

Multi-modal Gene/chemotherapy for Cancer: A Facile, Comprehensive, Tunable, and Versatile Approach

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Abstract

Most therapies tackle a single pathological target such as an effector protein or an abnormal genetic pathway, often resulting in limited, ancillary therapeutic effects. For example, cancers arise from complex molecular causes, making them difficult to treat by a single modal therapy. In order to rebalance the broken molecular homeostasis in chronic myelogenous leukemia (CML) as a simple, well-documented model, pro-apoptotic and pro-survival genes were simultaneously expressed and silenced in a CML cell, respectively, using a viral/nonviral chimeric nanoparticles (ChNPs) that were composed of the BIM-expressing adeno-associated virus (AAV) core and MCL-1 siRNA-encapsulating, acid-degradable polymeric shell. While BIM/MCL-1 ChNPs genetically rebalance the pathological genetic pathways, a targeted chemotherapeutics for CML, dasatinib, was additionally administered. The result demonstrated synergistically enhanced anti leukemic effects by the synergistically enhanced anti-leukemic effects by the combined multimodal gene and chemotherapy in vitro and in vivo, especially in a rapidly progressing disease stage of blast crisis. A computational simulation via multi-omics network analyses using machine learning also predicted the synergistically augmented apoptosis by the combined multimodal gene and chemotherapy. This study demonstrates the critical roles of engineering therapies that address the complex nature of a disease by integrating interdisciplinary principles.

Bio



Dr. Young Jik Kwon is a professor at UCI in the Pharmaceutical Sciences, Chemical & Biomolecular Engineering, Biomedical Engineering, and Molecular Biology & Biochemistry departments. Following his undergraduate education in Biological Engineering at Inha University, Dr. Kwon received his Ph.D. in Chemical Engineering from the University of Southern California in 2003 and did post-doctoral training in department of chemistry at UC Berkeley. He started his academic career in Biomedical Engineering at Case Western Reserve University in 2005 where he was the M. Frank and Margaret Rudy assistant professor and moved to UC Irvine in 2007. Dr. Kwon's work was awarded a Faculty

Early Career Development Award (CAREER) from the National Science Foundation in 2010 and a Medical Research Award from Gabrielle's Angel Foundation for Cancer Research in 2011. He was also an invited scholar to Federal University of Minas Gerais (UFMG) in Brazil and a Brain Pool Scholar in Korea University in Korea. He was also selected to be a Faculty Innovation Fellow of the Beall Applied Innovation at UCI.