Interaction between ferroptotic dying cancer cells and the immune system

S-01.2-3

L. Wyckaert[I], O. Van der Sypt[I], M. Vadi[II], W. Xie[I], **P. Vandenabeele**[I]

[I]Center for Inflammation Research, UGent-VIB, Gent, Belgium, [II]VIB-UGent Center for Inflammation Research, Gent, Belgium

Ferroptosis is a cell death modality elicited by perturbation of lipid redox metabolism, resulting in iron-dependent lipid peroxidation in the plasma membrane. Ferroptosis has emerged as a powerful strategy in anti-cancer therapy to bypass chemotherapy resistance, to sensitize radiotherapy and to eliminate metastatic tumors. Furthermore, newly developed ferroptosis inducers have been combined with nanotechnology-based targeting of tumor cells. Although killing by ferroptosis is an emerging strategy for anticancer therapy, its immunogenic potential in the context of anti-tumor responses is incompletely understood. Therefore we examined the immunogenic potential of ferroptotic dying cancer cells. The concept of immunogenic cell death (ICD) is based on the tripartite interaction between tumor-associated antigens (TAAs), adjuvanticity by Damage Associated Molecular Patterns (DAMPs) and immunoregulatory cytokines and chemokines elicited by dying cancer cells. Intruigingly, despite the massive release of DAMPs, the presence of TAAs and chemokines, ferroptotic dying cancer cells apparently interfere with antigen cross presentation by dendritic cells. Ferroptosis induction is associated with lipid droplet formation, COX2 activation, and PGE2 production, all factors that could possibly interfere with the antigen cross-presentation ability of DCs and as such stimulate tumor evasion. We will report on results that illustrate the impact of lipid peroxidation, lipid droplets formation, and related metabolites, and how these processes could be targeted to improve the anticancer immunogenic response during ferroptosis induction in cancer.