Evaluating Inflammatory and Genotoxic Consequences of Adiposity in Adolescents: a Non-Invasive Approach

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EVALUATING INFLAMMATORY AND GENOTOXIC CONSEQUENCES OF ADIPOSITY IN ADOLESCENTS - A NON-INVASIVE APPROACH

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The genome holds a substantial role in maintaining optimal cellular function. There are a variety of well-established genotoxicity tests that can evaluate acquired DNA damage and chromosomal instability. These types of tests can be utilized to inform susceptibility to disorders that are strongly associated with genome damage, such as cancer. A strong correlation has become evident between obesity and over ten different types of cancers. This association may be explained by the increased systemic inflammation and over-generation of reactive oxygen species (ROS) that is characteristic in individuals who possess excess body fat. The mutagenic effects of ROS are well-known and include oxidative base modifications and DNA single and double strand breaks. Emerging evidence indicates a correlation between increased adiposity and markers of oxidative DNA damage. One such marker is 8-OH-2-deoxy Guanosine (8-OHdG), a DNA lesion that is potentially mutagenic. Findings of other biomarkers indicative of DNA strand breaks in obesity include -H2AX foci, micronuclei and comet tails. Telomere attrition marks accelerated ageing and is another phenomenon identified in obese adults and children. Adolescent obesity is expected to rise and lead to morbidity. It is concerning that recent studies have suggested obese children to not only possess a reduced life expectancy, but a pre-disposition to age related disorders, including cancer. We propose biomonitoring of the genome to inform prioritization and severity of intervention measures. A combined laboratory ‘tool-kit’ to allow non-invasive biomonitoring of ‘genome health’ in adolescents and other large epidemiological studies is being developed. This investigation integrates the well-established micronucleus assay in exfoliated buccal epithelial cells, urinary 8-OHdG, salivary telomere length and salivary C-reactive protein to provide a comprehensive assessment of inflammation, cytotoxicity, chromosomal aberrations and DNA damage in a cohort of 11-15 year olds. Correlations of these markers is explored against three different measures of adiposity - waist to hip ratio, body fat percentage and body mass index. Findings from this study aim to establish the applicability of personalized, early detection of acquired DNA damage as a pre-cancerous biomarker in obesity and other pre-pathological conditions.