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Inhibition of HSP90 with AU922 Induces Synergy in HER2-Amplified Trastuzumab-Resistant Breast and Gastric Cancer
ABOUT THE COVER

The yeast Rad6 human homologues HHR6A and HHR6B (or Rad6A and Rad6B) encode ubiquitin-conjugating enzymes (or E2) that play a central role in substrate ubiquitination and E3 ligase selection. The ubiquitin-conjugating activity of Rad6 is essential for its function in postreplication DNA repair, damage-induced mutagenesis, and proteolysis. Using virtual screening of ZINC database against a pharmacophore model for consensus, E2-ubiquitin binding sites followed by biological evaluation of virtual hits, two small molecule compounds with a triazine core structure, and possessing Rad6 ubiquitin conjugation inhibitory activity were identified. These small molecules inhibit breast cancer cell proliferation, migration, and colony formation by blocking G2-M progression. For details, see article by Sanders and colleagues on page 373.