Description for the general public

Neutrophils are one of the most abundant white blood cells and conduct an effector function in the immune system. These cells are the first line of host defense against invading pathogens. For this purpose the use a wide arsenal of agents like proteolytic enzymes (bacteria destruction, complement activation). Neutrophil serine proteases (NSPs) are able to hydrolyze („cut") a various set of natural peptide substrates, activating cascades of reactions. These enzymes are stored within the neutrophil granules, in their active form, therefore they are ready for destruction of pathogens or cancer cells. Physiologically, the activity of NSPs is controlled by so called endogenous inhibitors, however an imbalance between enzymes and their inhibitors leads to many disorders, mainly pulmonary related diseases and cancer. Neutrophils, as an effector cells, are not only armed with different agents, but also use a set of various techniques for pathogen destruction. These cells are produced in bone marrow and transported to the circulation, where they circulate for a couple of hours. As a respond for inflammatory signal, they are getting closer to the blood vessels, crawling, attaching to it and migrating to the inflammation site. Here, they use different techniques for pathogen elimination like: (1) phagocytosis (e.g. bacteria engulfment and intracellular destruction) or (2) degranulation (release of the granules with agents to destroy bacteria). Also, neutrophils are able to (3) release their nuclear DNA to form so called traps, to catch bacteria in one site, decreasing its spreading. Neutrophils play a various functions within the organism employing NSPs, therefore we speculate that they differ in the amount of NSPs in the cells from entire population. This is called cells heterogeneity. Neutrophils heterogeneity was studied before and was connected with the amount of membrane bound receptors. This approach, however, did not allow for an adequate identification of neutrophil subpopulations. In our project we plan to identify neutrophils subpopulations differ in NSPs amount and activity. We propose an innovative view for neutrophils biology based on the amount of NSPs. This type of analysis has never been performed before. In our research we plan to incorporate new and unique chemical markers, that allow for detection of active form of enzymes. Moreover, these probes are selective, meaning that they bind only with targeted enzyme. These markers will be used to confocal microscopy analysis of subpopulations, that allow for an adequate analysis of such a small cell (7-10 uM), and even their granules. Also, we plan to incorporate flow cytometry that will allow us for an adequate analysis of correlation between subpopulations. We propose an innovative view for neutrophils biology based on the activity and amount of neutrophil specific serine proteases. Furthermore, the exact profile of healthy human NSPs profile in neutrophils, can serve as a scaffold to compare with neutrophils from disease. This may significantly change the way of neutrophil related treatment and help in targeted therapies in human.