Immunological, Biochemical and Therapeutical Research in Acetylcholine Receptor and Myasthenia Gravis

1990 Fiscal Year Final Research Report Summary

Immunological, Biochemical and Therapeutical Research in Acetylcholine Receptor and Myasthenia Gravis

Research Project

Project/Area Number

63480215

Research Category

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

Allocation Type

Single-year Grants

Research Field

Neurology

Research Institution

Kanazawa University

Principal Investigator

TAKAMORI Masaharu Kanazawa University Hospital ; Department of Neurology ; Professor, 医学部・附属病院・神経内科, 教授 (60039815)

Co-Investigator(Kenkyū-buntansha)

OKUMURA Seiichi Kanazawa University Hospital ; Department of Neurology ; Instructor, 医学部・附属病院・神経内科, 助手 (60152435)
IDE Yoshihiko Kanazawa University Hospital ; Department of Neurology ; Assistant Professor, 医学部・附属病院・神経内科, 講師 (10100835)
MATSUBARA Shiro Kanazawa University Hospital ; Department of Neurology ; Assistant Professor, 医学部・附属病院・神経内科, 講師 (00143884)

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Keywords

Myasthenia Gravis / Acetylcholine Receptor / Synthetic Peptides / Receptor Molecular Structure / Immune Cells / Antibody / Animal Model

Research Abstract

Upon the availability of amino acid sequences and transmembrane topography of acetylcholine receptor (AChR) alpha-subunit, the research attempted to localize myasthenic domains on AChR, such as the sites recognized by the "blocking antibody" which prevents the binding of ACh with AChR and by the "binding antibody" which accelerates the degradation of AChR, by use of peptides synthesized referring to AChR molecular structure, resulting in the following : (1) The synthetic peptide, alpha183-200, was immunogenic in the induction of myasthenia in animals and antigenic in the detection of antibody in human myasthenic patients. (2) Myasthenic patients treated with plasmaperfusion by use of the synthetic peptide (alpha183-200)-bound adsorbent showed

clinical improvement in association with the reduction of corresponding anti-peptide antibody and anti-native AChR blocking antibody in sera.
(3) Synthetic peptides, alpha67-76, alpha70-90 and alpha125-147, were stimulatory to the induction of myasthenia in animals, and were useful to detect myasthenic antibody in humman myasthenic sera. (4) Nineteen segments in the molecular structure of ACha alpha-subunit were found to be T-cell epitopes, but they were not potent to stimulate B-cells. (5) Artificially formed peptides were synthesized by coupling natural AchR peptides and theoretical amino acid sequences based on the concept that the induction of myasthenia gravis depends on linked recognition of the B-cell epitope expected at beta-turn structure and the T-cell epitope expected at amphipathic alpha-helical structure.
These conformationally modified AChR peptides were more immunogenic and antigenic than AChR peptides of natural sequences, and provided a provision for the antigenspecific therapy in myasthenia qravis.

Research Products (56 results)

All Other

All Publications (56 results)

[Publications] 高守 正治: "Myasthenogenic significance of synthetic α−subunit peptide 183−200 of Torpedo californica and human acetylchine receptor." J.Neurological Sciences. 85. 121-129 (1988)

[Publications] 高守 正治: "重症筋無力症ー蔵器特異的自己免疫病の発症機序に関する新知見" 臨床免疫. 20. 1116-1129 (1988)

[Publications] 高守 正治: "アセチルコリンレセプタ-" 代謝. 25. 341-346 (1988)

[Publications] 高守 正治: "アセチルコリン受容体と重症筋無力症" Medical Immurology. 16. 71-77 (1988)

[Publications] 高守 正治: "Experimntal autoimmune myasthenia gravis" Medical Immurology. 16. 113-121 (1988)

[Publications] 高守 正治: "抗アセチルコリン受容体抗体" 内科. 61. 1276 (1988)

[Publications] 高守 正治: "レセプタ-の構造と抗レセプタ-抗体の発現ー抗アセチルコリンレセプタ-抗体" 日本臨床. 46. 816-821 (1988)

[Publications] 高守 正治: "抗レセプタ-抗体による疾患とその治療" 治療学. 20. 353-358 (1988)

[Publications] 高守 正治: "重症筋無力症・Eaton−Lambert 症候群" 臨床医. 14. 66-69 (1988)

[Publications] 高守 正治: "自己免疫学的立場からみた内科疾患の病態と治療 ー重症筋無力症" 臨床成人病. 18. 1799-1805 (1988)

[Publications] 高守 正治: "筋無力症の薬物治療" Medicina. 24. 1876-1877 (1988)

[Publications] 高守 正治: "重症筋無力症,Lambert−Eaton 症候群" Medicina. 25. 2268-2271 (1988)

[Publications] 高守 正治: "主要疾患の最新の治療法 ー 重症筋無力症" Medical Practice. 14. 2069-2073 (1988)

[Publications] 高守 正治: "重症筋無力症の症状.病型.診断" ブレインナ-シング. 4. 1156-1165 (1988)

[Publications] 高守 正治: "重症筋無力症・Eaton−Lambert症候群" 臨床医. 14. 66-69 (1988)

[Publications] 高守 正治: "Conformational modification enhances myasthenogenicity in synthetic peptide of acetylcholine receptor α−subunit" J.Neurological Sciences. 99. 219-227 (1990)

[Publications] 高守 正治: "Effecto of calcitonin gene−related peptide on skeletal muscle via specific binding site and G protein" J.Neurological Sciences. 90. 99-109 (1989)

[Publications] 高守 正治: "重症筋無力症 ー 疾患催起抗原と免疫反応B細胞エピト-プを中心として" 最新医学. 44. 1689-1696 (1989)

[Publications] 奥村 誠一: "アセチルコリン受容体合成ペプチドの病的抗原性解析" 神経研究の進歩. 33. 999-1006 (1989)

[Publications] 奥村 誠一: "重症筋無力症の抗原特異的免疫吸着法 II.アセチルコリン受容体合成ペプチドの病的免疫原性検定とその臨床応用" 人工蔵器. 18. 19-23 (1989)

[Publications] 谷原 正夫: "重症筋無力症の抗原特異的免疫吸着法 I.アセチルコリン受容体部分合成ペプチドを固定化した吸着剤の作成" 人工蔵器. 18. 15-18 (1989)

[Publications] 吉川 弘明: "骨格筋におけるカルシトニン遺伝子関連ペプチドの生理,生化学的作用に関する研究" 金沢大学十全医学会雑誌. 98. 19-34 (1989)

[Publications] 高守 正治: "発症の免疫学的機序に関する最近の考え方 ー 重症筋無力症" 臨床医. 15. 1678-1681 (1989)

[Publications] 高守 正治: "免疫血清検査" 臨床検査. 33. 659-666 (1989)

[Publications] 高守 正治: "重症筋無力症 解明された分子レベルでのトピックス" Mebio. 6(7). 97-103 (1989)

[Publications] 高守 正治: "重症筋無力症Blocking抗体・Modulating 抗体産生による筋無力症の発生" Mebio. 6(10). 68-77 (1989)

[Publications] 高守 正治: "レセプタ-と疾患 ー 重症筋無力症" Clin.Neurosci.8. 57-59 (1990)

[Publications] 高守 正治: "抗レセプタ-抗体と疾患 ー 重症筋無力症" 免疫薬理. 8. 10-18 (1990)

[Publications] 高守 正治: "重症筋無力症治療の進歩 ー 重症筋無力症におけるわが国の現況" 神経内科. 32. 1-6 (1990)

[Publications] 高守 正治: "重症筋無力症" Clin.Neurosci. 8. 916-917 (1990)

[Publications] 高守 正治: "先天性筋無力症候群" 日本臨牀. 48. 1483-1488 (1990)

[Publications] 高守 正治: "重症筋無力症の新しい治療の展望 ー 受容体合成ペプチド固定化吸着剤を用いて" 神経内科治療. 7. 503-508 (1990)

[Publications] 高守 正治: "悪性腫瘍に伴う非転移性小脳方性症患者の腫瘍組織にみられるPurkinje 細胞抗原の特異的表現" 内科. 67. 126-127 (1991)

[Publications] 高守 正治: "A synthetic peptide,Torpedo californica α183ー200,of the acetylcholine receptor as a toal for immunoadsorption via plasmaperfusion in myasthenia gravis" Artif.Organs Tody. (1991)

[Publications] 高守 正治: "重症筋無力症" 臨牀と研究. (1991)

[Publications] 高守 正治: "重症筋無力症におけるアセチルコリン受容体合成ペプチドを吸着剤とした免疫吸着療法の検討" 集中治療. (1991)

[Publications] 井手 芳彦: "神経疾患の最近の経過と予後 ー 重症筋無力症" 神経内科治療. (1991)

[Publications] 坂戸 俊一: "代謝性ミオパチ-" Clin銃Neurosci.(1991)

[Publications] 松原 四郎: "多発性筋炎" 内科. (1991)

[Publications] 高守 正治: "Synthetic Peptides of Acetylcholine Receptor as myasthenogenic Antigens In:Neuroimmunological Diseases:Recent Advances in Pathogensis and Treatment" University of Tokyo Press, 235-240 (1988)

[Publications] 高守 正治 (分担執筆): "筋無力症候群 In:神経疾患の診かた ー 難しい症例をめぐる診断課程の着眼点" 医学書院, 235-246 (1988)

[Publications] 高守 正治 (分担執筆): "重症筋無力症 In:Practical Handbooks ー 神経疾患薬物療法" 南江堂, 144-147 (1988)

[Publications] 高守 正治(分担執筆): "重症筋無力症 In:診断治療マニュアル" 金原出版, 770-772 (1988)

[Publications] 高守 正治(分担執筆): "重症筋無力症 In:今日の診断指針 第2版" 医学書院, 547-550 (1988)

[Publications] 高守 正治: "アセチルコリン受容体と疾患 In:薬物活性シンポジウム講演集" 日本薬学会・日本薬理学会, 43-54 (1988)

[Publications] 高守 正治: "神経筋疾患 In:副腎皮質ステロイド剤の適応と使い方のこつ" 医薬ジャ-ナル, 115-128 (1990)

[Publications] 高守 正治: "重症筋無力症 In:今日の治療指針 1990" 医学書院, 228-230 (1990)

[Publications] 奥村 誠一: "生物学的免疫吸着剤によるMGの治療 In:体外免疫調節" 日本メディカルセンタ-, 180-188 (1990)

[Publications] 高守 正治: "吸着による血液浄化 ー 免疫吸着 ー 抗アセチルコリン受容体除去 In:シリ-ズ最新医工学治療 ー 吸着療法マニュアル" 金原出版, (1991)

[Publications] 高守 正治: "重症筋無力症 In:レセプタ- ー 基礎と臨床" 朝倉書店, (1991)

[Publications] 高守 正治: "重症筋無力症 ー 病因.病態.病理 In:新筋肉病学" 南江堂, (1992)

[Publications] Takamori, M., Okumura, S., Nagata, M. and Komai, K. :"Synthetic peptides of acetylcholine receptor as myasthenogenic antigens." Neuroimmunological Diseases. Recent Advances in Pathogenesis and Treatment (ed. by Igata, A.), University of Tokyo Press, Tokyo,. 235-240. (1988)

[Publications] Takamori, M., Okumura, S., Nagata, M. and Yoshikawa, H. :"Myasthenogenic significance of synthetic alpha-subunit peptide 183-200 of Torpedo californica and human acetylcholine receptor." Journal of the Neurological Sciences,. 85. 121-129, (1988)

[Publications] Takamori, M. and Yoshikawa. H. :"Effect of calcitonin gene-related peptide on skeletal muscle via specific binding site and G protein." Journal of the Neurological Sciences,. 90. 99-109 (1989)

[Publications] Takamori, M., Okumura, S., Komai, K. and Satake, R.: "Conformational modification enhances myasthenogenicity in synthetic peptide of acetylcholine receptor alpha-subunit." Journal of the Neurological Sciences,. 99. 219-227, (1990)

[Publications] Takamori, M., Okumura, S. and Ide, Y. :"A Synthetic peptide, Torpedo californica alpha183-200, of the acetylcholine receptor as a tool for immunoadsorption via plasma perfusion in myasthenia gravis." Artificial Organs Today,. (1991)