Defects in cellular control over apoptosis contribute to cancer development and drug resistance. This research investigated how a flexible heteroarotinoid (Flex-Het) compound, called SHetA2, controls apoptosis in ovarian cancer cells. Dr. Chenguza hypothesized that inhibition of the nuclear factor kappa B (NF-κB) survival pathway was involved in the mechanism of SHetA2-induction of the intrinsic apoptosis pathway, and would allow induction of the extrinsic apoptosis pathway by death-receptors (DRs). She demonstrated that SHetA2 inhibits kinase induction of NF-κB action, but that intrinsic apoptosis occurred independently of NF-κB inhibition. SHetA2 could circumvent ovarian cancer resistance to DR-mediated extrinsic apoptosis through a mechanism involving NF-κB inhibition and induction of DR expression through up-regulation of CHOP (CAAT/enhancer binding protein homologous transcription factor). Thus, SHetA2 could improve the efficacy of DR activating agents currently in clinical trials for ovarian cancer. SHetA2-mediating molecules identified in this study can be targeted for drug and biomarker development.