Neutrophil

Neutrophils are the immune system's first line of defense against infection and have conventionally been thought to kill invading pathogens through two strategies: engulfment of microbes and secretion of antimicrobials. In 2004, a novel third function was identified: the formation of Neutrophil extracellular traps.

Neutrophils (also known as neutrocytes) are the most abundant type of granulocytes and the most abundant (40% to 70%) type of white blood cells in most mammals. They form an essential part of the innate immune system. Their functions vary in different animals.

They are formed from stem cells in the bone marrow. They are short-lived and highly motile, or mobile, as they can enter parts of tissue where other cells/molecules cannot. Neutrophils may be subdivided into segmented neutrophils and banded neutrophils (or bands). They form part of the polymorphonuclear cells family (PMNs) together with basophils and eosinophils.

Patients after polytrauma suffer from posttraumatic immune system dysregulation and multiple organ dysfunction syndrome. Genome-wide microarray analysis inmonocytes revealed a regulatory network of inflammatory markers around the AP-1 transcription factor in severely injured patients. Recent research focuses on the role of neutrophils in posttraumatic inflammation. The aim of a study was, to evaluate the impact of this inflammatory network in neutrophils.

Blood sampling and neutrophil separation were performed on admission of the patient and at 6 h, 12 h, 24 h, 48 h, and 72 h after trauma. Neutrophil expression levels of the target genes c-Jun, c-Fos, BCL2A, MMP-9, TIMP-1, ETS-2, IL-1β, and MIP-1β were quantified by RT-qPCR. Patients were assorted into groups according to distinct clinical parameters like massive transfusion (>10 RBC units/24 h), injury severity (ISS), 90-d survival, and the presence of traumatic brain injury (defined by ICI on head CT). Statistics were calculated by Mann-Whitney Rank-Sum Test, Receiver Operating Curves, and binary multiple logistic regression.

Forty severely injured patients (mean ISS 36 ± 14) were included. BCL2A, MMP-9, TIMP-1, and ETS2 levels showed a significant correlation to 90-d-survival in the early posttraumatic period (6 h-24 h). Furthermore, differential BCL2A, IL-1β, MIP-1β, and MMP-9 regulation was observed in patients requiring massive transfusion. Bogner-Flatz et al. could further show a significant TIMP-1 response in trauma PMN associated with traumatic brain injury.

This study of seriously injured patients highlights very early posttraumatic transcriptional changes in polymorphonuclear neutrophils, which were clearly associated with posttraumatic events and outcomes [1)].

It is known that neutrophils (NEs) are BBB permeable and are capable of accessing glioma cells.

The adult central nervous system parenchyma is resistant to inflammation, but in juvenile rats the injection of inflammatory mediators, interleukin-1 beta for example, gives rise to extensive neutrophil recruitment and neutrophil-dependent blood-brain barrier breakdown. The factors that confer this resistant phenotype are unknown. In this study, the authors demonstrate that E- and P-selectin expression is increased to a similar extent in adult and juvenile brain after the intracerebral injection

of IL-1 beta. Thus, the refractory nature of the brain parenchyma cannot be attributed to an absence of selectin expression. However, in injuries where the resistant characteristic of the brain parenchyma is compromised, and neutrophil recruitment occurs, selectin blockade may be an advantage. The authors investigated the contribution that selectins make to neutrophil recruitment during acute inflammation in the brain. The authors examined neutrophil recruitment by immunohistochemistry on brain sections of juvenile rats killed four hours after the intracerebral injection of IL-1 beta and the intravenous injection of neutralizing anti-selectin monoclonal antibodies (mAb). The administration of the P-selectin blocking mAb inhibited neutrophil recruitment by 85% compared with controls. Surprisingly, E-selectin blockade had no effect on neutrophil recruitment to the brain parenchyma. Thus, P-selectin appears to play a pivotal role in mediating neutrophil recruitment to the brain parenchyma during acute inflammation [2)].

Tumor-associated NEs (TANs) have been found to lurk in the bed of malignant glioma cells promoting additional circulating NE recruitment.

Human gliomas were analysed for the infiltration of neutrophils using immunohistochemistry by staining sections for CD15-positive and myeloperoxidase-positive cells. Over 70% of all glioma samples analysed (n = 105) had significant neutrophil infiltration, but there was a marked and significant correlation between tumour grade and the extent of the neutrophil infiltration. In the low grade tumours only 40-50% had significant infiltration, while in glioblastoma multiforme over 85% of the samples analysed had significant infiltration. Numbers of neutrophils infiltrating glioblastoma multiforme tumours were also greater than in the other tumour groups. Circulating white blood cell counts were elevated above the normal range in all glioma patients, but this elevation was entirely due to increased numbers of circulating neutrophils. Again, the highest numbers of circulating neutrophils were seen in the glioblastoma multiforme patients. These experiments indicate that glioma-derived factors may directly or indirectly affect the number of circulating neutrophils and influence their infiltration into the tumours [3)].

In Nature Nanotechnology, Xue et al [4)] publish a novel, anticancer methodology for treating residual glioma cells immediately after surgical resection with NE-mediated nanoparticles.

These investigators recognized that tumor surgical resection leads to local inflammation involving the release of interleukin-8 (IL-8) and tumor necrosis factor α (TNF-α), cytokines that promote the migration of NEs to the brain [5)].

1)
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