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Short activating RNA (saRNA) targeting C/EBPA significantly inhibits cell proliferation of undifferentiated cancer cells

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In general, 'poorly' differentiated tumors have a worse prognosis when compared to more 'well' differentiated ones. Therefore, the use of a biological agent that could promote differentiation might have a therapeutic advantage. CCAAT enhancer binding protein alpha (C/EBPα) is a transcription factor known to be involved in the regulation of cell differentiation in a number of tissue types and has reported to inhibit the development of hepatocellular carcinoma. Here we report the effect of stimulation of C/EBPα expression by a specific small activating RNA (saRNA) on a panel of cell lines representing both well-differentiated and poorly-differentiated cancer cell types. The C/EBPα-saRNA inhibited proliferation of poorly differentiated small cell lung cancer and pancreatic cancer cell lines compared to treatment with scrambled double-stranded RNA controls. However C/EBPα-saRNA was not as effective in suppressing proliferation in well-differentiated insulinoma and breast cancer (MCF7) cell lines. Comparison of endogenous levels of C/EBPα, using qPCR and Western blots, showed that undifferentiated tumor cell lines expressed lower levels of C/EBPα when compared to the well-differentiated tumor types. Our results suggest that saRNA mediated stimulation of C/EBPα, could be of potential therapeutic value, especially in poorly differentiated cancers. Furthermore, intracellular expression levels of C/EBPα could be an important prognostic factor for predicting the therapeutic response in poor or un-differentiated tumors.

Biography

Nagy Habib, Professor of Hepatobiliary Surgery at Imperial College London is a Translational Researcher who pioneered the first clinical trial in the use of adenovirus and plasmid for the treatment of liver cancer, and the use of plasmid gene therapy in the hydrodynamic gene delivery. He was also the first to publish from the West a clinical trial on the use of adult bone marrow-derived stem cells for the treatment of patients with liver insufficiency. He has published on the evolution of molecular biology of tumors (oncogene, tumor suppressor gene, and epigenetic modification), gene therapy, stem cell therapy, saRNA and RNAaptamers.

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