



**Supplementary Figure 7.** A model for the inhibition of autophagy induced by MGCD0103 in primary CLL cells. MGCD0103 rapidly activates the PI3K/AKT/MTOR pathway, thus inhibiting autophagy at early time points. After onset of apoptosis, MGCD0103-induced caspase activation triggers the cleavage of key autophagy-related proteins, namely BECN1, ATG5, SQSTM1 and ATG4B, thus inhibiting autophagy at later time points. In cells from at least some CLL patients, caspase-mediated activation of calpain-1 is also involved in these cleavage processes. MGCD0103 modulates the expression of several autophagy-related genes at the transcriptional level, which may participate in the inhibition of the autophagic process.