Chapter 1
Developmental Origins of Health and Disease: Maternal and Paternal Exposures in Carcinogenesis

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ABSTRACT

There is an intricate relationship between the exposome and critical periods of gametogenesis, teratogenesis, and cancer development. Developmental Origins of Health and Disease (DOHaD) framework to cancer susceptibility examines the hypothesis that early-life environmental exposures can program long-term cancer risk. The authors review epidemiological studies demonstrating associations between developmental exposures and increased cancer risk. Case studies beginning from gametogenesis, debates on biological mechanisms, epigenetic modifications, and altered tissue development are discussed. The chapter also critically analyzes key controversies such as methodological limitations, the etiological complexity of cancer, issues of generalizability, and translational hurdles. This work demonstrates how environmental factors influence gamete formation, embryonic development, and carcinogenesis to highlight the need for addressing parental health and reducing health disparities.

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BACKGROUND ON DEVELOPMENTAL ORIGINS OF HEALTH AND DISEASE (DOHAD)

Lamarck's early theories on inheritance and environmental adaptation have influenced the concepts of the Developmental Origins of Health and Disease (DOHaD) (Zambrano & Ibáñez, 2025). DOHaD is the idea that environmental exposures during critical periods of development (in utero, infancy, early childhood) are essential. DOHaD believes that internal and external early life exposures can have epigenetic effects.

Exposome research purports that exposures of biological, environmental, and chemical origin influence human health. There are debates on Lamarckian ideas that also argue the link between DOHaD and cancer susceptibility. Arguments focus on how molecular markers for internal and external exposure vary in time and interact in complex ways. The tumorigenic effects can be cumulative, and the diagnosis of phenotypic plasticity based on morphological, physiological, and behavioral adaptations is obscure (Vineis & Dagnino, 2024). The eighth annual US DOHAD meeting calls for birth cohort studies, longitudinal cohorts, and innovative methodologies (Non, 2025). It aims to gain a modern understanding of how early-life environmental factors impact carcinogenesis across an individual's lifetime and future generations.

Exposome measurements examine colorectal cancer (CRC) risk using data from the UK Biobank. Findings revealed that risk factors such as ecosystem, healthy lifestyles, tobacco or alcohol use, socioeconomic status, and insufficient social support. Certain dietary factors, such as high intake of fat, red meat, processed meat, and dietary fiber, influence the risk of colorectal cancer. Conversely, nutritional variables like higher linolenic acid intake and lower coffee consumption are associated with squamous cell carcinoma. Cultural Practices, such as the use of betel quid, have been linked to increased oral and esophageal cancer risk. Poor living conditions that cause chronic inflammation, such as inflammatory bowel disease (IBD) and chronic hepatitis, can increase the risk of cancer development in affected tissues (Tortolero et al., 2024).