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The Impact of Obesity on Prostate Cancer

Introduction: Over the past four decades, the global prevalence of obesity (BMI > 30 kg/m2) has risen dramatically, alongside a steady increase in obesity-associated malignancies. Epidemiological data indicate that excess body weight is associated with an elevated risk of at least 13 distinct cancer types. The impact of obesity on prostate cancer pathogenesis is critical, given that prostate cancer remains the most frequently diagnosed non-cutaneous malignancy in men globally. Despite documented clinical correlations, the precise molecular mechanisms linking obesity to prostate cancer development and racial disparities remain highly complex and poorly understood.

Methods: Proteomic analysis quantified differential protein expression between obese and lean prostate cancer tissue samples from Black and White patients in the Louisiana cohorts. Notably, all patients in this study were untreated and had a Gleason score of 7.0. Identified proteins were mapped to distinct biological pathways, including peroxisomal metabolism, fatty acid and lipid metabolism, intracellular vesicular trafficking, post-transcriptional RNA processing, and mitochondrial bioenergetics. To validate these proteomic findings, histopathological alterations were assessed using Hematoxylin and Eosin (H&E) staining. Additionally, immunohistochemistry (IHC) was used to quantify progression biomarkers associated with obesity-induced prostate cancer, focusing on the lipid metabolism enzymes alpha-methylacyl-CoA racemase (AMACR) and glycerol-3-phosphate acyltransferase 4 (GPAT4).

Results: Proteomic analysis revealed that obesity inundates prostate tissue with lipids, prompting tumors to upregulate the alternative fat-burning HACL1 and lipid-building MCAT pathways. Furthermore, lipid overload stresses mitochondrial energy centers, including COQ8B, coinciding with the downregulation of structural anchors within the Keratin family and EPB41. The data demonstrate that these metabolic alterations are significantly more pronounced within this intermediate-risk cohort and correlate with higher AMACR and GPAT4 expression on IHC.

Conclusions: These findings suggest that obesity accelerates prostate cancer progression in part by driving a distinct lipid-mediated metabolic reprogramming of intermediate-grade tumors.

Limitations: The study used only 16 patient samples, and analysis of larger samples is needed to strengthen these conclusions.