Meta-Analysis of Cancer-Related Gene Sets: Linking Craniosynostosis and Endometrial Cancer

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Craniosynostosis, a congenital disease that affects 1 in 2000-2500 people, shares genetic mutations implicated in cancer progression, yet has not been studied as a potential predictive marker for cancers. In this study, a computational approach was designed to investigate craniosynostosis as a predictive marker of future cancer diagnosis. Craniosynostosis-mutated genes were identified using a literature review (N = 15) then molecular signatures in these genes were identified using the Molecular Signatures Database (MSigDB). Kaposi's sarcoma-associated herpesvirus (Kshv) Infection Angiogenic Markers Up signatures ($p < 1.96*10-9$) and Pathways in Cancer signatures ($p < 3.71*10-9$) were highly prevalent in craniosynostosis-mutated genes, highlighting the predictive power of craniosynostosis for cancers. The Cancer Gene Atlas (TCGA) was then used to rank cancers (N = 33) by mutation percentage (1 = highest mutation percentage, 2 = second-highest mutation percentage, etc.) for each craniosynostosis-mutated gene, from which the average rank was calculated. Craniosynostosis was highly correlated with endometrial cancer with an average rank of 1.12 and forty-five craniosynostosis-mutated genes had higher mutation percentages than the median mutation percentage of all mutated genes in endometrial cancer (N = 22,162; $p<2.94*10-5$), indicating that craniosynostosis may serve as a predictive biomarker for endometrial cancer. Therefore, this study supports early intervention and screening for at-risk women. In the future, similar computational approaches may determine predictive markers for disorders that are difficult to prognose and diagnose, such as pancreatic cancer, and other high mortality diseases.

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