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| Sommario/riassunto | In multicellular organisms, states with a high degree of tissue turnover like embryogenesis, development, and adult tissue homeostasis need an instantaneous, tightly regulated and immunologically silent clearance of these dying cells to ensure appropriate development of the embryo and adult tissue remodelling. The proper and swift clearance of apoptotic cells is essential to prevent cellular leakage of damage associated molecular patterns (DAMPs) which would lead to the stimulation of inflammatory cytokine responses. In addition to the clearance of apoptotic cells (efferocytosis), backup mechanisms are required to cope with DAMPs (HMGB-1, DNA, RNA, S100 molecules, ATP and adenosine) and other intracellular material (uric acid, intracellular proteins and their aggregates) released from cells, that were not properly cleared and have entered the stage of secondary necrosis. Furthermore, under certain pathologic conditions (e.g. gout, cancer, diabetes) non-apoptotic cell death may transiently occur (NETosis, necroptosis, pyroptosis) which generates material that also has to be cleared to avoid overloading tissues with non-functional cellular waste. Efficient efferocytosis is therefore indispensable for |

normal tissue turnover and homeostasis. The characterization of various signalling pathways that regulate this complex and evolutionary conserved process has shed light on new pathogenetic mechanisms of many diseases. Impaired clearance promotes initiation of autoimmunity as well as the perpetuation of chronic inflammation, but may also foster anti-tumor immunity under certain microenvironmental conditions. Immunological tolerance is continuously being challenged by the presence of post-apoptotic remnants in peripheral lymphoid tissues. Besides the autoimmune phenotype of chronic inflammatory rheumatoid disorders a plethora of pathologies have been associated with defects in genes involved in clearance, e.g. atherosclerosis, cancer, gout, diabetes, some forms of blindness, neuropathy, schizophrenia and Alzheimer’s disease.