Recent publications

Following you find a brief abstract of a scientific publication concerning LEUKOCARE's technologies. Please find the full text article at the given reference.

Immunobiology 2011 Mar, Volume 216, Issue 3

Stimulation of Fas signaling down-regulates activity of neutrophils from major trauma patients with SIRS

PAUNEL-GOERGUELUE A[1], LOEGTERS T[1], FLOHE S[1], CHINATL J[2], ALTRICHTER J[1], WINDOLF J[1], SCHOLZ M[1]

[1]Department of Trauma and Hand Surgery, University Hospital Düsseldorf, Germany, [2]Institute for Medical Virology, Johann Wolfgang Goethe University, Frankfurt am Main, Germany

Posttrauma apoptosis resistance of neutrophils (PMN) is related to overshooting immune responses, systemic inflammatory response syndrome (SIRS) and multiple organ failure (MOF). Recently, we have shown that the apoptosis resistance in circulating PMN from severely injured patients which is known to be mediated by high serum levels of pro-inflammatory cytokines can be overcome by the activation of Fas death receptor. Here, we aimed to study whether stimulation of surface Fas leads to the inactivation of hyperactivated PMN from critically ill patients with SIRS. PMN from 23 multiple trauma patients (mean injury severity score (ISS) 34 ± 1.9) were isolated at day 1 after admission to the trauma center. PMN from 17 volunteer blood donors served as controls. Neutrophil activity has been determined after ex vivo short (1 h) and long term (4 h) stimulation of freshly isolated PMN with immobilized agonistic anti-Fas antibodies. We found neutrophil chemotactic migration in response to IL-8, phagocytosis and oxidative burst to be significantly inhibited in control cells already after short term (1 h) Fas stimulation. In contrast, inactivation of trauma PMN by agonistic anti-Fas antibodies was found to be efficient only after long term (4 h) incubation of cells with agonistic antibodies. Thus, in trauma PMN down-regulation of neutrophil activity seems to be delayed when compared to cells isolated from healthy controls, suggesting impaired susceptibility for Fas stimulation in these cells. Interestingly, whereas Fas-mediated inhibition of phagocytosis and oxidative burst could be prevented by the broad range caspase inhibitor t-butoxycarbonyl-aspartyl(O-methyl)-fluoromethyl ketone (BocD-fmk), the chemotactic activity in response to IL-8 was unaffected. In conclusion, we demonstrate that stimulation of neutrophil Fas does not only initiate apoptosis but also induces inhibition of neutrophil functions, partially by non-apoptotic signaling.