

Neutrophils are very Interesting Cells

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Editorial

Neutrophils have been the object of exhaustive study in recent years and they were implicated with a role in activation and regulation of innate and adaptive immunity [1].

Polymorphonuclear (PMN) neutrophils are cells that not only act as phagocytes and reactive oxygen species releasers, but also they have another function as defense mechanism called neutrophil extracellular traps (NETs), which were described by Brinkmann et al in 2004 [2]. NETs trap a wide variety of microorganisms including bacteria, viruses, fungi and parasites. NETs have not only been involved as defense mechanisms, but they have also been linked to autoimmunity, cancer immunoediting [3], tissue damage and thrombosis [4]. NETs are constituted by chromatin and granular proteins, and they can be generated in inflammatory conditions [5,6]. It has been observed, as a sterile stimulus, that the monosodium urate crystals in patients with gout trigger the formation of NETs [7].

Stunningly, neutrophil leukocytes are able to express Major Histocompatibility Complex class II (DR) antigen (HLA-DR) and the costimulatory molecules CD80 and CD86 on their surface, which enables them as potential antigen-presenting cells (APC) [8,9]. The B7-1 (CD80)/B7-2 (CD86):CD28/CTLA-4 pathway is the best characterized T-cell costimulatory pathway [10,11]. Recently we found CD80 and CD86 colocalized in NETs in autologous leukocytes cultures, after lipopolysaccharide (LPS) or ovalbumin (OVA) stimulation [12,13]. The presence of costimulatory molecules in NETs would have implications for the rupture of self-tolerance, which in future investigations could contribute to explain the immunopathogenesis of autoimmune diseases.

The presence of these molecules in the cellular microenvironment can determine the stimulation or inhibition of the immune response, considering the complexity of diverse populations of T cells, naives and effectors [14]. The neutrophil phenotype as a probable APC has been described on in vitro and in vivo activated human PMN and in murine models with the expression of HLA-DR, CD80 and CD86 molecules [8,15].

All these antecedents give rise to multiple and varied questions to be elucidated by the scientific researchers, includes us. In agree with the results of several research papers, arises the concept of "neutrophil phenotypes", but there are heterogenea descriptions in literature, because parameters, methods, specie, tissue, biomarkers, are different [16].

Argentina is one of the countries with high prevalence of Chagas' disease. Chagas disease is a parasitic disease produced by the protozoan *Trypanosoma cruzi* and it is transmitted to humans by a blood-sucking bug of Reduviidae family [17]. It affects about 10 million people in Latin America although due to migration, it has

become a global health problema [18,19]. In the chronic stage of the disease immunological cells have been implicated in the development of chagasic heart disease [20-22]. In the pathogenesis of Chagas disease has been implicated autoimmunity due to the breakdown of self-tolerance [20,22].

Neutrophils are not directly implicated in the pathophysiology; however, we have observed that in human blood samples with positive serology for Chagas disease, neutrophils have a longer half-life in autologous cultures, as well as neutrophils with ring shaped nuclei [18].

In human neutrophils ring nucleus were observed earlier by Cabral in 1987 in chagasic patients and healthy individuals [23,24]. The occurrence of extracellular traps are most commonly found in cell cultures of total blood leukocytes from chagasic patients and greater expression of CD80 was observed in LPS-stimulated leukocyte cultures of chagasic blood samples [19]. These findings could be related to the possibility of rupture of self-tolerance in agree with the autoimmunity hypothesis of immunopathogenesis of Chagas disease.

IL-10-producing neutrophils were found in a murine model of Chagas disease, and they reduce inflammation and mortality during *T. cruzi* infection through IL17RA-signaling [22]. Further studies are needed to elucidate the molecular mechanisms that underlie the immunopathogenesis.

On the other hand, neutrophils are very versatile cells; they are implicated in cancer, too. About of the role of PMNs in tumor development, polarization of Tumor-Associated Neutrophil (TAN) was reported [25].

Advances in neutrophil biology knowledge have made it possible to explain some pathophysiological mechanisms that were previously unclear, both in autoimmune diseases, cancer and infectious diseases. They are very interesting cells.

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