Technology Offer

Protein nanoparticles for the targeted therapy of aggressive tumours and metastasis

Summary

Directed delivery of targeted therapies has become the main goal in cancer therapy.

The proper selection of functional peptides, to be rationally combined in modular, multifunctional proteins is a convenient approach to generate smart nanocontainers for small molecules and therapeutic proteins, DNA or RNA delivery. Such vehicles can self-assemble as nanoparticles, recognize specific cell-surface markers and deliver the pharmaceutical into the cytoplasm or nuclear compartments. Cellular targeting to colorectal cancer cells permit therapeutic doses with low product amounts, and much more efficient treatment of Colorectal cancer (CRC) than that achieved with conventional drugs.

According to the American Cancer Society, CRC has a global incidence of nearly one million new cases every year and is the third most common type of cancer.

The U.S. colorectal cancer market is forecasted to grow from $3,900 million in 2011 to 6,050 million by 2016, at a compound annual growth rate of 8.6 percent*.

*Source: Frost & Sullivan

We have developed a new drug delivery system for the selective treatment of colorectal tumor cells. We are seeking a company partner to further develop the technology through a co-development and license agreement.

Innovative aspects and applications

- Highly targeted drug delivery system for the treatment of aggressive tumours and metastasis. Excellent biodistribution pattern.
- Precise adjustment of the dosage regimen, allowing a considerably important reduction of side effects.
- This system allows for personalizing CRC therapy because peptide nanoparticles can bind to and transport a wide range of therapeutic molecules such as small molecules, siRNA, etc.

State of development

Modular nanoparticle prototypes have been developed and tested in cell culture for targeted delivery of a payload construct DNA and its expression, and for targeted delivery of fused functional polypeptides.

So far, *in vivo* delivery tests have been successful, showing specific and receptor-mediated cell internalization of the nanoparticles in tumor and metastasis tissues at low doses.

Furthermore, the nanoparticles have shown high stability into the animal for at least 24h, without apparent toxicity.

In vivo results in Orthotopic Mouse Models have shown that nanoparticles loaded with a fluoropyrimidine derivative are able to target the metastasis foci in a very effective and selective way.

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The Invention

We have developed modular, single chain polypeptides obtained by recombinant DNA procedures able to deliver therapeutic proteins or DNA to specific cell types involved in the development and progression of colorectal cancer. The basis of this technology is the proper selection of targeting peptides directed to specific cell markers (CXCR4), and the optimization of cell internalization and trafficking routes of protein particles of a nanosize scale, compatible with efficient nuclear import. As shown in Figure 1, tagged particles are able to internalize desired therapeutic molecules into the cytoplasm or even the nucleus of cultured tumor cells.

Our peptide nanoparticles, improve the performance of metal nanoparticles, since they are highly customizable, can bind a wide range of therapeutic molecules such as nucleic acids (shRNA, siRNA) or therapeutic proteins and show no toxicity in animals.

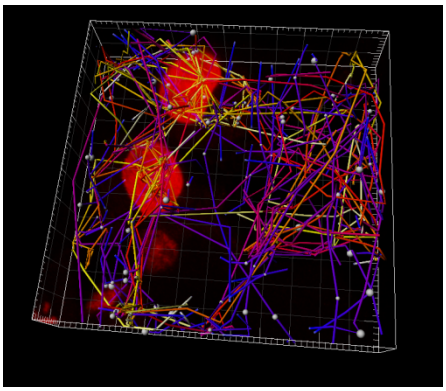
This allows an individualized and selective therapy scenario.

The surface receptor to which our tag binds (CXCR4) to is overexpressed in aggressive tumors and metastasis. So far, we have focused on the treatment of CRC. In the near future, we are planning to target other tumor types, such as glioblastoma, pancreas or hematological neoplases.

Ongoing research

We are currently assessing the potential in different animal models using a variety of associated therapeutic molecules.

Figure 1



Intracellular trafficking and nuclear delivery of self-assembled, modular protein particles, based on cationic peptides, after its exposure to cultured HeLa cells. Modified from: Vazquez et al, Nanomedicine 2010. 5, 259

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