# Old protein, new function: tBID can directly trigger cell death

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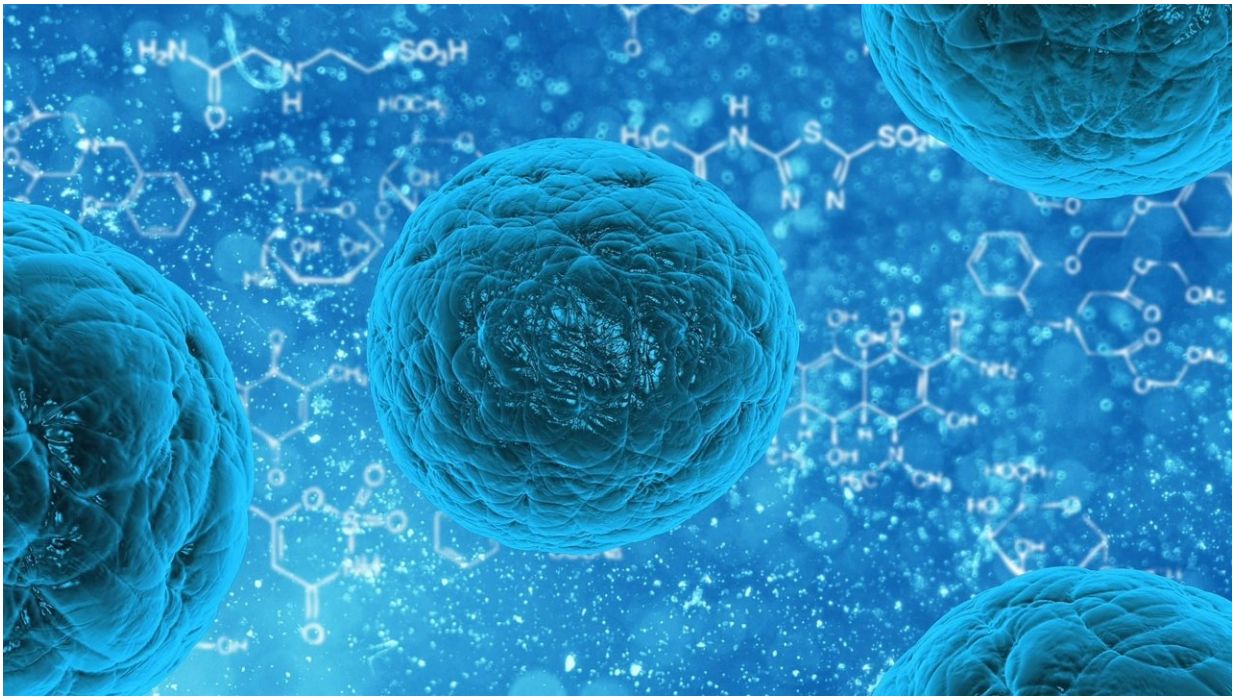

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The protein tBID can trigger programmed cell death (apoptosis) by inducing damage in the energy suppliers of the cells, the mitochondria. Apoptosis is essential for maintaining tissue balance. In addition, apoptosis plays a critical role as a defense 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. The article "tBID can act as a BAX-like effector of apoptosis" has now been published in *The EMBO Journal*.

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 analyze 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 signaling 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."

The work for this study started at the IFIB (Interfaculty Institute of Biochemistry) in Tübingen and was further developed at the CECAD Research Center, Institute for Genetics, in Garcia-Saez's core laboratory, together with the laboratories of Professor Dr. Hamid Kashkar und Dr. Lukas Frenzel as well as external collaborators from the University of Nebraska and the laboratory of Andreas Villunger (University of Innsbruck and CeMM Research Center, Austria).

**More information:** Hector Flores-Romero et al, BCL-2-family protein tBID can act as a BAX-like effector of apoptosis, *The EMBO Journal* (2021). DOI: 10.15252/embj.2021108690

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