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Precision genome editing with engineered nucleases

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A major concern in DNA vaccination and gene therapy protocols using non-viral vectors is the low efficiency of gene delivery. This is mainly attributed to the several physical, enzymatic and diffusional barriers that plasmid vectors must overcome during the traffic to the target cells nuclei. Our group has been working on the development of delivery particles formed by the combination of recombinant proteins, specifically designed for plasmid DNA (pDNA) delivery, and lipids. We propose that these particles, also called "artificial viruses", will rely on the high efficiency of cell internalization of the lipids and then, exploit the cell machinery for intracellular trafficking via the recruitment of dynein molecular motors for the transport towards the nucleus. In this work, recombinant dynein light chains (LC8 and RP3) were fused to synthetic DNA binding domains, maintaining the ability to interact with dynein intermediate chain. We confirmed the ability of the proteins to interact and condense pDNA, forming positive particles with size ranging from 100 to 900 nm, depending on the protein construct. Transfection studies indicated that addition of fusion proteins to pDNA (pVAX1Luc) increased the transfection efficiency of mammalian cells (HeLa) up to almost ten thousand times, comparing to naked DNA. Even higher transfection efficiencies are achieved by complexes formed by protein, pDNA and LipofectamineTM, with reduced cytotoxicity. The development of non viral vectors that mimic strategies used by virus to infect mammalian cells may, in the near future, reduce the current advantage of viral vectors, providing new tools for gene therapy studies.

Biography

Jin-Soo Kim is an entrepreneur and a chemist-turned-biologist. He graduated from Seoul National University in 1987 with a major in chemistry. He earned a master's degree in chemistry from Seoul National University in 1989 and a Ph. D. in biochemistry from the University of Wisconsin-Madison in 1994. After postdoctoral training at Howard Hughes Medical Institute/Massachusetts Institute of Technology, He came back to Seoul in 1997 to serve as a Principal Investigator at Samsung Biomedical Research Institute. In 1999, he co-founded a biotechnology company, ToolGen, Inc., focused on zinc finger technology, and served as CEO and CSO of ToolGen for the subsequent six years. He joined the faculty of the Department of Chemistry at Seoul National University in 2005. Jin-Soo Kim has published 40 research articles mostly on zinc finger technology, which include 3 papers in Nature Methods, 2 in Nature Biotechnology, and 4 in Genome Research, and filed 20 patent applications.

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