TIMS/MANA JOINT SEMINER

題目： POLYMERIC MICELLES FOR NANO-COMBINATION DRUG DELIVERY

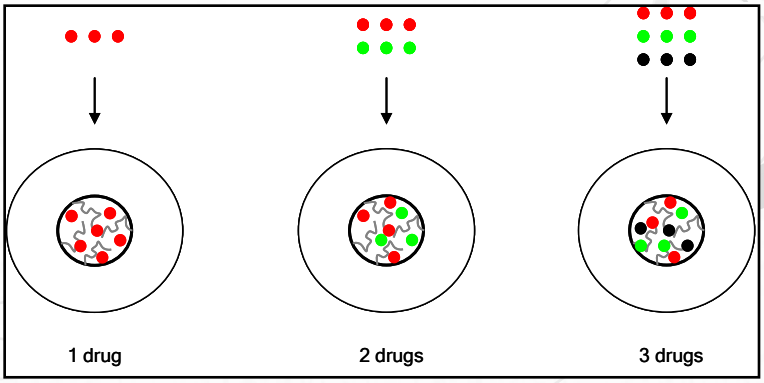
講師：Dr. Glen S. Kwon
Professor
School of Pharmacy, University of Wisconsin, Madison, WI, 53705, USA

日時：10月2日(金)　16 :00-18:00

場所： 総合研究棟B　0110教室

Abstract

We have discovered that poly(ethylene glycol)-*block*-poly(lactic acid) (PEG-*b*-PLA) micelles can take up and solubilize multiple anti-cancer agents, providing a novel and simple approach for combination cancer therapy (Figure 1), aiming for synergistic anti-tumor efficacy involving combinations of chemotherapy and signal transduction inhibitors. We are interested in a novel 3-drug anti-cancer combination involving pacli-taxel, rapamycin, and 17-allylamino-17-demethoxygeldanamycin (17-AAG). Pre-clinical data suggests that paclitaxel exerts synergistic anti-tumor activity in murine tumor models with rapamycin or 17- AAG. While acting via different mechanisms of action and on different targets, both rapamycin and 17- AAG act on cancer survival pathways and are potent angiogenesis inhibitors. Notably, 17-AAG, a prototype heat shock protein 90 (Hsp90) inhibitor, knocks out kinases (AKT, Raf), activated by the inhibition of the mammalian target of rapamycin (mTOR) by a feedback mechanism, providing a basis for enhancing the activity of rapamycin, the first mTOR inhibitor. In this work, PEG-*b*-PLA micelles solubilize paclitaxel, rapamycin, and 17-AAG as nano-combinations, offering safety over surfactants and cosolvents, physical stability against drug precipitation, ease of production and scale-up, and low prospects for PK interactions; all facilitating ease of entry into clinical trials for a 3-drug combination of paclitaxel, rapamycin, and 17-AAG.



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