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Targeting of Cancer associated fibroblast in NSCLC by new aptamer-based approaches

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References:


Background: The identification of effective therapies represents a crucial challenge in non-small-cell lung cancer (NSCLC) often associated with resistance to conventional therapies, relapses and poor prognosis. Recent studies indicate that cancer associated fibroblasts (CAFs) participate in tumor progression by establishing a favorable microenvironment thus representing a key therapeutic target.

Methods and Results: We addressed CAF targeting by using nucleic acid aptamers. To this end, we applied cell-SELEX using primary NSCLC CAFs as target to identify CAF-specific aptamers. We isolated different molecules efficiently discriminating NSCLC CAFs from normal lung fibroblasts. The analyses of aptamer specificity and functionality is currently ongoing. In addition, we characterized the functional effects of an aptamer conjugate able to specifically silence STAT3 that has been reported as a fundamental player in the CAF-NSCLC cell cross-talk. We demonstrated that this molecule effectively delivers STAT3 siRNA in NSCLC cells, blocking CAF-induced growth and migration in both continuous and primary NSCLC cultures.

Conclusions and Significance: We provide evidence of new molecules able to specifically recognize CAFs and/or inhibit with their pro-tumorigenic functions. 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.


**Thematic area:** Nucleic acid-based therapeutics

**Infrastructures:** Not applicable