

Endocrine Dismodulation and Cancer

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Carcinogenesis has generally been viewed as a genomic disease resulting from genetic mutations occurring at critical locations in the genome in a particular sequence. In the last 10 years, scientists have increasingly identified changes in the levels, frequency and types of endocrine hormones as important contributors to the major cancers faced by western populations. Many of the cancers occurring with highest frequency have large fractions attributed to alterations in circulating endocrine hormones; examples include breast cancer (estrogen, progesterone, prolactin), prostate cancer (estrogen, testosterone), endometrial cancer (estrogen) and thyroid cancer (TSH, T3, T4). In addition, a number of chemicals in the environment either mimic the role of these hormones to bind to receptors (e.g. phytoestrogens as estrogen mimics), alter signaling pathways (e.g. retinoids), inhibit steroid hormone synthesis (such as some fungicides) or alter steroid hormone metabolism (such as TCDD altering the metabolism of both estrogen and thyroid hormones). Genomic and non-genomic endocrine signaling pathways are extensively present in the body and function in a complicated fashion. In order to fully understand the basis for endocrine-induced cancers, one must simultaneously study the various receptors, ligands, enzymes, proteins and organs which all contribute to endocrine system function. Mechanism-based mathematical models are the only analysis tool available to address these complicated networks. In addition, cross-talk between various endocrine systems is common and this is key to understanding a potential role of melatonin on human cancer risks. Melatonin has a major role mediating the effects of photoperiod on reproduction, metabolism, thermoregulation, immunity and possibly aging. This talk will focus on what is known about endocrine-mediated carcinogenesis, discuss the various mechanisms involved in the formation and promotion of the resulting cancers and discuss targets for future research on the role of melatonin and light in promoting cancer.