

# Scientists develop 3-D model of regulator protein bax

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Scientists at Freie Universität Berlin, the University of Tübingen, and the Swiss Federal Institute of Technology in Zurich (ETH) provide a new 3D model of the protein Bax, a key regulator of cell death. When active, Bax forms pores in the membranes of mitochondria, causing the release of proteins from the intermembrane space into the cytoplasm. This in turn triggers a series of operations ending in cell death, which are often impaired in cancer cells.

Using Double Electron-Electron Resonance spectroscopy, a research group headed by Professor Enrica Bordignon at Freie Universität has now shown that active Bax is present on the [membrane](#) in the form of dimeric assemblies whose clamp-like structures have a central role in the pore formation process. Previous scientific efforts could only provide the crystal structure of the truncated core domain of Bax, but the full-length structure of the protein has remained elusive to date. The 3D model presented by the scientists can explain the way Bax functions and thereby may help future development of new cancer drugs. The findings were published in the prestigious online journal *Molecular Cell*.

Active Bax is organized at the membrane as assemblies of dimers. Two protein core domains build a stable interaction along helices 2-5. By contrast, helices 6 to 9 of Bax re-organize: they are dislodged from the core domain and adopt a dynamic configuration at the membrane. The most significant conformational change is the opening of the hairpin formed by helices 5-6 in each monomer to assemble a clamp-like dimeric structure. This new conformation is proposed to pinch the

membrane bilayer forming a toroidal pore.

The model proposed by the Berlin-based scientist Enrica Bordignon and her colleagues emphasizes the significant transformation of Bax from the aqueous inactive state to the membrane-bound active state. This makes earlier models based on the permanent preservation of 5 to 6 hairpins obsolete. "If we understand how the Bax protein deforms the membrane and forms pores, we are one step closer to understanding how cells die, and thus one step closer to the development of new cancer drugs which should promote [cell death](#)," says Enrica Bordignon.

Enrica Bordignon was born in 1975 in Italy. She earned a degree in chemistry at the University of Padua, Italy, where she also completed a doctorate in physical chemistry in 2003. Her doctoral advisor was Prof. Dr. Donatella Carbonera. From 2003 to 2008 Bordignon was a postdoctoral researcher in the Prof. Dr. Heinz-Jürgen Steinhoff's laboratory of the University of Osnabrück, where she started investigating the structure and dynamics of membrane proteins. From 2008 to 2013 she further specialized in this field while working as senior researcher in Prof. Dr. Gunnar Jeschke's laboratory at ETH Zurich in Switzerland. Bordignon has been a professor of biophysics at the Department of Physics, Freie Universität Berlin, since September 2013.

**More information:** Stephanie Bleicken, Gunnar Jeschke, Carolin Stegmüller, Raquel Salvador-Gallego, Ana J. García-Sáez, Enrica Bordignon. 2014. Structural Model of Active Bax at the Membrane, in: *Molecular Cell*, Elsevier Inc.

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