Integrating Redox-Metabolic Regulation of Adipose Tissue within the Exposome Framework: From Cold Exposure to Obesity and Cancer

IST1-02

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The exposome framework, encompassing external (like diet, temperature) and internal (such as metabolic stress) environmental exposures, highlights adipose organ as a key interface for energy and redox processes influencing metabolism. Exposure to low environmental temperatures triggers brown adipose tissue (BAT) to activate non-shivering thermogenesis. This process harnesses energy from food and mobilizes lipids from white adipose tissue (WAT), all coordinated through intricate redox processes to effectively sustain heat production. Mitochondrial reactive oxygen species (ROS) are crucial in mediating thermogenic activation and uncoupling protein 1 in BAT. ROS and reactive nitrogen species also promote WAT browning into beige adipocytes, offering anti-obesity strategies. However, in obesogenic states, WAT shows redox imbalance linked to oxidative damage, mitochondrial dysfunction, disrupted insulin signaling, and impaired adipokine production, increasing risks of insulin resistance and metabolic disorders. In obesity-related cancers like breast cancer, adipose organ undergoes changes, with tumors exploiting cancer-associated adipose tissue (CAAT) via redox and metabolic rewiring to access nutrients supporting growth. The recent studies of breast cancer reveal Nrf2's role in mediating redox coupling between tumors and CAAT. Loss of Nrf2 disrupts this communication, redox balance, and alters tumor mitochondrial dynamics, emphasizing bidirectional interactions governed by Nrf2. These findings show the exposome as a valuable perspective on redox-metabolic regulation in adipose organ in health and disease, from cold exposure to obesity and cancer. Incorporating the exposome into adipose and cancer research offers a path to precision redox medicine for treating metabolic diseases, including cancer.
Acknowledgement: This work was supported by the Science Fund of the Republic of Serbia, project #7750238 “Exploring new avenues in breast cancer research: Redox and metabolic reprogramming of cancer and associated adipose tissue” - REFRAME and the Ministry of Science, Technological Development and Innovation of the Republic of Serbia, (grant #451-03-137/2025-03/200178 and #451-03-136/2025-03/200007).