ImmunoTools *special* Award 2015

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Malaria pigment hemozoin and lipoperoxidation product 4-hydroxynonenal affect the dendritic cell development in the in vitro malaria model.

Malaria is a disease still claiming to 660,000 million deaths and 200 million new cases per year, as WHO estimated in 2010. Most frequent complications are severe anemia, cerebral malaria and immunodepression, the latter constantly present in all forms of malaria. One of the important feature of malaria infection is formation of malaria pigment hemozoin (HZ) during malaria parasite growth and HZ sequestration by host phagocytes. Ultimately it was proposed that HZ plays important roles in monocyte/neutrophil functionality; modulation of immunity; pathophysiology of organ malaria (cerebral malaria, dyserythropoiesis and anemia, placental dysfunctions, respiratory distress); and alteration of cytokine equilibria. Furthermore, HZ was described to be target of aminoquinolines, artemisia and other antimalarials.

Oxidative stress interferes with many cellular functions, such as cell proliferation, inflammatory responses, cell adhesion, and chemotaxis - as regulatory or as toxicity element when in excess. Experimental evidence suggests that cellular dysfunctions under oxidative stress are frequently mediated by products of nonenzymatic degradation of polyunsaturated fatty acids (PUFAs). Among these products, hydroxyaldehydes, like 4-hydroxynonenal (4-HNE), are of particular interest because they reach relative high concentrations and are stable as radicals and able to diffuse inside or even outside the cell to reach distant target molecules that they attack to form covalent conjugates. Target molecules are proteins, DNA, and phospholipids. The importance of biological features of 4-HNE opens the door for studying the role of this molecule in malaria and potentially in all diseases accompanied by oxidative stress.

In previous studies HZ was shown to contain high amounts of lipoperoxidation products, included 4-HNE, generated non-enzymatically via heme-catalysis from PUFAs.

Present studies we base on previous observations in HZ-fed monocytes, also found to contain high 4-HNE levels which can affect monocyte phagocytosis and oxidative burst ability, MHC class II expression. Protein kinase C (PKC) involvement was proposed after detection of direct PKC modifications by 4-HNE. Secondly, the studies of our group and others indicate the modulatory role of HZ and HNE on dendritic cells (DC).

Now we plan to deep in action of HZ and 4-HNE on the process of monocyte differentiation to immature DC, and immature DC maturation. Involvement of membrane receptors for GM-CSF/IL-4, essential to induce DC differentiation, the possible targets of 4-HNE, will be studied.

For this research we will apply a variety of molecular- and cell biology methods, cytokine profile studies (PCR, ELISA kits) will be performed as well. For DC differentiation and maturation IL-4, GM-CSF, TNF-alpha will be used. DC subpopulation distribution will be studied by flow cytometry using corresponding antibodies to DC markers: CD1a, CD11c, HLA-DR and others. The cytokine expression and release, as IL-6, IL-8, IL-10, TNF-a, and others, monitored in differentiating Mo, in immature and mature DC under experimental conditions, will be studied. The special attention we will pay to eventual apoptosis of DC, which will be evaluated by Annexin-V staining combined with other DC markers. Finally I want to thank ImmunoTools for eventual support of my research by awarded reagents!

ImmunoTools *special* AWARD for **Oleksii Skorokhod** includes 24 reagents

FITC - conjugated anti-human HLA-DR, IL-6, Annexin V,

PE - conjugated anti-human CD11c, IL-8, TNF alpha, Annexin V,

APC - conjugated anti-human CD14, Annexin V,

human ELISA-set for 96 wells, human IL-6, human IL-8, human IL-10, human TNF-a, (each 3 reagents),

recombinant human cytokines: rh GM-CSF, rh IL-4, rh TNFα

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