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Updates to the documentation system for R

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OBJECTIVES/SPECIFIC AIMS: This research seeks to create a next generation documentation system that exists independent of but is complimentary to the packaging system in R. The new documentation can be manipulated programmatically as with all R objects. It also implements multiple translators for creating documentation from different sources, including documentation pages written in latex and code comments. METHODS/STUDY POPULATION: This work is based on input from the R Documentation Task Force, which is a working group, supported by the R Consortium and the University of Utah Center for Clinical and Translational Science, consisting of R Core developers, representatives from the R Consortium member companies and community developers with relevant interest in documentation. An abstraction of the documentation currently in use was created and extended. This abstraction was translated to a class system in R so that documentation can be stored and manipulated in R. RESULTS/ANTICIPATED RESULTS: The class system representing the documentation and the tools for creating the translators are currently being implemented in R. A preview of the system is scheduled to be available at the time of the conference. DISCUSSION/SIGNIFICANCE OF IMPACT: Good documentation is critical for researchers to disseminate computational research methods, either internally or externally to their organization. This work will facilitate the creation of documentation by making documentation immediately accessible and promote documentation consumption through multiple outputs which can be implemented by developers.

2109

Interleukin 4-induced protein 1 as a biomarker and treatment option in multiple sclerosis

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OBJECTIVES/SPECIFIC AIMS: The overall objective of this proposal is to establish and modulate the inflammatory profile of individuals across the spectrum of multiple sclerosis (MS), with a focus on determining the potential of interleukin 4-induced protein 1 (IL4I1) as a possible marker of progression and modulator of inflammation in human blood samples. METHODS/STUDY POPULATION: The proposed experimental approach involves isolating plasma and peripheral blood mononuclear cells (PBMCs) from individuals across the spectrum of MS phenotypes, and analyzing these samples primarily by quantitative polymerase chain reaction (qPCR) and enzyme-linked immunosorbent assay (ELISA) methods. Specifically, study groups include: (1) actively relapsing-remitting MS (a-RRMS), (2) non-actively relapsing-remitting MS (n-RRMS), (3) non-active secondary-progressive MS (SPMS), (4) other autoimmune diseases (OAD), (5) healthy controls (HC). RESULTS/ANTICIPATED RESULTS: We expect that IL4I1 treatment increases regulatory cytokine (eg, IL10, TGFb) expression while decreasing Th1 and Th17-derived cytokines (IFNg, IL17), as well as increasing relative composition of regulatory cells (Th2, Treg, M2) as compared with Th1, Th17, M1 (aim 1). Preliminary data on healthy control cells support this prediction. Our central hypothesis is that IL4I1 level indicates the body's ability to repair itself. As such, we anticipate that all MS groups are deficient in IL4I1, to varying degrees, such that HC > n-RRMS > a-RRMS > SPMS. HC have full repair capacity. RRMS > SPMS as remission indicates existent repair capacity, which is lost in SPMS. n-RRMS > a-RRMS since both, as RRMS, capable of repair response, but a-RRMS triggered this response more recently in response to more recent relapse. In all groups, we expect IL4I-treatment to mitigate inflammation (aim 2). Finally, we expect that H_2O_2 production by IL4I1 is a key player in IL4I1 function, and that H2O2 will preferentially induce oxidative stress to pro-inflammatory subsets of PBCMs (aim 3). DISCUSSION/SIGNIFICANCE OF IMPACT: MS is a chronic inflammatory neurodegenerative disease of the central nervous system that, with an average age of onset of 34, afflicts over 2.3 million individuals worldwide during many of the most productive years of their lives. The pathogenesis of MS, which involves autoimmune destruction of myelin, is poorly understood. Accurate biomarkers, which could predict disease progression, are yet to be identified and would provide valuable information to patients and their treating clinicians. Likewise, effective treatments are few and in high demand. IL4I1 is a promising candidate for both roles.

2120

Antipsychotic-induced weight gain arises, in part, from alteration of feeding circuitry in the lateral hypothalamic area

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OBJECTIVES/SPECIFIC AIMS: To demonstrate that olanzapine recapitulates the effect of increased lateral hypothalamic (LH) GABAergic activity in the DRN and the DBB. This will provide a potential neural substrate for the observed increase in consumption of food and weight gain. METHODS/STUDY POPULATION: (1) We will examine electrophysiological activity of the DRN and the DBB in response to optogenetic stimulation of LH fibers to these nuclei. (2) We will identify the behavioral phenotype of stimulating these same projections using optogenetic techniques. (3a) Identify the behavioral phenotype of mice possessing cre-loxp-dependent knockout (KO) of LH GABAergic activity, DRN serotonergic activity, and inhibition of DBB cholinergic activity. (3b) Using these mice, we will establish behavioral response to olanzapine in ad libitum feeding and fast-refeeding condition. (4) Using baseline and post-treatment body mass index (BMI), PANSS, and side effect profile scores from a recently completed prospective cohort study of treatment-naive schizophrenic patients receiving atypical antipsychotics for 1 year, we will sequence multiple single nucleotide polymorphisms and explore the correlation of serotonergic, dopaminergic, and cholinergic receptor mutations with the increase in BMI and changes in PANSS score and side effect scores. RESULTS/ANTICIPATED RESULTS: (1) Our preliminary data indicates that the LH exclusively sends GABAergic input to the DBB, and the large majority of its projections to the DRN are GABAergic. (2) We have identified that stimulating LH– > DBB projections produces intense feeding and drinking behavior, a real-time place preference for laser stimulation, and a conditioned place preference for laser stimulation. Preliminary data shows that the LH- > DRN also produces feeding behavior. (3a) Our lab has demonstrated that transgenic mice with LH-specific GABA release KO are smaller, have increased anxiety-like behaviors such a repetitive grooming and open field aversion, and have reduced feeding after fasting conditions. We expect the DRN serotonergic KO mice to have increased body weight and reduced anxiety-like behaviors. (3b) Our pilot study demonstrated that the LH GABA KO mice administered olanzapine have a greater consumption of food over 1 hour than controls ($n = 7$, 5, respectively; $p = 0.08$). DRN serotonergic KO mice and mice with inhibition of choline will have an increased baseline feeding behavior, but will not be affected by olanzapine. (4) We believe that SNPs in serotonergic receptors such as 5HT2C, and those affecting dopaminergic and cholinergic receptors, will be more common in schizophrenic patients with increased BMI than those without. Further, we believe that a reduction in the PANSS items reflecting anxiety and aversiveness will correlate with increased BMI, since we

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