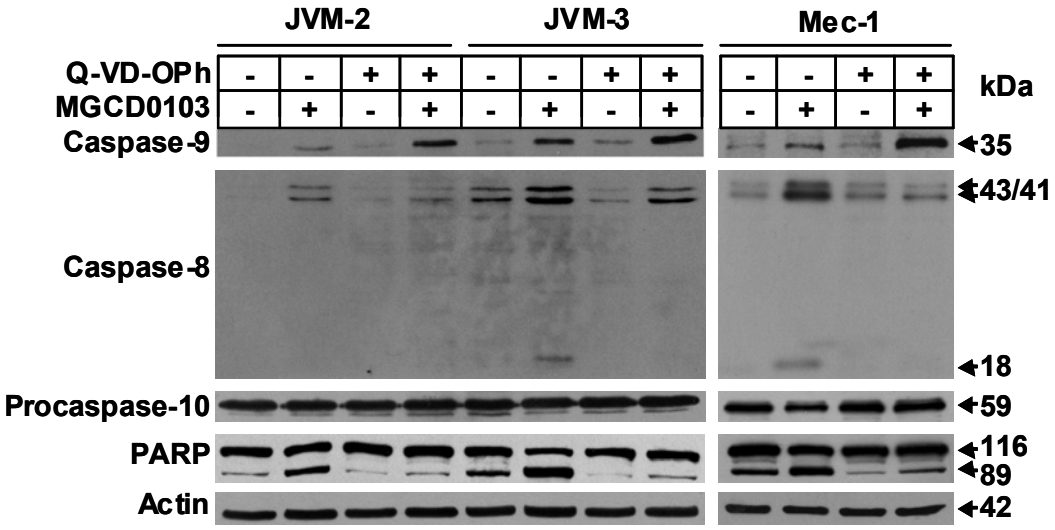
Supplementary Data

Supplementary Figures legends

Supplementary Figure S1. MGCD0103 can induce both the intrinsic and extrinsic pathways of apoptosis in leukemic/lymphoma cell lines. JVM-2, JVM-3 and Mec-1 cells were incubated with MGCD0103 (3 μM) alone or in the presence of Q-VD-OPh (15 μM) for 24 h (JVM-2 and JVM-3) or 48 h (Mec-1). The status of the indicated proteins was analyzed by immunoblotting, using actin as a loading control.

Supplementary Figure S2. Proposed model for the mechanism of MGCD0103-induced apoptosis in CLL cells. MGCD0103 stimulation induces translocation of Bax to the mitochondria and loss of $\Delta\Psi_m$, leading to cytochrome c release and caspase-9 activation. Caspase-9 activates caspase-3 which in turn activates caspases-6 and -8. Caspase-6 then activates caspase-10 and may also participate in caspase-8 activation. This apoptotic cascade contains several positive feedback loops since caspase-3 activates caspase-9, and caspase-6 activates caspase-3. Caspase-3 activation may also result in the cleavage and inactivation of the calpain inhibitor calpastatin, thereby triggering an additional amplification loop to accelerate the apoptotic process. Thus, inactivation of calpastatin, together with the release of the Ca^{2+} stored in the mitochondria following the drop of $\Delta\Psi_m$, leads to the activation of calpain and its translocation to the mitochondria where it can cleave p21 Bax, generating p18 Bax. p18 Bax increases the disruption of mitochondrial integrity and thus the release of cytochrome c in the cytosol.

Supplementary Figure S1



Supplementary Figure S2