

IS01-1 Protein Knockdown: Targeted Destruction of Pathogenic Proteins by SNIPER Compounds

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Protein knockdown by SNIPER (Specific and Nongenetic IAP-mediated Protein ERaser) is a technology that can induce selective degradation of target proteins in cells. SNIPER is a hybrid molecule composed of a ligand for cIAP1 (BS: bestatin) linked to another ligand for a target protein (X), which is designed to cross-link cIAP1 and the target protein, thereby inducing IAP-mediated ubiquitylation and proteasomal degradation of the target protein (Fig. 1). We initially employed *all-trans* retinoic acid (ATRA) to target cellular retinoic acid binding protein-II (CRABP-II), and the SNIPER(CRABP) reduced the CRABP-II protein within several hours. With its modular structure, SNIPER technology can be easily applied to other target proteins. By using tamoxifen as a ligand, we also developed SNIPER(ER) to target estrogen receptor-alpha (ER α). The SNIPER(ER) induces degradation of ER α and necrotic death of breast cancer cells. Thus, SNIPER can target a variety of pathogenic proteins for degradation via the ubiquitin-proteasome system, which might be useful for biological researches and therapeutic purposes.

