Analysis of the lipid binding properties of mutant murine Bid proteins

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Bid is a BH3-only member of the Bcl-2 family that regulates cell death at the level of mitochondrial membranes. It is generally assumed that the full length Bid protein becomes activated after a proteolytic cleavage catalized by apical caspases, like caspase 8. The cleaved protein then re-locates to mitochondria and promotes membrane permeabilization, presumably by interaction with mitochondrial lipids and other Bcl-2 proteins that facilitate the release of apoptogenic proteins like cytochrome *c*. The un-cleaved Bid also has proapoptotic potential when ectopically expressed in cells or *in vitro*. It has been demonstrated that full length Bid can insert specific lysolipids into the membrane surface and this lipid transfer activity participates to the release of apoptogenic factors from mitochondria. The binding properties of Bid are still unknown. In this work we will present new full length Bid mutants that possess altered lipid binding properties and proapoptotic activities *in vitro*. We have analysed the binding properties of Bid mutants to LPC species and MCL (or LPG) in order to investigate the protein dual specificity for the diverse lysolipids.

Keywords: Bid, Bcl-2, lysolipid, apoptosis, mitochondria.