Advanced glycation end products: A tumor promoting consequence of Nutrition

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Our research has demonstrated that advanced glycation end products (AGEs) derived from diet can directly impact both pubertal developmental programs and neoplastic growth to increase cancer risk and progression. Most people are unaware of what AGEs are or the damage they can cause, but we are exposed to them every day through the lives we lead and the foods that we eat. The Western diet together with more sedentary habits means that lifestyle-associated AGEs are accumulating in our bodies at a faster rate than ever before. Changes in the AGE equilibrium due to lifestyle cause protein dysfunction, reduced genetic fidelity, and aberrant cell signaling activation which we believe contribute to cancer outcomes. Disparity populations defined by AGE-associated risk factors such as diet, smoking, drinking and physical inactivity often bear a greater cancer burden when compared to the general population (reviewed by the PI, Cancer Research 2015). Lifestyle associated AGEs therefore may represent a unifying biological consequence of the social, demographic and environmental risk factors that contribute to increased cancer incidence and mortality. Early life exposures during mammary development influence the breast microenvironment to increase breast cancer risk. We show that due to an innate ability to influence the cellular matrix, dietary AGEs disrupt mammary development during puberty and accelerate tumor growth and progression. Critically, dietary-AGE mediated effects on pubertal development and tumor growth were dependent upon the stromal activation of the receptor for AGE (RAGE). Our studies show that dietary-AGE activation of RAGE alters cytokine profiles and increases immune cell recruitment to produce an activated stroma. An activated stroma was characterized by the increased recruitment and activation of fibroblasts and macrophages. stromal cells adopt distinct metabolic patterns which function to maintain the energy requirements needed for cell differentiation and functionality. Pathway analysis of expression data from excised tumors shows that AGE consumption significantly impacts energy metabolism through the aberrant expression of MYC regulated transcriptional targets. Our combined data show that AGEs contained in the foods we eat can impact cancer risk and progression. Due to their links with lifestyle, both pharmacological and/or interventional strategies aimed at reducing the AGE accumulation pool may be viewed as universal health care preventive and/or therapeutic initiatives. This may be an attractive option for populations where lifestyle change is not feasible due to poverty, inability, illness, treatment side effects, time, apathy and/or depression.

Biography

David Turner has accumulated over 20 years of basic and translational cancer research experience in the UK, Europe and USA and has a track record of success. Through peer reviewed publications, multiple intercontinental collaborations, and numerous scientific meetings around the world his work is internationally recognized. His research program has been dedicated to defining the biological mechanisms involved in promoting cancer with a emphasis on the effects of lifestyle and diet. In order to be successful in his chosen field he has established working collaborations with a multidisciplinary team of investigators including clinicians, epidemiologists as well as behavioral and population scientists in order to fully comprehend the translational link between lifestyle, cancer and cancer disparity. He continues to show a strong commitment to community outreach and has developed bridges with numerous community leaders and has presented at many community events.

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