Defining the Effects of a High Advance Glycation End Product Diet on Mammary Development during Puberty

The mammary gland is a unique organ because its functional development and differentiation are completed postnatally during puberty, pregnancy, lactation and involution. These cycles of mammary gland development are potential windows of breast cancer susceptibility. Due to links between diet and increased risk of breast cancer, we hypothesized that consuming large amounts of sugar derived metabolites known as advanced glycation end products (AGEs) during puberty may cause mammary gland dysregulation and increase the risk for future pre-neoplastic lesions. AGEs are a heterogeneous group of macromolecules that are generated through non-enzymatic glycation and oxidation of proteins, lipids, and nucleic acids. Accumulation of AGEs leads to pro-inflammatory and pro-oxidant effects which can contribute to the development and complications associated with multiple chronic diseases. Our previous research showed that consuming a high AGE diet causes the formation of hyperplastic lesions which resembled pre-neoplastic lesions. This study expands on our findings by examining the effects of diet switching on the formation of the hyperplastic lesions. Mice (3 weeks old) were initially fed the high AGE diet for 4 weeks followed by a regular diet (regular mouse food) for 5 weeks. At the experimental endpoint of 12 weeks, mice were sacrificed and mammary tissues were collected for whole mounting and hematoxylin and eosin staining. This model mimics the concept of “metabolic memory” which postulates that events that occur early in disease onset are imprinted within cells and promote disease progression later in life. Our data showed that consuming a high AGE diet during pubertal development altered mammary gland morphology forming abnormal cell structures and promoted the formation of hyperplastic lesions, despite intervention with the regular diet. In summary, the data supports the hypothesis that a diet high in AGE metabolites during puberty may induce metabolic memory and may represent a window of susceptibility for breast cancer.