ABSTRACT

Immunostimulatory potential of tumor cells depends on various factors, including primarily tumor antigen repertoire and the capacity to emit molecules associated with cellular stress or injury, so called DAMPs, during immunogenic forms of cell death. These molecules mainly act on dendritic cells (DCs), thus activating the antitumor immune response. Several immunogenic cell death (ICD) inducers have been described in the past years. The contribution of my PhD thesis into this topic was the characterization of the apoptotic pathways activated by high hydrostatic pressure (HHP). HHP induces rapid tumor cell death accompanied by DAMP release (mainly calreticulin (CRT), HSP70, HSP90, HMGB1 and ATP) that is characterized by the overproduction of reactive oxygen species (ROS) causing the establishment of integrated stress response. ROS-PERK-eIF2α-caspase-2-caspase-8 signaling pathway plays an essential role in CRT translocation to the tumor cell surface upon HHP treatment, thus influencing the immunogenic potential of these cells. Moreover, the importance of ICD concept was also confirmed *in vivo*. The results point out that the presence of CRT on the surface of malignant blasts from AML patients correlates with the activation of specific antitumor immune response and improved clinical outcome. Another study focuses on the optimalization of DC manufacuring protocol in GMP conditions. Data obtained in this project shows that DCs differentiated during 3 days are similarly potent in inducing antigen-specific $CD8^+$ T cells as DCs produced by the standard 5 day protocol. The data included in this thesis also show that the efficacy of immunotherapy based on DCs pulsed with HHP-inactivated tumor cells for the treatment of poorly immunogenic tumors can be potentiated by combination with suitable chemotherapy.