Recognition of self-derived molecules in the regulation of inflammation and anti-tumor immunity

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Abstract

When we initiated our studies on the molecular characterization of cytokines, namely interferons and interleukins, the conventional wisdom was that they are soluble molecules secreted upon activation of cells by various stimuli, such as viruses. It was in this context that we discovered a family of transcription factors, termed interferon regulatory factors (IRFs), which is now a large focus in terms of its contribution in immunity and oncogenesis. In recent years, we focused our study on a new class of cytokines that function not only as secreted molecule, but also within distinct cellular compartments to exert seemingly unrelated biological activities. High-mobility group box protein1 (HMGB1) is a typical example of this class, which is the most abundantly expressed and extensively studied, thus far, for its role as a transcriptional regulator in the nucleus and inflammatory cytokine-like molecule when secreted. I will present our new data obtained using recently generated HMGB1 conditional knockout mice in the context of inflammation, infection and oncogenesis. I will also present recent results that show for how innate antitumor responses are orchestrated by recognition by an innate receptor(s) of tumor-associated molecular patterns (TAMPs) for the elimination of tumor cells. In the context of tumor immunoediting, we also present data indicating that the immune system via Dectin1 selects against expression of Dectin-1 ligands on tumor cells.