Chitosan nanoparticles directed for the selected release of a Tumor suppressive miRNA (miR126) in metastatic melanoma cells resistant to therapy

KEYWORDS

- ❑ CHITOSAN NANOPARTICLES
- ❑ miR126
- ❑ METASTATIC MELANOMA

AREA

- ❑ PHARMACEUTICAL

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Patent Type
Patent for invention

Ownership
Sapienza University of Rome 100%

Inventors
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Industrial & Commercial Reference
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Time to Market
The developed technology was validated on a laboratory scale, corresponding to the TRL4 level

Availability
Research, Development, Experimentation, Collaboration and Start-up

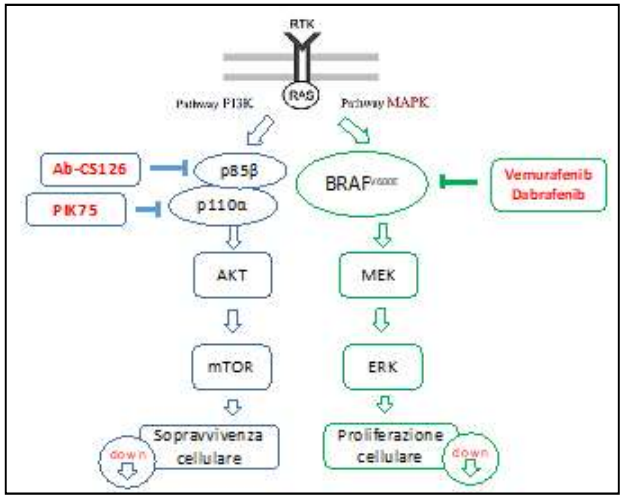

Fig. 1 Proposed mechanism of action [Figure modified from Pedrini F. et al., Mol Oncol, 2019]

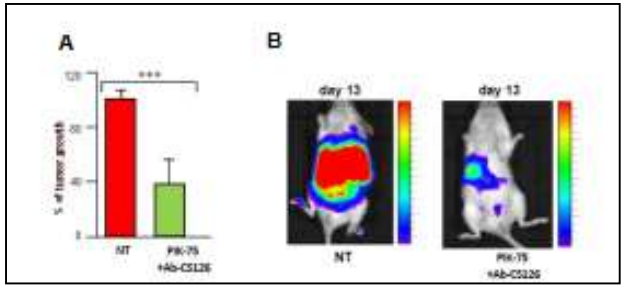

Fig. 2 In vivo experiment: statistical analysis of tumor growth (A) and IVIS images of a mouse representative of two treatment groups (B) [Figure modified from Pedrini F. et al., Mol Oncol, 2019]

Abstract
Our research group has demonstrated a tumor-suppressive role of microRNA-126 (miR126) in advanced and therapy-resistant melanoma. For this reason purpose we have formulated and created a vehicle made up of chitosan nanoparticles (CS), capable of incorporating effectively miR126 and coated by the variable part of an antibody (scFv) specific for a melanoma cell membrane protein (CSPG4). To carry out this study we developed a mouse model of liver and lung metastases from a dabrafenib-resistant melanoma line (A375M-DR) and used this model to study the effectiveness of scFv-CS126 + PIK-75 in containing growth and the spread of the tumor. The results obtained highlighted a significant reduction in tumor growth in the primary (hepatic) site and a surprising inhibition of metastasis in the lung site.

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Technical Description

More generally, the use of nanotechnology in anti-tumor therapies has aimed to improve the pharmacokinetics and reduce the systemic toxicities of chemotherapies through the selective targeting and delivery of these anticancer drugs to tumor tissues. Chitosan based nanoparticles (CSs) have been identified as a promising candidate for drug nucleic acids delivery due to their positive charge in acid environment, biocompatibility and stability. The inventors of the present application have developed a new therapeutic agent for the treatment of metastatic melanoma resistant to therapies. In particular, they have found how to delivery miR126-modified sequence (OMe-126) directly to melanoma tumor cells. The system is based on the use of loaded chitosan particles functionalized with a single chain antibody against a specific tumor marker. These nanoparticles have proven to be extremely effective in the treatment of metastatic melanoma resistant to targeted therapy in preclinical models

Technologies & Advantages

Liposomes, polymeric, supermagnetic or gold nanoparticles, dendrimers are some examples of innovative approaches in experimentation for the transport of drugs into target cells. This is in fact a rapidly expanding sector and the applications are numerous, ranging from electronics to materials physics, from pharmacology to industrial catalysts. Nanomaterials for drug transport have very important chemical-physical properties in this field because they have a fundamental role in degradation processes, vascular dynamics and targeting. For example, colloidal nanoparticles produced with biological polymers such as chitosans can give rise to "intelligent" targeting systems, capable of changing the chemical-physical properties based on external stimuli. The inventors of the present patent application have developed a new therapeutic agent for the treatment of metastatic melanoma resistant to traditional therapies. In particular, they discovered how to deliver the modified sequence of miR126 (OMe-126) directly to melanoma tumor cells. The system is based on the use of chitosan nanoparticles loaded and functionalized with a single-chain antibody against a specific tumor marker. These nanoparticles have proven to be extremely effective in treating metastatic melanoma resistant to targeted therapy in preclinical models.

Applications

The main application field of our invention is undoubtedly pharmacological. Despite recent advances in the treatment of metastatic melanoma (immunotherapy and targeted therapy), a high percentage of patients (about 40%) still do not respond to treatments, and an equally high percentage, after initial regression, develops resistance to the treatments. For these reasons, the pharmaceutical industry may show interest in our approach. However, the system we propose not only represents a therapeutic possibility for advanced melanoma patients but also serves as a model applicable to other diseases, especially other forms of neoplastic disease. In particular, for certain types of lung tumors and ovarian cancer, miR126 plays a tumor-suppressive role, and CSPG4 (recognized by our nanoparticles) is a specific marker.

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