



Office of Patents and Licensing Central Nervous System

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A Computational Method for the Prediction of Amyloid Fibril Formation (*Welsh, RWJ 02-92*) CNS

Background

Amyloid fibril formation, or amyloidosis, is observed in human neurodegenerative and neuromuscular diseases such as, Alzheimer's, Parkinson's, and Huntington's Diseases. It has also been associated with Type II (or Late-Onset) diabetes mellitus, and the so-called prion diseases, also known as spongiform encephalopathies. The amyloid fibril formation occurs as a consequence of increase in β strands in amyloidogenic proteins. However, sequence analyses have failed to reveal consensus sequences predictive of the β strand propensity in proteins. Many currently existent secondary structure prediction algorithms, such as the PHD algorithm, that predict native secondary structure based on sequence information, fail to predict consistently the tendency of α -helical or random coil sequences to transform into non-native β strands under physiological conditions. **Thus, there exists an unmet medical need for a method that can consistently and accurately detect hidden β strand propensity in proteins. Such a method would have utility in the identification of therapeutic agents capable of breaking β strands.**

Description of the Technology

UMDNJ researchers have developed a computational method for predicting sequences in proteins with hidden propensities for amyloid fibril formation. The computational method of the present invention has, without exception, correctly identified sequences that have been shown to initiate amyloid fibril formation under both *in vitro* and *in vivo* conditions. This invention has applications for the discovery of agents that specifically target these sequences for the prevention, treatment, and diagnosis of amyloid diseases

Applications

- To design peptides or agents that can be used to break β strands
- To predict tendency of proteins to form amyloid fibrils
- The neural network program can be used for the rapid prediction of β strand propensity for any protein or peptide

Patent Status:

United States provisional patent application filed.

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A Method for Increasing Synaptic Growth or Plasticity (*Black, RWJ 02-79*) CNS

Background

Studies have shown that neurotrophins such as Brain Derived Neurotrophin (BDNF) modulate synaptic strength and affect learning and memory. Transcription and translation of certain genes induced by endogenous BDNF have been shown to be necessary for learning. Previous studies have utilized transcriptional profiling to identify genes associated with learning. However, genes associated with BDNF-induced plasticity and the correlation of their expression with learning has not been studied. The present invention relates to the identification of differentially expressed genes involved in BDNF-induced synaptic activity and plasticity.

Description of the Technology

UMDNJ researchers have utilized whole-cell patch-clamp recordings in conjunction with differential display and single-cell transcriptional analysis to identify genes whose expression is altered during BDNF-induced plasticity. The present invention also provides a method for increasing synaptic growth or plasticity by increasing the expression of genes inducible by BDNF.

Applications

- To increase the synaptic growth or plasticity by modulating the expression of BDNF induced genes.
- To treat diseases associated with damaged or diseased synapses

Patent Status

Application was published on May 21, 2004 (WO 2004/041778 A2)
PCT application filed.

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Methods for Determining Autism Spectrum Disorder (*Millonig, CABM 03-16*) CNS

Background

Despite intense research in Autism field, there is no known cause for autism; however, abnormalities in brain structure or function are generally associated with the disease. Diagnosis is often based on observation of patient's communication, behavior, and developmental levels. Due to the fact that there are no reliable diagnostic tests, there is a critical need for the development of such tests for accurate diagnosis of autism. Since research to date indicates a possible genetic basis for susceptibility to the disease, a genetic marker would be a valuable diagnostic tool to detect individuals at risk. The present invention relates to the identification of genes for use as diagnostic tools for autism and methods for identifying subjects susceptible to autism.

Description of the Technology

The homeobox transcription factor, Engrailed2 (En2), was investigated for possible association with autism spectrum disorder. Linkage/disequilibrium tests in En2 in 137 triads of autistic individuals and their parents indicated that two single nucleotide polymorphisms, Intron A/G and Intron C/T, are critical. The A allele of Intron A/G and the C allele of Intron C/T were transmitted preferentially to autistic individuals, indicating that EN2 locus predisposes individuals to autism. Studies conducted in 29 additional families, confirmed that there is a statistically significant association between susceptibility to autism and the presence of these polymorphisms. Thus, A, C haplotype could be used as a diagnostic marker in the identification and screening of individuals at risk for developing autism.

Applications

- The A/C haplotype can be used in diagnostic tests for the identification individuals that have autism spectrum disorder.
- Screening tests can enable early diagnosis and prognosis of autism and lead to better healthcare outcome

Patent Status

United States Provisional Patent application filed.

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Assessment and Quantification of Risk for the Development of Schizophrenia (Johnson, RWJ 96-16) CNS

Background

Schizophrenia is a developmental disorder caused by brain damage in a fetus due to maternal genetic and environmental factors. The genetic factors have not been definitively identified due to several factors: 1) involvement of more than one gene 2) uncertainty in the mode of inheritance 3) a high frequency of the allele being tested in the population being screened. The environment around the developing fetus is contributed by maternal components and there is a growing appreciation that a combination of fetal environmental and maternal genetic factors during the second trimester of pregnancy contributes to the development of schizophrenia. A resolution of the precise nature, components, and manner of interaction of the genetic and environmental factors could lead to the prevention of this disease and other developmental disorders that are believed to share common etiological factors.

Description of the Technology

A 19 base pair deletion in the enzyme dihydrofolate reductase (DHFR) has been shown to have a significant predictive value for the identification of individuals at risk for the development of schizophrenia. Models for the determination of gene inheritance pattern using patient derived tissue samples have been developed. Further, the dietary content of folate, cobalamin, and pyridoxine of pregnant and susceptible individuals has been determined to be predictive of the susceptibility to schizophrenia.

Applications

- To screen and identify individuals genetically susceptible to give birth to schizophrenic individuals
- To screen and identify individuals susceptible to schizophrenia
- For the development of a database of environmental reference sets for the identification of environmental factors capable of triggering the disease in genetic carriers or genetically prone individuals or their off-springs
- For the development of treatment modalities for individuals identified as susceptible to developmental disorders

Patent Status

United States patents: US 6,210,950 B1 & 6,912,492

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Erythropoietin-Derived Short Peptide and Its Mimics as Immuno/Inflammatory Modulators (*Yuan, Rui Rong RWJ 05-14*) CNS/Therapeutic

Background

Erythropoietin (Epo) is a hematopoietic growth factor widely used in the treatment of anemia and has been claimed to have direct neuroprotective effects. However, long-term Epo therapy can elevate patient's red blood cells and platelets excessively in non-anemic individuals. A short Epo-derived peptide has recently been shown to induce differentiation and prevent cell death in rodent and human neuronal cell lines, while lacking the erythro-proliferative effects.

Description of the Technology

The present invention relates to the fact that the Epo-derived short peptide protects against tissue damage by significantly diminishing tissue responses to injury which are mediated by the inflammatory network. The Epo-derived short peptide reduces the MHC class I and II over-expression in peripheral lymphoid tissue, as well as, brain tissue thereby decreasing cytotoxic effects of cytokines produced by mononuclear and T cell populations. Additionally the peptide has been shown to not increase red cell indices in rodent animal models.

Applications

The Epo-derived peptide has potential for clinical application in the treatment of CNS and PNS diseases associated with acute and chronic injury including demyelinating diseases, traumatic injury of the brain, spinal cord injury, and stroke. The beneficial effect of this peptide is not limited to the nervous system, and can be useful in the treatment of autoimmune disorders, for suppression of graft rejection following organ transplantation, as well as, for tissue protection in other non- CNS or PNS systems such as heart and joints.

Patent Status

United States Provisional Application for Patent Filed

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Method for Producing a Functional Neuron (*Rameshwar, NJMS 04-50*) *CNS/Stem Cells*

Background

Experimental evidence shows that stem cells could have future benefits in the area of regenerative medicine. Mesenchymal stem cells (MSCs) are major adult bone marrow stem cells with multilineage potential. They are easily obtained from adult bone marrow, and can be expanded by *in vitro* procedures. MSCs have been shown to transdifferentiate into cells of other germ layers and the generation of MSCs into neurons as characterized by morphology and action potential has been studied. However synaptic transmission has not been reported for neurons derived from MSCs. **The present invention describes a method for generating functional neurons from adult human MSCs.**

Description of the Technology

The present invention is a method for producing a functional neuron. The transdifferentiation of MSCs into neurons is determined by phenotypic and electrophysiological analysis. In particular embodiments, the functional neurons are subsequently polarized by contacting the functional neuron with at least one selected growth factor. Isolated functional neurons and polarized functional neurons are also provided. The neurons provided by the method of the present invention are capable of synaptic transmission, as evident by immunofluorescence for synaptophysin, and can be used in neuronal repair.

Applications

- For treatment or amelioration of a variety of diseases or conditions including, but not limited to, neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, Down's syndrome, prion disease, polyglutamine disease, and amyotrophic lateral sclerosis; cerebral ischemia; demyelination; head injury; spinal damage; cerebral infarct and the like.

Patent Status

United States patent application filed in November, 2005

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Compound Human α -synuclein Transgenic Mouse Model of the Parkinson's Disease Phenotype (*Richfield, EOSHI 06-52*) *Research Tools/Mouse Models*

Background

A role for both the wild-type and mutated forms of α -synuclein in humans with Parkinson's disease has been implicated. It is not yet known if both forms have the same mechanism or differ. Nor is it known how either contributes to the disease. UMDNJ researches have created several lines of transgenic mice with Parkinson's disease phenotype that will allow for better understanding of the roles of these genes in contributing to Parkinson's disease. Testing of interventions to slow or halt the progression of the disease would be best tested in the compound transgenic mice.

Description of the Technology

A transgenic mouse model of the Parkinson's disease phenotype was originally created in the C57BL/6J line. One line contained the wild-type human α -synuclein gene under control of the rat tyrosine hydroxylase promoter. The other line contained a doubly-mutated form of human α -synuclein. The transgenes have been crossed into a line of C57BL/6J mice that are spontaneously deleted in the mouse α -synuclein gene. The major advantage of this cross is that the actions of the human α -synuclein gene will not be altered by the action of the endogenous mouse α -synuclein gene. The different lines have transgene specific consequences on the dopaminergic neurons of the substantia nigra pars compacta which decline in humans and are responsible for many of the adverse effects in the disease. These consequences include loss of locomotor activity with aging associated with loss of striatal levels of the neurotransmitter dopamine.

Applications

- To study mechanisms of cell dysfunction and death in regions of the brain vulnerable in Parkinson's disease.
- For testing of interventions to slow or halt the progressive features or to provide symptomatic therapy.

Patent Status

Provisional Application Filed 2006

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Method of Quantifying Disease Biomarkers in the Lens of the Eye (*Frederikse NJMS 06-04*)
CNS/Medical Device/Biomarkers

Background

Age related neurodegenerative disease is a growing problem due to the aging of the population. Alzheimer's and other related diseases, associated with the aging process, are difficult to diagnose in early stages; despite the fact that early detection is the key to prophylactic treatment. To further complicate assessment of disease state or progression, many of the currently available diagnostic methods are qualitative. However, recent studies have shown that changes in the eye can provide information about corresponding changes in the brain related to the presence of age-related degenerative disease. Further, there is also evidence that the presence and concentration of specific disease-related biomarkers in the eye can be measured and that a correlation exists with the levels of such biomarkers in the brain.

Description of the Technology

The invention consists of disease related biomarkers and a non-invasive, non-contact optical method and instrument for the measurement of those biomarkers that have been shown to be indicative of the disease state. The instrument uses standard light source and CCD detection optics. A compact prototype has been built and tested on animals and human cadaver lenses.

Advantages

- Non-invasive, non-contact
- Short measurement time
- Can be performed in physician's office
- Relatively low-cost instrumentation
- Quantitative
- Allows measurement of progression over time

Applications

The applications for this technology include early detection of senile cataracts, complications of diabetes, Alzheimer's disease, and Wilson's disease.

Patent Status

U.S. Provisional patent has been filed.

Licensing Opportunity

This technology is available for exclusive or non-exclusive license. For more information, please contact Judith Ladd at the Office of Patents and Licensing.

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