

A6**An Anti-apoptotic Protein Human Survivin is a Direct Inhibitor of Caspase-3 and -7**

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Survivin, an apoptosis inhibitor/cell-cycle regulator, is critically required for suppression of apoptosis and ensuring normal cell division in the G2/M phase of the cell cycle. It is highly expressed in a cell cycle-regulated manner and localizes together with caspase-3 on microtubules within centrosomes. Whether survivin is a physiologically relevant caspase inhibitor has been unclear due to the difficulties with obtaining correctly folded survivin and finding right conditions for inhibition assay. In this study, recombinant, active human survivin was expressed in *Escherichia coli* and purified to homogeneity. The protein, existing as a homodimer in solution, binds caspase-3 and -7 tightly with a dissociation constant of 20.9 nM and 11.5 nM, respectively, when evaluated by surface plasmon resonance spectroscopy. Consistently, survivin potently inhibits the cleavages of a physiological substrate poly(ADP-ribose) polymerase and an artificial tetrapeptide by caspase-3 and -7 *in vitro* with an apparent inhibition constant of 36.0 nM and 16.5 nM, respectively. The data suggest that sequestering caspase-3 and -7 in inhibited states on microtubules is at least one mechanism of survivin in the suppression of default apoptosis in the G2/M phase. The localization of survivin on microtubules, which is essential for its function, should increase the protective activity at the action site.