Sputum-Based mRNA-Targeting Probes in Lung Cancer: A Noninvasive Early Diagnostic Tool

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Lung cancer, the leading cause of cancer death, has no simple, non-invasive early detection tests. This project aims to create a multiplex sputum-based RNA probe through the targeting of the mRNAs for tumor marker genes. These genes are significantly overexpressed in the disease and present in sputum. First, the mRNA sequences of EGFR, KRAS, and ALK genes were recorded from UCSC Genome Browser. RNA secondary structures for the sequences were identified. Six fully/mostly open regions (with no base pairing) of 21 nucleotides in length were located per gene, and complementary sequences (to act as probes) were generated. Then, each probe was tested using the RNAhybrid tool in Linux against the targeted mRNA sequence and reconfirmed with the DuplexFold Web Server. The three probes for each gene with the most negative minimum free energy (MFE) values, meaning the highest hybridization efficacy with the target gene, were chosen. All probes were then tested in RNAhybrid against 3 lung-specific genes, AGER, CLDN18, and SFTPC (controls). The chosen probes interact far more strongly with their targets than with control genes, with average percent changes in MFE from control genes to the target genes being 92.1%, 77.9%, and 69.5% for KRAS, EGFR, and ALK probes respectively. Probes were additionally tested to rule out dimerization, and 1 ALK probe was removed due to higher probability of self-hybridization. Future experimentation would include clinically testing the probes on sputum samples from patients with and without cancer and eventual creation of an off-the-shelf test.

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