

# オリゴヌクレオチドを用いた悪性グリオーマに対する遺伝子療法

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# 1994 Fiscal Year Final Research Report Summary

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

Research Project

### Project/Area Number

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05454395

### Research Category

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Grant-in-Aid for General Scientific Research (B)

### Allocation Type

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Single-year Grants

### Research Field

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Cerebral neurosurgery

### Research Institution

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Kanazawa University

### Principal Investigator

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### Project Period (FY)

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1993 - 1994

### Keywords

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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

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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 develop 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) ▼
- [Publications] 山下純宏: "脳腫瘍に対する遺伝子治療法における三重鎖DNA形成の効果" 日本脳神経財団、1992年度研究報告. 1-7 (1994) ▼
- [Publications] 新多 寿: "Annual Review神経1994" 悪性神経膠腫の放射線治療, 159-169 (1994) ▼
- [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) ▼
- [Publications] Takashi Okada et.al.: "Triplex-Forming Oligonucleotide Binding Represses Transcription of the Human c-erbB Gene in Glioma" Growth Factors. 11 (4). 259-270 (1994) ▼
- [Publications] Junkoh Yamashita et.al.: "Antigene Strategy by Triplex-Forming Oligonucleotides" nanoGIGA. 24 ; (Japanese). 1618-1622 (1994) ▼
- [Publications] Junkoh Yamashita et.al.: "Growth Inhibition of Human Glioma Cells by PDGF Receptor Antisense Oligomers" The Sagawa Foundation for Promotion of Cancer Research. 4 ; (Japanese). 115-120 (1994) ▼
- [Publications] Junkoh Yamashita et.al.: "Antigene Strategy for Brain Tumors" Japan Brain Foundation Report. (1992) (Japanese). 1-7 (1994) ▼
- [Publications] Hisashi Nitta et.al.: Radiation Therapy in Malignant Glioma. Annual Review (Shinkei) (Japanese), 159-169 (1994) ▼
- [Publications] Junkoh Yamashita et.al.: Glioblastoma. TODAY'S THERAPY IN NEUROLOGY AND NEUROSURGERY IGAKU-SHOIN (Japanese), 262 (1994) ▼

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