## Lecture 3: “Targeting Bcl-2 family proteins in cancer”

The Bcl-2 oncogene was discovered nearly 30 years ago as overexpressed gene in B-cell follicular lymphoma. It became rapidly clear that Bcl-2 represented the prototypical member of a new class of oncogenes which was found to promote tumour progression by inhibiting the cell death rather than promoting cell proliferation. It is now well acknowledged that proteins belonging to the Bcl-2 family control a central event of the apoptosis execution: the increase of the mitochondrial outer membrane permeability (MOMP) with the subsequent release of apoptotic factors. Structurally, these proteins contain one to four B-cell homology (BH) domains as well as a hydrophobic C-terminus transmembrane domain. Functionally, they are divided in two antagonistic subgroups; on the one side, the activators of the MOMP called “pro-apoptotic” Bcl-2 members and on the other side, the repressors of this process called the “anti-apoptotic” Bcl-2 proteins. Upregulation of the anti-apoptotic members in wide range of cancers including breast cancer is often correlated with chemotherapy resistance and poor prognosis. Thus targeting the activity of Bcl-2 family proteins using BH3 mimetics or BH4-derived peptides represent promising strategies for the elaboration of cancer therapeutics.

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