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.

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Mcl-1-mediated impairment of the intrinsic apoptosis pathway in circulating neutrophils from critically ill patients can be overcome by Fas stimulation.

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The systemic inflammatory response syndrome and subsequent organ failure are mainly driven by activated neutrophils with prolonged life span, which is believed to be due to apoptosis resistance. However, detailed underlying mechanisms leading to neutrophil apoptosis resistance are largely unknown, and possible therapeutic options to overcome this resistance do not exist. Here we report that activated neutrophils from severely injured patients exhibit cell death resistance due to impaired activation of the intrinsic apoptosis pathway, as evidenced by limited staurosporine-induced mitochondrial membrane depolarization and decreased caspase-9 activity. Moreover, we found that these neutrophils express high levels of antiapoptotic Mcl-1 and low levels of proapoptotic Bax protein. Mcl-1 up-regulation was dependent on elevated concentrations of GM-CSF in patient serum. Accordingly, increased Mcl-1 protein stability and GM-CSF serum concentrations were shown to correlate with staurosporine-induced apoptosis resistance. However, cross-linking of neutrophil Fas by immobilized agonistic anti-Fas IgM resulted in caspase-dependent mitochondrial membrane depolarization and apoptosis induction. In conclusion, the observed impairment of the intrinsic pathway and the resulting apoptosis resistance may be overcome by immobilized agonistic anti-Fas IgM. Targeting of neutrophil Fas by immobilized agonistic effector molecules may represent a new therapeutic tool to limit neutrophil hyperactivation and its sequelae in patients with severe immune disorders.