Bob's Corner

Alzheimer's disease (AD) is an age-dependent form of neurodegenerative disease with years of preceding neuropathology including deposition of β-amyloid, tau protein and neurofibrillary tangles associated with ultimate and progressive cognitive dysfunction and loss of memory. Although apolipoprotein E4 is the strongest genetic predictor of disease, most AD is sporadic. Because aging without AD has an epigenetic basis, similar molecular mechanisms could contribute. At present, DNA methylation abnormalities found in the brain of AD patients are most often located outside of gene promoters. Thus, the purpose of this study, from the Michigan and University of Toronto groups, was to analyze sites of DNA methylation in neurons from AD brain using a genome-wide approach. Of note, novel gene regulatory regions were identified that may contribute to why AD is age-dependent.

Article:

Abstract
Epigenetic control of enhancers alters neuronal functions and may be involved in Alzheimer's disease (AD). Here, we identify enhancers in neurons contributing to AD by comprehensive fine-mapping of DNA methylation at enhancers, genome-wide. We examine 1.2 million CpG and CpH sites in enhancers in prefrontal cortex neurons of individuals with no/mild, moderate, and severe AD pathology (n = 101). We identify 1224 differentially methylated enhancer regions; most of which are hypomethylated at CpH sites in AD neurons. CpH methylation losses occur in normal aging neurons, but are accelerated in AD. Integration of epigenetic and transcriptomic data demonstrates a pro-apoptotic reactivation of the cell cycle in post-mitotic AD neurons. Furthermore, AD neurons have a large cluster of significantly hypomethylated enhancers in the DSCAML1 gene that targets BACE1. Hypomethylation of these enhancers in AD is associated with an upregulation of BACE1 transcripts and an increase in amyloid plaques, neurofibrillary tangles, and cognitive decline.

The Centers for Disease Control and Prevention

The Centers for Disease Control and Prevention has asked CU and research institutions across the country to provide information for the National Inventory for Poliovirus Containment to support the World Health Organization's Global Polio Eradication Initiative and Global Action Plan. As a first step, the University Office of Environmental Health and Safety has prepared a short survey to identify principal investigators who may possess potentially infectious materials containing poliovirus. Based on the survey results, the University Biological Safety Officer will work with the identified principal investigators to compile an inventory to be submitted to the National Inventory for Poliovirus Containment. The survey must be completed by Wednesday, June 5.
Research Corner

Thomas Delong, PhD, is an Assistant Professor in the Department of Pharmaceutical Sciences in the Skaggs School of Pharmacy. He received his PhD in chemistry and biochemistry at the University of Erlangen (Germany) and performed his postdoctoral fellowship in the Department of Immunology at the University of Colorado. Dr. Delong joined the faculty at the Skaggs School of Pharmacy in 2017.

Dr. Delong’s research is focused on better understanding the etiology and pathogenesis of the human autoimmune disease type 1 diabetes (T1D). He is particularly invested in identifying targets for immune-based therapies for T1D and identifying biomarkers that could improve disease staging and the assessment of therapeutic outcome. As a type 1 diabetic himself, he recognizes the pressing need for such advances in the field.

During his time as a postdoctoral fellow and later as a research assistant professor, Dr. Delong used his expertise in chemistry to approach long-standing questions about the immunology of T1D in new ways. His work led to the discovery of chromogranin A and islet amyloid polypeptide (IAPP) as autoantigens in the primary mouse model of T1D, the non-obese diabetic (NOD) mouse, and he later helped confirm that chromogranin A is an antigen in human T1D. In a seminal publication in the field, he demonstrated that pancreatic beta cells contain a novel class of post-translationally modified peptides, hybrid insulin peptides (HIPs), that consist of insulin sequence fused to peptides from other proteins present in the beta cell. With collaborators, he also showed that HIPs are recognized by autoreactive CD4 T cells in both NOD mice and human donors with T1D.

Dr. Delong’s current research is focused on using proteomics-based approaches, particularly tandem mass spectrometry, to further elucidate the role of HIPs as autoantigens in human T1D. His lab is developing new techniques for confidently identifying diverse HIPs in human islets and is investigating the mechanisms that lead to their formation. He is also heavily involved in clinical studies examining HIP-reactive CD4 T cell responses in T1D patients and is exploring the possibility that other types of hybrid peptides are involved in different autoimmune diseases.

In addition to running a successful research program, Dr. Delong is an expert pretzel maker, much to the enjoyment of his lab members.

National Institute of Health (NIH)

Clinical Trial Requirements for Grants and Contracts

If you are submitting a grant application or responding to a contract proposal to NIH that includes a clinical trial, or are involved with conducting, managing, or overseeing clinical trials, learn about NIH policies, and find resources to guide you in your work.

Application Submission Policies

Learn about the policies that may impact your application submission, including late applications, due dates on holidays/weekends, post submission application materials, continuous submission, guidelines for applicants experiencing system issues, resubmission policies, overlapping applications, weather and other disasters, and more.