Inhibition of transcription of the human EGFR gene in glioma by site-specific oligonucleotides designed to form DNA triple helices

1994 Fiscal Year Final Research Report Summary

INHIBITION OF TRANSCRIPTION OF THE HUMAN EGFR GENE IN GLIOMA BY SITE-SPECIFIC OLIGONUCLEOTIDES DESIGNED TO FORM DNA TRIPLE HELICES

Research Project

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05454395

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Research Institution

Kanazawa University

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DNA triplex, antigene, EGFR,Sp-1, human glioma, human squamous cell carcinoma, retrovirus vector, gene therapy / アンチジーン / 上皮成長因子受容体 / 癌遺伝子 / グリオーマ / 扁平上皮癌 / レトロウイルスベクター / 遺伝子療法

Research Abstract

Mixed purine-pyrimidine anti-gene oligodeoxynucleotides were designed to form collinear DNA triplexes with pyrimidine-rich elements in the human epidermal growth factor receptor (EGFR) gene promoter as gene code blocker. Their effects as suppressors of the EGFR gene transcription were evaluated using human squamous cell carcinoma (A431) and human glioma (U251MG and U87MG) cell lines. Gel shift analyzes indicated that the oligonucleotide forms a collinear triplex within the Sp-1 binding site. An in vitro assay revealed a correlation between the triplex formation and the suppression of EGFR transcription. We postulate that guanine residues are not always optimum in apposition to G-C pairs to form triple helices in the target. We found that oligonucleotides designed to form a triple helix with enhancer elements of the EGFR gene promoter can suppress mRNA formation and also the proliferation of a human glioma cell line. Anti-gene binding to a DNA duplex may serve as a basis for an alternative program of gene control in vitro. We are trying to develope retrovirus vectors which allow expression of anti-genes. We also consider the feasibility of an anti-gene strategy as adjuvant therapy of glioma.

Research Products (12 results)

All Other

All Publications (12 results)

[Publications] Okada T: "Triplex-forming oligonucleotide binding represses transcription of the human c-erbB gene in glioma" Growth Factors. 11. 259-270 (1994)

[Publications] 山下純宏: "三重鎖DNA形成を利用した遺伝子治療" nanoGIGA. 3. 1618-1622 (1994)

[Publications] 山下純宏: "PDGF受容体アンチセンスオリゴマーによるヒトグリオーマ細胞株に対する増殖抑制効果" The Sagawa Foundation for Promotion of Cancer Research. 4. 115-120 (1994)

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[Publications] 山下純宏: "今日の神経疾患治療指針、亀山正邦、高倉公明(総編集)" 神経膠芽腫, 262 (1994)

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