Personalized Treatment of Schizophrenia and Related Disorders with Selective Agonists and Antagonists of VPAC2R

Tech ID: 21872 / UC Case 2011-199-0

BACKGROUND

Rare copy number variants (CNVs) have a prominent role in the aetiology of schizophrenia and other neuropsychiatric disorders. Substantial risk for schizophrenia is conferred by large (0.500-kilobase) CNVs at several loci. However, these CNVs collectively account for a small fraction (2 to 4 percent) of cases, and the relevant genes and neurobiological mechanisms are not well understood. A majority of the rare CNVs that have been implicated in schizophrenia involve large (500 kb) genomic regions where local segmental duplication architecture promotes frequent and nearly identical rearrangements by non-allelic homologous recombination (NAHR). Because of the high structural mutation rates at these loci, the strong phenotypic effects of the causal variants, and the excellent power of most array platforms to detect such large CNVs, these genomic hotspots were the first to be detected in studies of CNVs in schizophrenia.

Vasoactive intestinal polypeptide (VIP) and pituitary adenylate cyclase-activating peptide (PACAP) are two closely related peptides that bind two homologous G protein-coupled receptors, VIP/PACAP receptor 1 (VPAC1R) and VIP/PACAP receptor II (VPAC2R). Vasointestinal Peptide Receptor 2 (VIPR2) encodes the vasoactive intestinal peptide (VIP) receptor VPAC2, a G protein-coupled receptor that is expressed in a variety of tissues including, brain, suprachiasmatic nucleus, hippocampus, amygdala, and hypothalamus. VIPR2 is known to play a role in the cardiovascular and gastrointestinal system and it is this application that has driven early efforts to develop selective agonists and antagonists of VPAC2R. Peptide derivatives and small molecules have been identified that are selective VPAC2 agonists or antagonists.

TECHNOLOGY DESCRIPTION

Scientists at UC San Diego have developed a novel approach to the personalized treatment of schizophrenia and autism consisting of applying novel diagnostic and therapeutic technologies to the analysis of DNA and human cells from patients. Specifically, this invention includes generic methods for the identification of patients that carry mutations in VIPR2, and further detection of mutations in DNA that impact the function of VIPR2. These methods include DNA sequencing-based methods and microarray, PCR, and mass spectrometry-based methods for detection of DNA copy number. The invention demonstrates that the patients carrying the mutations in VIPR2 are likely to benefit from treatment with selective agonists or antagonists of VPAC2R, and/or vasoactive intestinal peptide or derivatives. As a direct implication of this finding, specific compounds that selectively modulate the activity of the VPAC2R receptor encoded by VIPR2 (e.g. selective agonists, antagonists, VIP, and/or VIP derivatives) are treatments for these and related disorders. The invention further provides a novel approach to using genetic testing to guide the selection of appropriate drugs for modulation of VPAC2R activity and consequently to treat brain disorders, such as schizophrenia and autism.

This approach to personalized treatment of schizophrenia and autism consists of applying the diagnostic and therapeutic inventions described above to the analysis of DNA and human cells from patients. Overall, these findings implicate altered vasoactive intestinal peptide signaling in the pathogenesis of schizophrenia and indicate the VPAC2 receptor as a potential target for the development of new antipsychotic drugs.

RELATED MATERIALS

- Vacic, V. et al. Duplications of the Neuropeptide Receptor Gene VIPR2 Confer Significant Risk for Schizophrenia, Nature 2011 Mar 24;471(7339):499-503. - 03/24/2011

CONTACT
University of California, San Diego
Office of Innovation and Commercialization
innovation@ucsd.edu
tel: 858.534.5815.

INVENTORS

- Sebat, Jonathan

OTHER INFORMATION

CATEGORIZED AS

- **Medical**
  - Diagnostics
  - Disease: Central Nervous System

RELATED CASES

2011-199-0

University of California, San Diego
Office of Innovation and Commercialization
9500 Gilman Drive, MC 0910, ,
La Jolla,CA 92093-0910

Tel: 858.534.5815
innovation@ucsd.edu
https://innovation.ucsd.edu
Fax: 858.534.7345