Seminars in Biotechnology BTEC 592 & BTEC 692

"Synthesis, characterization and anti-carcinogenic effects of X-aptamers against Growth Hormone Releasing Hormone (GHRH)"

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13:30

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Ajda Çoker Gürkan has been working as a faculty member at Istanbul Kültür University, Department of Molecular Biology and Genetics since 2010. Lecturing undergraduate courses such as molecular biology techniques, human genetics, transgenic animal models, Preimplantation genetic diagnosis, Dr. Çoker-Gürkan completed her undergraduate education at Marmara University. She completed his master's study on single nucleotide changes in cytokine genes associated with autoimmune diseases in 2005, and her doctoral dissertation on Growth Hormone (GH) gene cloning and in vitro demonstration of biological functions of GH gene mutations in Marmara University Biology Program in 2009. Caenorhanditis elegans continues her in vivo studies on neurodegenerative disease in animal models by elucidating the molecular action mechanisms of candidates of various drugs in colon, breast and pancreatic cancer cells through intracellular signaling pathways, investigating the molecular mechanism of new drug targets. She has been working on the synthesis and characterization of aptamer-based drugs and modeling their anti-carcinogenic effects. She is the co-founder of a startup firm called DAPGenomics. Prof. Dr. Ajda Çoker Gürkan has 52 articles within the scope of international SCI, 103 international papers, four of which are oral, one of which is invited speaker, and 4 international book chapters. She actively participated in the International Polyamine Congress (2012) and many national symposium organizations held in Istanbul. Prof. Dr. Ajda Çoker Gürkan has 2 TUBİTAK 1001, 3 TUBİTAK 1002 project executives, 1 TUBİTAK 1001, 1 COST-AB project research manager and TUBİTAK-1512 co-director.

Abstract

Cancer is a complex disease in which cells undergo malignant transformation *via* various genomic and proteomic alterations, leading to uncontrollable cellular growth and proliferation [1]. Cancer cells are known to produce growth factors that induce their proliferation, and thus cell division is continually stimulated in these cells [2]. Growth Hormone Releasing Hormone (GHRH) is a hypothalamic neuropeptide that stimulates the pituitary gland for the production and secretion of Growth Hormone (GH) [3]. Instead of the neuroendocrine function, the peripheral expression of GHRH and its receptor was evident in various surgical samples of the prostate, breast, ovarian, and endometrial cancers [4]. The expression and secretion of GHRH in non-pituitary cell types imply the effect of GHRH on the regulation of cell proliferation, differentiation, and carcinogenesis [5]. GHRH peptide antagonist triggered apoptotic cell death via inhibiting GHRH signaling in prostate, endometrial, colon, lung cancer *in vitro*, and *in vivo* [6], [7]. Aptamers are single-strand nucleic acid molecules (DNA or RNA) that can bind to target molecules such as proteins, peptides, carbohydrates, bacteria, viruses, and also cancer cells for detection and diagnosis [7]. VEGF aptamer (Macugen) is used for the treatment of macular degeneration [8]. Recently, new generation aptamer synthesis has been performed by using a magnetic bead-dependent modified ssDNA library for target binding and amplification of candidate sequences termed as X-aptamer technology [9]. Our aim is to synthesize, select X-aptamers against GHRH NH2 (1-44) and NH2 (1-29) peptides, and also illustrate the binding affinity of selected putative X-aptamers against its target molecule with regarding their anti-carcinogenic effect on colon and pancreatic cancer cell lines. Aptamers against GHRH NH2 1-44 and NH2 1-29 peptide were synthesized and binding affinity (Kd) of 24 putative X-aptamers was determined by the dot-blot method, co-immunofluoresences staining and, SPR analysis. Serum stability of 4 X-aptamers were 90-120 h, respectively. The dose-dependent binding of 3 of 24 putative X-aptamers on GHRHR in MIA PaCa-2 was approved by co-IF assay results. Moreover, SPR analysis indicated the Kd (47.5, 12.1 and 40 nM) levels of 3 putative X-aptamers, respectively. Our results illustrates the synthesis of 24 putative X-aptamers against GHRH peptide and 3 X-aptamers has apoptotic effect on MIAPaca-2 pancreatic and HT29 colon cancer cell lines.

References:

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