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Titel des Beitrags: Consensus guidelines for the detection of immunogenic cell death.

Abstract: Apoptotic cells have long been considered as intrinsically tolerogenic
or unable to elicit immune responses specific for dead cell-associated antigens. However, multiple stimuli can trigger a functionally peculiar type of apoptotic demise that does not go unnoticed by the adaptive arm of the immune system, which we named "immunogenic cell death" (ICD). ICD is preceded or accompanied by the emission of a series of immunostimulatory damage-associated molecular patterns (DAMPs) in a precise spatiotemporal configuration. Several anticancer agents that have been successfully employed in the clinic for decades, including various chemotherapeutics and radiotherapy, can elicit ICD. Moreover, defects in the components that underlie the capacity of the immune system to perceive cell death as immunogenic negatively influence disease outcome among cancer patients treated with ICD inducers. Thus, ICD has profound clinical and therapeutic implications. Unfortunately, the gold-standard approach to detect ICD relies on vaccination experiments involving immunocompetent murine models and syngeneic cancer cells, an approach that is incompatible with large screening campaigns. Here, we outline strategies conceived to detect surrogate markers of ICD in vitro and to screen large chemical libraries for putative ICD inducers, based on a high-content, high-throughput platform that we recently developed. Such a platform allows for the detection of multiple DAMPs, like cell surface-exposed calreticulin, extracellular ATP and high mobility group box 1 (HMGB1), and/or the processes that underlie their emission, such as endoplasmic reticulum stress, autophagy and necrotic plasma membrane permeabilization. We surmise that this technology will facilitate the development of next-generation anticancer regimens, which kill malignant cells and simultaneously convert them into a cancer-specific therapeutic vaccine.

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