Many cancer cells do not release cytochrome c from the inter-membrane space of mitochondria when intrinsic apoptosis is stimulated. Bcl-2 family proteins such as Bcl-2 and Bcl-XL regulate intrinsic apoptosis by inhibiting mitochondrial outer membrane (MOM) permeability. Jingzhen used comprehensive site-specific photo-crosslinking to determine the interface formed by a full-length pro-apoptotic protein (Bax) with Bcl-2 or Bcl-XL in detergent micelles of MOM-mimic liposomal membranes or native MOM. She found that pro-apoptotic Bax interacts with either Bcl-2 protein through two interfaces on the cytosolic side of MOM, a previously discovered canonical BH3 helix:BH1-3 groove and a new interface consisting of the BH4 regions of both proteins. A point mutation in each sub-interface blocks the formation of both interfaces, rescuing MOM permeability and releasing cytochrome c like the BH3 mimetic ABT-737 which Jingzhen showed targets the same interactions. Jingzhen’s studies therefore indicate that formation of Bax:Bcl-2 protein sub-interfaces is coupled and is a target for novel apoptosis activators for cancer therapy.