Characterization of an RNA aptamer hampering CAF-cancer cells interplay in NSCLC

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Background: Despite significant advances in early diagnosis and the introduction of highly effective targeted therapies, Non-Small Cell Lung Cancer (NSCLC) still represents the most lethal cancer worldwide, driven by frequent recurrence and the emergence of therapeutic resistance. Multiple reports have highlighted the crucial contribution of the tumor microenvironment (TME) in supporting NSCLC progression and impacting treatment efficacy. Among the different TME components, cancer-associated fibroblasts (CAFs) are the predominant stromal population and have been shown to actively promote tumor growth, epithelial-to-mesenchymal transition (EMT), metastasis, and resistance to anticancer therapies. Method: Thus, targeting CAFs represents a promising strategy to improve NSCLC treatment outcomes. Here, we describe Apt1sh, an aptamer selected through a modified cell-internalizing Systematic Evolution of Ligands by EXponential enrichment (SELEX) approach, capable of specifically binding and internalizing into NSCLC-CAFs. Results: When treated with Apt1sh, CAFs showed to have a decreased migratory ability, and in co-culture models of CAFs and NSCLC cell lines, Apt1sh disrupted the tumor-promoting interaction between stromal and cancer cells, leading to decreased NSCLC cell viability and migration. Furthermore, Apt1sh's ability to internalize within target cells makes it suitable as CAF-specific carrier of secondary therapeutics. Conclusion: Overall, our findings identify Apt1sh as a promising tool for the selective targeting of CAFs within the NSCLC microenvironment. By interfering with CAF-mediated tumor support, Apt1sh may represent a novel therapeutic strategy to restrain NSCLC progression and enhance the efficacy of current anticancer treatments.