Missense Mutations in Colorectal Cancer: Targeting Pathways in Early vs. Late Stages--Could There be a Role for Early Intervention with Better Outcomes?

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Colorectal cancer arises from genetic aberrancies classified as driver mutations, which actively promote disease progression, and passenger mutations that provide no evident selective growth advantage. A driver can consist of both driver and passenger mutations. Missense mutations account for a large percent of genetic irregularities within the transforming cancer cell and can either operate as driver or passenger mutations. The role of driver status missense mutated genes was revealed through the Chi-Square test, Cramer's V, Odds Ratio, and Polynomial Regression Analysis. The cBIO, INTOGEN, COSMIC, and Venny bioinformatics tools facilitated in the acquisition of driver missense mutated genes for each stage. While the Chi-Square test and Cramer's V demonstrated a strong association between a missense mutated gene having a driver status and the progression of disease, the Odds Ratio test illustrated driver status missense mutated genes present in more than one stage are a greater relative risk for the development of each stage. Additionally, a missense distribution less than or equal to 50% favored the presence of stage 1 and 2, while greater than 50% favored stage 3 and 4. An accelerated rate of change between stage 2 and stage 3 depicted in the polynomial regression models confirmed this distribution shift. Thus, an increase in the distribution of missense mutation directly corresponds to the onset of metastasis—early targeting will lead to better outcomes because drivers with low missense mutation distribution will be prevented from "setting the stage" for distant metastasis.

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