial cells which induce cell rolling are called selectins and have been the subject of intensive study for decades. However, all studies to date have utilized simple adsorption of selectins to surfaces which are unstable and not translatable to an implantable device. A team led by Professor Jeffrey M. Karp at the HST Center for Biomedical Engineering at the Brigham and Women's hospital, in collaboration with Michael King at the University Rochester, and Institute Professor Robert Langer at the Massachusetts Institute of Technology, has developed new technology to enhance the stability of selectins on implant surfaces.

Recently, they have demonstrated a 30 fold increase in the stability of selectins - they tested these surfaces up to 28 days and believe they may work much longer. Through enhancing the stable presentation of selectins within a device which may be directly connected to blood vessels, particular cell types traveling through the bloodstream such as cancer cells or stem cells can be captured. A concept developed by Prof. Michael King involves adds additional functionality to the device to reprogram the rolling cells. For cancer, this may involve a kill-signal to prevent cancer metastasis or for stem cells, the ability to stimulate them to form various tissues.

These results are directly applicable to the design of therapeutic or diagnostic devices. CellTraffix Inc. is presently translating this result to animal studies to capture hematopoetic stem cells and circulating cancer cells from whole blood.

Karp also holds appointments at Harvard Medical School and MIT. King is also a member of the scientific advisory board of CellTraffix, Inc. Coauthors include first author Seungpyo Hong, a postdoctoral associate in MIT's Department of Chemical Engineering; MIT undergraduates Huanan Zhang, Jennifer Q. Zhang, and Jennifer N. Resvick, also of chemical engineering; graduate student Dooyoung Lee of the University of Rochester; assistant professor Ali Khademhosseini of the Harvard-MIT Division of Health Sciences and Technology and Brigham and Women's Hospital, and MIT Institute Professor Robert Langer

Reference:

Seungpyo Hong, Dooyoung Lee, Huanan Zhang, Jennifer Q. Zhang, Jennifer N. Resvick, Ali Khademhosseini, Michael R. King, Robert Langer, and Jeffrey M. Karp. Covalent Immobilization of P-Selectin Enhances Cell Rolling. Langmuir (published by the American Chemical Society), 20 October, 2007. Available here.

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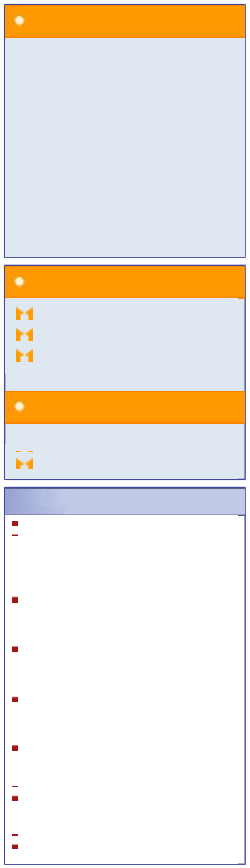

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