Effects of Diabetes and Diet on Spinal Pathology
James C. Iatridis, PhD; Andrew C. Hecht, MD; Sheeraz A. Qureshi, MD; Helen Vlassara, MD; Svenja Illien-Juenger, PhD

Intervertebral disc (IVD) degeneration and degenerative spinal changes are major causes of back pain and recent epidemiology suggests that obese and diabetic individuals are at increased risk for back pain and spine surgery complications. However, little research has been done to investigate possible links between diabetes mellitus (DM) and IVD degeneration (IDD). Research into mechanisms for type 2 DM (T2DM) induced IDD is a major research priority due to the increased numbers of back pain patients who are diabetics and because such links are likely to expand and enhance current knowledge on mechanisms for IDD in the general population. Our previous study is one of the first to show direct links between DM, IDD and vertebral pathology in mice, and the results implicated the accumulation of advanced glycation endproducts (AGEs) as a potential mechanism for these effects. Of all DM patients 90% suffer from T2DM, and the development of T2DM is associated with hyperglycemia as well as the consumption of modern diets rich in AGEs (which accumulate in foods cooked at high temperatures). Our overall goal is to characterize how T2DM and diet can induce IDD, and to identify potential mechanisms for these effects. The proposed project tests our primary hypothesis that T2DM induces spinal pathology involving IDD and vertebral pathology due to hyperglycemia and the accumulation of AGEs that lead to inflammation, catabolism, ectopic calcification, and protein crosslinking. Hypothesis 2 is that IVD and vertebral pathology are predominantly associated with AGE accumulation that can occur through excess dietary AGE ingestion (i.e., without hyperglycemia found in T2DM). Our third hypothesis is tissue AGE accumulation correlates with irregular calcifications observed in vertebral endplates (EPs) and IVD tissues, which may be one of the initiators of important degenerative changes. We test this hypothetical model by comparing spinal pathologies observed in T2DM mice with those fed a high AGE diet. We expect the spinal pathologies induced in T2DM mice (Aim 1) and high AGE diet fed mice (Aim 2) to be similar and to include IDD (i.e., degenerative morphology and loss of glycosaminoglycans), vertebral pathology (i.e. increased cortical bone mineral density but lower bone lower trabecular bone quality), and accumulation of AGEs co-incident with ectopic calcifications. This project is highly significant because of the tremendous health burden of both T2DM and IDD, and the increasing prevalence of back pain patients who suffer from T2DM. The approach is innovative because there are remarkably few studies relating T2DM and IDD, and because our hypothetical model provides a framework that may provide future treatments for IDD of both diabetic and non-diabetic patients. This fundamental information is required to design treatments and management strategies for back pain patients with T2DM, and will better understand the role of inflammation and AGE accumulation in spinal pathologies.