As diabetes becomes a growing health concern, affecting nearly 25.8 million people in the United States and nearly 220 million people worldwide, there has been an increased awareness of environmental factors like diet that are contributing to the disease. In diabetic patients, a major causal factor contributing to progression of the disease is hyperglycemia. While we know that early intensive glycemic control reduces the risk of cardiovascular complications in humans and rodent models, there is a large gap in studies of the etiology of hyperglycemia-induced alterations in the disease. To combat high sugar diets that contribute to diabetes and subsequent hyperglycemia, non-caloric artificial sweeteners have become one of the most utilized food additives worldwide due to their consideration as a low caloric substitute. However, supporting scientific data as to the safety of these non-caloric artificial sweeteners is limited and controversial. The negative implications of consuming a high sugar diet on overall health have long been linked to diabetes, obesity, and resulting systemic health problems; however, it was not until recently that the negative impact of consuming artificial sweeteners in the place of sugar had been increasingly recognized. This presentation will focus on research to decipher the underlying molecular mechanisms influenced by these high glucose and artificial sweetener diets.