Old protein – new function: tBID can directly trigger cell death
This opens up a new approach in cancer therapy

23.12.2021 - The protein tBID can trigger programmed cell death (apoptosis) by inducing damage in the energy suppliers of the cells, the mitochondria. Apoptosis is essential for maintaining tissue balance. In addition, apoptosis plays a critical role as a defence mechanism and in the elimination of damaged or redundant cells in our bodies. Impaired apoptosis has been linked to many human diseases, from cancer and autoimmune diseases to neurological disorders and heart failure. The discovery by Professor Dr Ana Garcia-Saez and her collaborators and colleagues at the University of Cologne’s CECAD Cluster of Excellence for Aging Research that tBID, previously thought to be a signal transducer, can also execute apoptosis could open up new therapies to treat malignant cells such as cancer cells.

Scientists have discovered a new function of the protein tBID, which until now had only been associated with its regulatory role in cell death and cancer. However, tBID can also directly mediate controlled cell death (apoptosis). Symbolic image

The protein tBID belongs to the family of BCL-2 proteins, which are fundamentally important for the self-determined apoptosis of cells and tissue balance. Because of the overlapping functions of this protein family, studying them individually is particularly challenging. Garcia-Saez and her team set out to characterize the roles of the various family members. Using cell lines lacking much of the BCL-2 proteins, they were able to determine the function of tBID. In addition, state-of-the-art microscopy (confocal, STED and electron microscopy) was used to analyse in detail the effects of tBID at the mitochondrial membrane in the cell. Activating tBID was also able to combat cellular infection with the bacterium Shigella flexneri and kill blood cancer cells (leukemia). In addition, the researchers showed that apoptosis triggered by tBID is independent of other known apoptosis induction pathways.

‘For us, it was amazing to see that proteins which are quite well known still surprise us after four decades. The realization that a protein that was considered a signal transducer for twenty years has an effector function under certain conditions is mind-blowing,’ Garcia-Saez remarked. This newly discovered function of tBID could in the future become useful...
in medicine. ‘For example, activating tBID could induce apoptosis when other known apoptosis signalling pathways fail or lack the proteins that carry it out,’ said Garcia-Saez. ‘Activating tBID could also help with Shigella infections, where the proteins that usually induce apoptosis are not activated.’

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