

45. Programmed Cell Death

1 unit, Emily Cheng, November 3, 2025

Classification of cell death

BCL-2 defines a novel class of oncogenes

BCL-2 family proteins are classified into three subfamilies—multidomain anti-apoptotic, multidomain pro-apoptotic, and BH3-only molecules

Multidomain pro-apoptotic BAX and BAK are essential effectors of mitochondrion-dependent apoptosis

BH3-only molecules activate multidomain pro-apoptotic BAX and BAK or inactivate multidomain anti-apoptotic BCL-2 subfamily

Mitochondrion-dependent cell death program

MOMP (mitochondrial outer membrane permeabilization) versus MIMP (mitochondrial inner membrane permeabilization)

Intrinsic versus extrinsic apoptotic pathways

Activation of caspases – apoptosome versus DISC complex

IAP family proteins

Necroptosis, pyroptosis, and ferroptosis

Apoptosis and tumorigenesis

Apoptosis and cancer therapy

Targeting apoptotic pathways in cancer therapy

Small molecule inhibitors of BCL-2, BCL-X_L, and MCL-1 for cancer therapy

Immunogenic cell death

Discussion

McArthur K, Whitehead LW, Heddleston JM, Li L, Padman BS, Oorschot V, Geoghegan ND, Chappaz S, Davidson S, San Chin H, Lane RM, Dramicanin M, Saunders TL, Sugiana C, Lessene R, Osellame LD, Chew TL, Dewson G, Lazarou M, Ramm G, Lessene G, Ryan MT, Rogers KL, van Delft MF, Kile BT. BAK/BAX macropores facilitate mitochondrial herniation and mtDNA efflux during apoptosis. *Science* 359, eaao6047 (2018).

Background

Moyer A, Tanaka K, Cheng EH. Apoptosis in Cancer Biology and Therapy. *Annu Rev Pathol.* 20: 303-328 (2025).

Tait SW, Green DR. Mitochondria and cell death: outer membrane permeabilization and beyond. *Nat Rev Mol Cell Biol.* 11:621-32 (2010).

Wallach D, Kang TB, Dillon CP, Green DR. Programmed necrosis in inflammation: Toward identification of the effector molecules. *Science* 352: aaf2154 (2016).