Targeting necroptosis and ferroptosis in cancer treatment

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Necroptosis is a regulated form of necrotic cell death that is tightly regulated in normal development and pathophysiological processes. The escape of host cells from apoptosis, induced by infectious agents such as viruses or bacteria, seems to enforce natural selection of necroptosis as an alternative protective pathway. The significance of necroptosis in several pathophysiological conditions, including viral infection, ischemia-reperfusion injury, pancreatitis, neurodegeneration, and systemic inflammatory response syndrome, has recently been revealed, along with necroptosis signaling pathways. Although necroptosis is an effective cell death mechanism, most cancer cells escape from necroptosis, but the underlying mechanism is largely unknown. In this talk, I will discuss our recent finding of the reciprocal regulation between necroptosis and oncogenic signaling.

Ferroptosis, a new form of regulated necrosis, is an iron-dependent cell death that is triggered by the excessive accumulation of lipid ROS. Under normal conditions, glutathione peroxidase 4 (GPX4) but not other GPx family members catalyses the reduction of lipid peroxides, thereby removing lipid ROS and protecting cells from ferroptosis. Emerging studies have revealed that ferroptosis is involved in various human diseases such as neurodegenerative diseases, ischaemia/reperfusion injury of the kidney and heart, and cancer. I will discuss about the role of lipid metabolism on ferroptosis in chemoresistant tumors.