

## W0532

**The Crystal Structure of BCL-XL in Complex with Full-length BAD.** Kwang-Hoon Lee, Ji-Hye Baek, Byung-Ha Oh, Pohang Univ. of Science & Technology, Namgu Hyojadong San 31, Pohang, Korea.

The BCL-2 family of intracellular proteins is the central regulator of apoptosis. We overproduced a complex between an antiapoptotic member BCL-XL (residues 1-196) and a proapoptotic member BAD (residues 43-204). Here, the 2.3 Å ring; crystal structure of BCL-XL:BAD complex shows that BAD is totally disordered except for 27 amino acids occupying the extended BH3-binding groove of BCL-XL. The structure indicates that BAD is a natively unstructured protein, but becomes partly structured upon binding to the proapoptotic partner proteins, in a sharp contrast with another BH3-only protein BID, which adopts an  $\alpha$ -helical fold. The snapshot of the structure of BCL-XL disabled by BAD-binding in conjunction with the  $\sim 40$  nM dissociation constant between the two proteins supports that BAD exerts the proapoptotic activity by displacing other proapoptotic proteins responsible for mitochondrial dysfunction. The structure also shows that Ser155 of BAD is completely buried in the binding groove of BCL-XL, which explains why the survival factor-mediated phosphorylation of this residue inactivates BAD and protects cells from apoptotic stimuli.