Genetically Engineered RNA Microvesicles (RNAmv) for Cancer Gene Therapy

RNTein Biotech Lab., based in Los Angeles, California, USA, is a new type of biotech company dedicated to human cancer gene therapy. RNTein Biotech Lab. has been working on research projects and development of human gene therapy vectors since 2001. By registered as a small business entity in USA in 2008, RNTein Biotech Lab. has generated various types of DNA nanoparticles for cancer gene therapy, such as Lentiviral vectors AJS2001 and AJS2010, DNA nanoparticles vlp-vectors, and Cytomox. Now we announce we have developed new type of RNA nanoparticles called engineered RNA microvesicles, RNAmv.

Completely different from DNA nanoparticles which pose potential threats against host genome, and which is generated in self-assembling polycationic polymers and cloned DNA that would causes destruction of cell membrane, RNAmv, or RNA nanoparticles, produced as micorvesicle in donor cells and released or budding to outside of the cell, play a role in gene regulation and participate in various kinds of cellular events directly without disturbing host cell genome integrity. Therefore, RNAmv is more safer in terms of medical application.

RNTein Biotech Lab makes RNAmv using a technology called RNA controlled cellular distribution (CCD). We have developed unique transgene vectors from which the transgene will be transcribed in RNA inside the donor cells and the specific transcripts will be processed in a form of nuclear core that lets transgene RNA to be assembled and encapsulated with provided exogenous envelopes. These macromolecular complexes are formed as nanoscale endocytic membrane vesicles, or various kinds of microvesicles, or exosomes, or shedding vesicles, or apoptotic bodies. They are released into extracellular environment on fusion with cytoplasmic membrane.

With this discovery, researchers and biotech engineers from RNTein Biotech Lab., who have been in participating in the Tokyo clinical trial and who have been involved in biotechnology development create a new type of anti-cancer transgene vectors that carry 5’ upstream sequences of human telomerase reverse transcriptase gene (hTERT, which protects chromosome end's integrity) that are used for actively processing, stimulating, and enhancing microvesicles emitting or releasing out of the donor cells. When collected and purified, these genetically engineered cellular microvesicles, RNAmvs, are ready for treatment of cancer patients in clinical trial.

Research results have shown that tumors possess a unique physiology of fenestrated vasculature and poor lymphatic drainage, a characteristic that is now

wildly known as enhanced permeability and retention (EPR) effect. Relatively larger gaps between adjacent endothelial cells in tumor neovasculature allow bionanoparticles, such as RNAmvs, passing blood vessel barriers in a way of passive targeting the tumor foci, while poor lymphatic drainage creating relatively higher retention of macromolecular bionanoparticles within tumor mass. Therefore, RNAmvs are able to "enter" and "exit" cells and to spread extracellularly to have cancer cells in the vicinity "infected". This kind of extracellular RNA microvesicles delivers the transgene RNA to target cells naturally and safely. The RNA molecules delivered in targeted cells can be translated into transgene products, or cancer-cure proteins, or perform RNA interference as short-hairpin RNA (shRNA), or as long non-coding RNA (lncRNA ）to suppress lost-controlled tumor growth.

Assembled with VSV-G envelope protein, similar to recombinant pseudo-typed lentiviral particles, but functioning as non-viral vector, RNAmvs are compatible with cellular membrane, make it possible that transgene RNA and proteins are able to be administrated systemically in multiple times, having the cancer-cure components kept at sustainable treatment levels. The RNA microvesicles, created from the RNTein Biotech Lab., therefore, will be the most efficient cancer-fighting therapeutics for medical application.

As fast development of biotechnology and application of human genome projects cancer treatment is now in transform from conventional surgery, chemotherapy, and radiotherapy into combination of conventional therapies with gene therapy and immunotherapy. For each cancer patient, specific gene therapy approaches are set up according to results of gene tests and laboratory tests to let medical providers to run personal medicine, or precision medical treatment.