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Integrating Physical Activity and Diet into Mechanisms of Metabolic Dysregulation and Cancer Risk: Insights from the MeDOC Consortium

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Obesity and associated metabolic dysfunction are increasingly recognized as major contributors to cancer risk across diverse populations. The National Cancer Institute's Metabolic Dysregulation and Cancer Risk (MeDOC) Consortium brings together six transdisciplinary research teams to identify mechanisms linking metabolic perturbations to cancer development and to identify actionable strategies for prevention. Given the importance of lifestyle factors, MeDOC is integrating harmonized measures of physical activity and diet to characterize behavioral contributors to metabolic health. The International Physical Activity Questionnaire (IPAQ) was implemented for studies enrolling participants prospectively and MeDOC harmonized physical activity assessed via questionnaire in historical cohorts. With dietary intake captured by food frequency questionnaires (FFQs), MeDOC is jointly assessing the roles of diet and physical activity in relation to metabolic dysregulation and cancer risk. Data harmonization enables evaluation of dietary patterns, while also positioning physical activity as a primary determinant, mediator, or effect modifier of metabolically driven cancer risk. MeDOC's scientific aims are advanced through five synergistic projects. A-FABP focuses on fatty acid-binding protein-mediated lipid dysregulation's impact on breast cancer biology and tumor-associated macrophages. CerMet examines the role of ceramides in colorectal cancer risk and tests ceramide-lowering interventions. iDOC leverages well-characterized large cohorts and deep inflammatory proteomics profiling to identify pathways most representative of the metabolically unhealthy obese state associated with colorectal and liver cancers. REMEDY investigates metabolic and inflammatory drivers of early-onset colorectal cancer, with particular attention to populations experiencing metabolic obesity at lower BMI levels. WELCOM evaluates obesity-altered gut microbiome-immune interactions that may influence breast cancer initiation. The George Washington University-based Coordinating Center provides oversight of harmonization efforts, data infrastructure, and cross-project collaboration. MeDOC's integrated behavioral, metabolic, and mechanistic approaches offer new opportunities to understand how physical activity and diet may counteract metabolic dysregulation to reduce obesity-associated cancer risk.

Keywords

Physical Activity; Diet; Metabolic Dysregulation; Cancer Risk

Conflict of Interest & Ethical Approval

yes

Abstract submitters declaration

yes

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