Molecular Cancer Therapeutics

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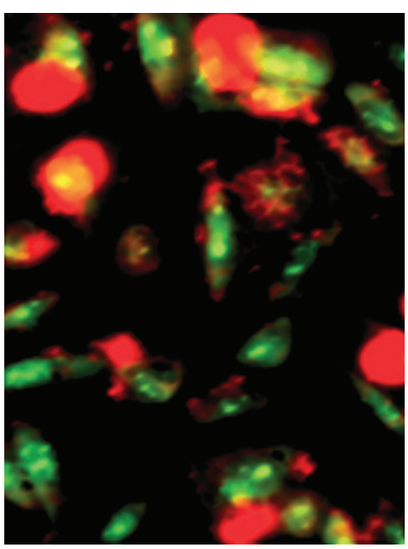
ABOUT THE COVER

The yeast RAD6 homologues HHR6A (a.k.a. RAD6A or UBE2A) and HHR6B (a.k.a. RAD6B or UBE2B) encode ubiquitin conjugating enzymes or E2s that play a central role in translesion DNA synthesis (TLS), damage-induced mutagenesis and proteolysis. Consistent with RAD6 function, treatment of breast cancer cells with a RAD6-selective small molecule inhibitor SMI#9 restores chemosensitivity by inhibition of TLS. Delivery of SMI#9 is challenging due to its poor aqueous solubility. Saadat and colleagues synthesized SMI#9 as a prodrug-gold nanoparticle (GNP) conjugate to overcome its solubility limitations and to effectively deliver therapeutic SMI#9 to triple negative breast cancers (TNBCs). As depicted on the cover, both blank and SMI#9 conjugated GNPs are endocytosed into the TNBC cells but cell death is only induced by SMI#9-GNP as detected by acridine orange/ethidium bromide staining. GNPs delivering SMI#9 prodrug exhibited improved in vivo pharmacokinetics and inhibited TNBC growth in vivo. The GNP platform allows for SMI#9 conjugation and delivery to treat TNBCs, a breast cancer subtype with poor prognosis and lacking targeted therapies.



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