NASA-BASED siRNA NANOPARTICLES

A giant leap has been made by researchers developing nanoparticles for the delivery of siRNA to cancer cells. Mauro Ferrari explained the team's multistage vectors as "similar in concept to the system NASA used to bring people on the moon: multiple stages each designed to carry out part of the trip—while a single spaceship would not have been able to make it."

The sustained delivery of siRNA will allow the targeting of many established oncogenes that are not druggable using standard small-molecule agents. The team had previously demonstrated that biodegradable and biocompatible mesoporous silicon particles could be used to deliver nanoparticles to endothelial cells.

The recent study built on this work to produce multistage particles that can deliver a sustained dose of siRNA to the bloodstream. As Ferrari elaborates "the specific multistage system we have used features nanoporous silicon as the first stage (the 'mothership'), and neutral charge liposomes for the second stage. The latter contain and deliver the siRNA to the cancer cells."

In ovarian cancer mouse models, treatment with this system containing siRNA targeted against the oncogene *EphA2* resulted in targeted gene silencing for at least 3 weeks with no toxic effects observed. In addition, this single administration substantially reduced tumor burden, angiogenesis and cell proliferation.

According to Ferrari the analysis of this study demonstrates that "the multistage vectors create vascular depots in various parts of the body, and from there release therapeutic siRNA over time. This is the very first vascular depot system for siRNA, or any other drug, anywhere, anytime."

A central focus of the team going forward will be double targeting with a first stage targeted to the cancer vasculature and second stage to the cancer cells.

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Original article Tanaka, T. *et al*. Sustained small interfering RNA delivery by mesoporous silicon particles. *Cancer Res.* **70**, 3687–3696 (2010)