神経研究所

National Institute of Neuroscience
National Center of Neurology and Psychiatry

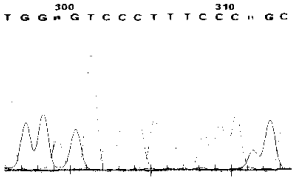
神経研究所の概要

National Institute of Neuroscience: An overview

国立武蔵療養所神経センターは、精神障害、神経障害・筋障害・発達障害などの病態や病因の解明及びそれらの治療法の開発を目指して設立された。昭和61年10月1日に、国立精神・神経センターの設立に際して「神経研究所」と改称され現在に至っている。当研究所には遺伝子工学、免疫学、形態学、生化学、発生学などを武器とした7つの基礎研究部門、神経・筋疾患、精神疾患、発達障害などを対象とした7つの臨床研究部門及び実験動物とアイソトープに対する研究管理部門がある。

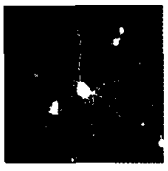
National Institute of Neuroscience (NIN) has its origin in 1978 when Neurological Research Center was established with the aim of elucidating the pathogenesis and etiology of psychiatric disorder, neurological disorder, and muscular diseases and for developing therapeutic means for these disorders. It was renamed as NIN on the October 1st, 1986, when National Center for Neurology and Psychiatry (NCNP) was established. In NIN, there are seven departments for basic neuroscience research and seven departments for clinically oriented research as well as administration sections for experimental animal research and for experiments assisted with radioisotope. In the basic research departments, scientists are actively undertaking research by applying the methodology of molecular biology, immunology, morphology, biochemistry and developmental biology. Clinically oriented departments are engaged in the research related to neurological diseases, muscular diseases, psychiatric diseases and developmental disorder.

遺伝子解析Genetic analysis
(The Institute is a leader in genetic research and analysis in Japan.)



動物実験 Anima1 experiments

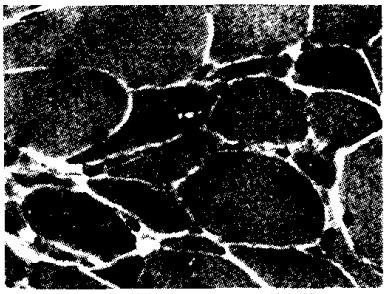
培養神経細胞 Culture of neurons



疾病研究第一部
Department of Neuromuscular Research

遺伝性筋疾患を初めとする各種神経・筋疾患の病因・病態の解明と、一日も早い治療法の開発を目指した研究を行っている。これらの疾患は、根本的治療法がないばかりか、依然として病態不明のものが大多数であり、臨床医学、病理学、分子生物学、細胞生物学という様々な角度からのアプローチを駆使して、病因・病態の解明から、一日も早い治療法の開発を目指して研究を進めている。また、武蔵病院DNA診断・治療室との協力の下、神経・筋疾患の診断サービスを提供している。

The Department of Neuromuscular Research undertakes research aimed at elucidating the causes and clinical conditions of various neuromuscular diseases, including hereditary muscular diseases, in order to develop effective treatments and cures for these conditions as early as possible. There are still numerous diseases for which there are no basic cure or the clinical conditions are still unclear. The department is moving ahead with research aimed at elucidating the causes and clinical conditions of disease in order to find and develop suitable cures as quickly as possible. A wide variety of approaches is brought to bear in these efforts including clinical medicine, pathology, molecular biology, and cellular biology. The department also provides diagnostic services for neuromuscular diseases in cooperation with the DNA Diagnostic Testing and Treatment Section of Musashi Hospital.



縁取り空胞を伴う遠位型ミオパチーの筋組織
Muscle pathology of distal myopathy with rimmed vacuoles

疾病研究第二部
Department of Mental Retardation and Birth Defect Research

知的障害、脳性麻痺その他の脳の器質的または機能的異常に起因する発達障害の研究を、主として神経学的及び生物学的実験方法を用いて行っている。胎児環境や周産期における外因（薬物、胎児環境、分娩時低酸素など）と各種の脳形成障害や代謝性脳障害などを起こす内因（遺伝子異常、染色体異常など）を取り扱い、その病態を主に生化学的、病理学的に研究し、新たな治療法や予防法の開発を目指している。

The Department pursues research on developmental disorders such as mental retardation and cerebral palsy, which are derived from the organic and functional abnormalities of the developing brain mainly by the methods of neurological and biological experimental procedures. We investigate extrinsic factors (drugs, fetal environment, perinatal hypoxia and so on) and intrinsic factors (gene mutation, chromosome abnormality and so on), which result in brain malformation and metabolic brain disorders. Our aim is to understand the pathogeneses biochemically and pathologically, and ultimately to develop a new therapeutic and/or preventive measure for the diseases.

疾病研究第三部
Department of Mental Disorder Research

原因が充分解明されていない二大精神疾患である、統合失調症と躁うつ病について、新しい診断および治療法の開発を目指して生物学的研究を行っている。また、武蔵病院などと連携して、遺伝子研究や生物学的診断法の開発を行っている。さらに遺伝子異常や心理的ストレスが脳や神経細胞に及ぼす影響について動物や培養細胞を用いた実験を行っている。

Schizophrenia and manic-depressive illness are two major forms of functional psychoses. The Department of Mental Disorder Research performs biological research in order to elucidate the pathogenesis of these illnesses and pursues the development of new diagnostic measurements and treatments. The Department engages in molecular genetics and clinical studies developing biological markers in collaboration with National Center Hospital for Mental, Nervous and Muscular Disorders and other facilities. Experiments on animals and cultured neurons are ongoing to examine effects of genetic abnormalities and psychological stress on behavior and neuronal function.

疾病研究第四部
Department of Degenerative Neurological Diseases

パーキンソン病、脊髄小脳変性症、筋萎縮性側索硬化症など神経変性疾患の発症にまつわる現象を分子レベルで解明し、根本的な治療法を開発することを目指している。1999年に神経変性モデルマウス（gadマウス）の原因遺伝子を解明し、神経変性疾患におけるユビキチンシステムの重要性を世界に先駆けて示すとともに今日の「神経変性におけるユビキチン研究」の隆盛を築いた。神経変性疾患では原因遺伝子産物の除去、神経機能不全の修復、変性ニューロンの再生が根本治療の扉を開くことは疑いの余地がなく、目標達成のため一丸となって研究を展開している。

The aim of the department is to elucidate the molecular pathogenesis of various neurodegenerative diseases including Parkinson's disease, spinocerebellar ataxia and amyotrophic lateral sclerosis. In 1999, the department demonstrated that the gracile axonal dystrophy (gad) mouse is the first mammalian model of neurodegeneration with a defect in the ubiquitin system. The gad mouse lacks the expression of ubiquitin C-terminal hydrolase L1 that is a member of the deubiquitinating enzyme family. The finding has led many researchers to focus on the direct link between the ubiquitin system and neurodegeneration. The department also aims to develop essential therapies for the diseases. To cure the diseases, the elimination of the causal gene products, repair of neuronal dysfunction, and the regeneration of degenerated neuron are very important subjects to be addressed. The department is expanding its research activities and making every effort to achieve the subjects.

疾病研究第五部
Department of Inherited Metabolic Disease

先天代謝異常症の病態解明と治療法の開発研究を目的として、研究を行っている。筋糖原病、HHH症候群、Alexander病などの症例における遺伝子解析と遺伝子治療及びプログラム細胞死、ERストレスによる細胞死、コンフォメーション病におけるカスパーゼカスケード活性化の機構についての研究を行っている。

The department aims at elucidating the pathological mechanisms of and developing new therapies for inherited metabolic diseases. The researches include genetic analyses of inherited diseases, such as muscle glycogenoses, HHH syndrome, van der Knaap disease, and Alexander syndrome, and developing gene therapy, as well as clarifying the mechanisms of programmed cell death, ER stress-mediated cell death, and cell death in conformation diseases.

疾病研究第六部
Department of Demyelinating Disease and Aging

若年性痴呆などの脳器質疾患の病因解明、予防・治療法開発を目指した研究に取り組んでいる。武蔵病院等と連携の下、各種痴呆疾患の遺伝子解析を実施し、新たな遺伝子変異の発見などの新知見を得ている。アルツハイマー病の分子病態解明研究では病原因子βアミロイド蛋白の生成・蓄積機構を培養細胞やモデル動物を用いて解析し、国際的な成果をあげている。

The Department of Demyelinating Disease and Aging is actively involved in research aimed at preventing and treating the causes of organic brain disorders such as juvenile dementia. It carries out genetic analyses of various types of dementia disorders in cooperation with Musashi Hospital and other facilities, and has obtained new findings including the discovery of new gene mutations in familial Alzheimer's disease. In research to elucidate the molecular pathologic conditions of Alzheimer's disease, the department has achieved international recognition for its accomplishments in analyzing the mechanism behind the formation and accumulation of β amyloid proteins using cultured cells and laboratory animals as models.

疾病研究第七部
Department of Cortical Function Disorders

高次脳機能障害を呈する疾患としての「プリオン病」に関する基礎研究と治療法開発研究、及び機能性疾患の病態、治療に関する基礎研究を行うことを目的としている。主な研究内容としては、感染型プリオン蛋白質生成等に関与する新しい分子シャペロン因子に関する研究、正常型プリオン蛋白質の生理機能解明、プリオン病治療法の開発、新しい組織解析法（ナノ分子病理学）の開発、神経伝達物質受容体関連の研究を行っている。その他、社会的活動として、各種のプリオン病感染対策マニュアルの邦訳、並びに「クロイツフェルト・ヤコブ病感染予防ガイドライン」の作成等を行っている。

The Department of Cortical Function Disorders pursues basic research into "prion disease" that presents symptoms of impairment of higher brain function, and therapeutic research into the development of a cure for the condition. The main content of its research activity focuses on an identification of new molecular chaperone factors that are involved in infectious prion protein formation as well as an elucidation of the physiology of normal cellular prion protein. The department also carries out basic research into the disease mechanism and treatment of functional diseases including (epilepsy). Other research activities include efforts to develop a general therapeutic method for various neurological disorders and a novel method of histopathological analysis. As part of its social activities, the department has also prepared various manuals and materials on the measures against various prion disease contagions, and "Guidelines for the Prevention of Infections of Creutzfeldt-Jakob Disease."

診断研究部
Department of Biochemistry and Cellular Biology

タンパク質の働きを通じて、脳の機能を解明する研究に取り組んでいる。発達障害およびそれに起因する精神疾患などの病因解明、診断、治療法の開発を目指して、とくに脳が発達する過程で、遺伝的要因と環境要因がどのように相互作用しているかという点に注目し、この作用が顕著な臨界期に、神経細胞の形と機能、さらに神経回路が形成される機構を解析している。

The department of Biochemistry and Cellular Biology is actively engaged in research to understand the developmental and molecular basis of brain function. The department analyses the developmental process as well as the signal transduction mechanism of neural cells morphology, synaptic function, and neural circuit formation. Particular attention is focused on how genetic and environmental factors interact with each other to yield a neural networks and a behavior, aiming of revealing the causes of developmental and mental disorders. Thus, these research would shed light on the development of early diagnosis and treatment of such diseases.

微細構造研究部
Department of Ultrastructural Research

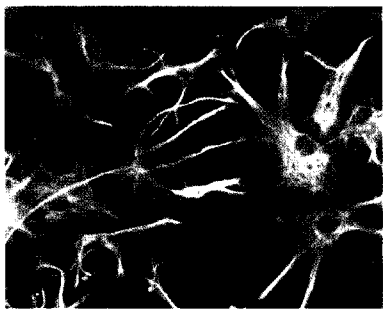
神経系の発生、神経回路形成から高次脳機能発現に至る分子細胞生物学的機構の解明を、電子顕微鏡技術を含めた形態学的手法と発生工学的手法を統合して進めている。ニューロン、アストログリアの発生・分化を制御する因子、特異的神経結合形成にかかわる接着因子の機能形態学的解析を行うとともに、情動に関わる神経構築の発生と機能発現の分子生物学的解析を行い、精神・神経疾患の原因究明、治療法開発の基盤形成を目指している。

The Department of Ultrastructural Research is actively engaged in the studies on the molecular and cell biological mechanisms of the neural development and neural circuit formation which leads to the expression of higher brain function. These studies are in progress based on the integration of the morphological methods including advanced electron-microscopic technique and the developmental engineering technology. The aims of this department are to get fundamental knowledge for the elucidation of pathogenesis and the development of treatment of the neurological and psychiatric disorders through the research such as the functional and morphological analysis of the factors controlling the development and differentiation of neuron and glia, the functional and morphological analysis of the cell adhesion molecules involved in the formation of specific neural connection, and the molecular biological analysis of the development and functional expression of neuronal structures involved in the emotion.

代謝研究部
Department of Neurochemistry

ヒトの神経系は神経細胞とそれを取り巻くグリア細胞、血管細胞などから成りたっている。代謝研究部では、特に神経細胞とグリア細胞の相互作用という観点から、神経細胞の発生分化・成長・生存維持・再生という様々な現象を支えている分子メカニズムについて研究を行っている。これらの基礎的な研究を通じて、様々な神経疾患の病態の解明・治療法の開発に貢献できるように日夜励んでいる。

The work in our department focuses on molecular mechanisms responsible for development of brain, neuronal survival and regeneration, in special reference to the neuron-glia interaction. The final goal of our study is to understand the molecular basis of neuronal diseases.1) One of our major concerns in the brain is microglia. Iba1 is a molecule that we identified as a calcium binding protein specifically expressed in microglia. We found that Iba1 regulates ruffling and phagocytosis by mediating the activation of Rac. Recently, we characterized ATP as an activator for microglia via Gi/o-coupled receptor P2Y12,13. To investigate the molecules responsible for neuronal regeneration, we employ the facial nerve axotomy in rodents. By screening the subtracted cDNA library constructed between facial nuclei of axotomized and control, we identified a number of novel and known genes that may play an important role in the regeneration of neurons.



ラットの初代神経培養の蛍光顕微鏡写真
赤が神経細胞、緑がグリア細胞

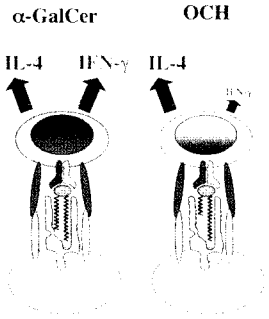
A fluorescent microphotograph of primary rat neurons. Neurons are stained in red, while glial cells are in green.

免疫研究部
Department of Immunology

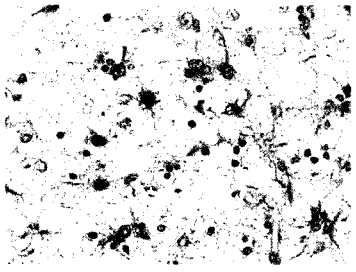
免疫の関係する神経疾患の病態の解明と治療法の開発に関する研究を進めており、特に多発性硬化症（MS）の免疫異常、MSの動物モデルの研究で成果をあげている。近年の成果としては、MSの治療薬として有望な物質（糖脂質OCH）の発見がある（ネーチャー誌に発表）。この物質には、NKT細胞というリンパ球を刺激する活性があり、現在臨床応用を目指した研究を進めている。

The Department of Immunology is engaged in research that seeks to understand and reveal the pathogenesis of immune-mediated neurological diseases and to develop more effective therapies for treating such conditions. An area of particular interest is the immunopathology of multiple sclerosis (MS) and animal models of MS. A notable result of the past year is the discovery of a substance (glycolipid OCH) that shows promise as an effective therapeutic agent for MS (published in the journal, Nature). This substance activates lymphocytes known as NKT cells. Research work is currently proceeding aimed at clinical applications.

OCHの作用機構
The action mechanism of OCH



MSの脳における14-3-3蛋白の発現
Appearance of 14-3-3 protein in the brain of a patient with MS



遺伝子工学研究部
Department of Molecular Genetics

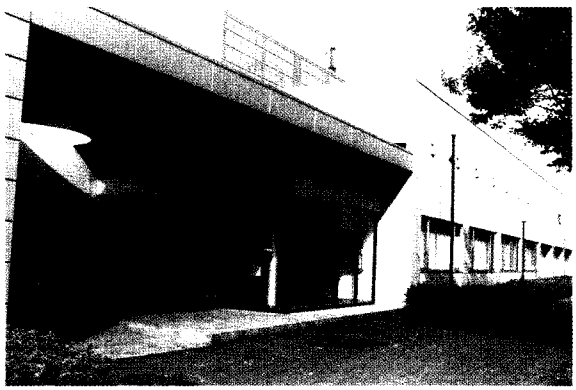
新規ガス性生体内活性物質としての硫化水素を世界にさきがけて提案し、生理活性脂質リソフォスファチジン酸とともに、神経系での役割と神経疾患への関与について研究を行っている。また、アルツハイマー病関連遺伝子の解析や、ヒトA群色素性乾皮症（XPA）とB群コケイン症候群（CSB）に対するモデルマウスを解析し、発症機序解明を目指している。

The Department of Molecular Genetics made the first demonstration that hydrogen sulfide functions as a novel gaseous mediator. The department is further studying the role of this substance, together with bioactive lipid lysophosphatidic acid, in the nervous system and their involvement in neurological disorders. It is also investigating the genes related to Alzheimer's disease and analyzing model mice of human A group xeroderma pigmentosum (XPA) and B group Cockayne syndrome (CSB) to elucidate the underlying mechanisms of these disorders.

遺伝子疾患治療研究部
Department of Molecular Therapy

筋ジストロフィーを始めとする遺伝性神経・筋疾患に対して根治的な治療法を確立するために、平成12年4月設立された。神経・筋難病に対する治療法には、遺伝子治療、幹細胞移植治療、新たな薬物治療があるが、特にアデノ随伴ウイルスベクターを用いた遺伝子導入と筋細胞に分化し得る幹細胞に注目している。新たな治療法を臨床に応用するためには、モデル動物が重要であり、平成13年3月竣工した中型実験動物研究施設で、筋ジストロフィー犬を用いた病態研究と治療研究を行っている。

The Department of Molecular Therapy was founded in April 2000 with the goal of establishing treatments for hereditary neuromuscular diseases, including Duchenne muscular dystrophy (DMD). The department is paying particular attention to potential benefits of gene transfer using micro-dystrophin and adeno-associated virus vectors, new drug treatments and transplantation of stem cells that can differentiate into muscle cells. Experiments using animal models for DMD are important to establish a new treatment. Hence, a new medium-sized laboratory animal research facility was constructed in March 2001, and researchers are currently analyzing molecular pathology of newly generated dystrophy dog model, CXMDJ and trying to develop medical treatment for DMD.



中型実験動物研究施設
Medium-sized laboratory animal research facility

モデル動物開発部
Department of Animal Models for Human Disease

種々の神経・筋疾患の病態及び病因の解明や治療法開発の研究に有用な疾患モデル動物を開発することを課題として、1 人や霊長類を対象とした高次脳機能障害に関する研究、2 自然発症ミュータントの遺伝子解析と治療法開発に関する研究、3 マウスを用いたウィルスの脱髄性脳脊髄炎に関する研究、4 遺伝子操作による疾患モデルマウスの作製と筋ジストロフィーの研究を行っている。

In order to elucidate the causes and pathology of various neuromuscular diseases and to develop disease model animals that are useful in research into the development of cures, the department has been focusing its efforts into research concerning the 1) disorder of higher brain function in human and non-human primates, 2) genetic analysis of spontaneous mutations and the development of therapeutic treatments, 3) demyelinating encephalomyelitis virus used in mice, and 4) development of disease model mice through gene manipulation and research for muscular dystrophy.