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CASPASE-INDEPENDENT PROGRAMMED CELL DEATH IS NOT NECESSARILY NECROPTOSIS

To the Editor:

How to regulate cell death has always been an important means for people to intervene in the development of disease and improve prognosis. With the development of research, the mechanism of caspase-independent programmed cell death has been improved continuously, including the necroptosis and the ferroptosis, which is defined as a mode of caspase-independent regulated necrosis that is dramatically characterized by iron-dependent lipid peroxide accumulation.[1] It is reported that ferroptosis is governed by 3 antioxidant axes, ie, the cyst(e)ine/GSH/GPX4 axis, the GCH1/BH4/DHFR axis, and the FSP1/CoQ10 axis, all of which are fueled by nicotinamide adenine dinucleotide phosphate.[2]

Ueda and colleagues from Kyoto University considered that terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL)-positive and caspase-3–negative cells were counted as necroptotic cells, and TUNEL-positive and caspase-3–positive were counted as apoptotic cells in immunofluorescence.[3] However, the caspase-independent cell death form is not only necroptosis. That is to say TUNEL-positive and caspase-3–negative cells also possibly include ferroptotic cells and other caspase-independent cells that have not been reported. This approach is not rigorous and needs to be improved.

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