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New aptamer-based approaches for the targeting of cancer associated fibroblast in NSCLC

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The aim of the research. Non-small cell lung cancer (NSCLC) represents about 80 % of all lung cancer cases and is often associated with drug resistance, relapses and a poor prognosis. Therefore, the identification of effective therapeutic strategies represents a crucial challenge in oncology. A key limit of conventional anticancer treatments is that they do not target the permissive tumor microenvironment, of which key components are cancer-associated fibroblasts (CAFs). It has been shown that CAFs are able to regulate malignant progression and drug resistance. However, a detailed characterization of CAF profile and the targeting of their pro-tumor effects still remain an ambitious challenge and have a primary importance for the identification of new effective therapies.

Material and methods. We aimed to develop innovative strategies based on nucleic acid aptamers to address these fundamental issues. Firstly, we applied an aptamer conjugate (named Gint4.T-STAT3), containing a STAT3 siRNA linked to an aptamer binding and inhibiting the PDGFR β , to specifically silence STAT3 reported as a fundamental player in the cross-talk between CAFs and epithelial NSCLC cells.

Results. We demonstrated that this molecule effectively delivers STAT3 siRNA in NSCLC cells, blocking CAF-induced cell growth and migration in both continuous and primary NSCLC cultures. In addition, in order to address CAF specific targeting and profiling, we developed an innovative differential cell-SELEX approach by using primary NSCLC CAFs as selection target. Such a strategy allowed the isolation of different aptamers discriminating NSCLC CAFs from normal lung fibroblasts. The analyses of aptamer specificity and functionality is currently ongoing.

Conclusion. Our data represent the first ever attempt in CAF targeting using aptamer-based drugs, and can open innovative horizons in the current therapeutic approaches for NSCLC.

Key words: aptamers, cancer cell, fibroblast, non-small cell lung cancer.

Conflict of interest. The authors declare the absence of obvious and potential conflicts of interest associated with the publication of this article.

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