PLEKHA7: Assessing Locational Responses to Induced Cellular Stress to Uncover Junctional Mechanisms in Colorectal Cancer

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Carcinomas are cancers originating in epithelial cells that cover the lining of internal organs or the external skin, and whose study remains significantly relevant in today's field of medicine, as over 90% of all cancers diagnosed are defined as carcinomas. The principles of epithelial cell homeostasis and junctional mechanisms are critical to understanding the epithelial cell's responses to the mechanical, oxidative, genotoxic, and metabolic stresses of cancer. As such, the purpose of this study was to identify the responsive behavior of a critical junctional protein PLEKHA7 to cancer-related cellular stress and map its altered localization under such conditions to better understand how to restore its functionality in affected tissues. PLEKHA7 is known for its role as an E-cadherin–p120 catenin (p120) binding partner, but recent studies have revealed its critical role in recruiting the microprocessor complex (DROSHA, DGCR8) to the zonula adherens (Kourtidis, A., & Anastasiadis, P.). Through this mechanism, PLEKHA7 regulates levels of a set of miRNAs to suppress expression of mRNAs that promote cellular transformation, thus maintaining the normal epithelial phenotype. Lower levels of junctional PLEKHA7 in cancerous epithelial cells suggest disrupted cellular homeostasis, leading to anchorage independent cell growth and other abnormal cell behaviors. Immunofluorescent staining revealed co-localization of PLEKHA7 with stress-granule proteins in the cytoplasm under conditions of stress that accompany cancer, thus suggesting the potential role of PLEKHA7 as an RNA-binding protein within these stress granules. Further analysis of PLEKHA7's intrinsic disorder profile revealed three intrinsically disordered regions, a primary characteristic of RNA-binding proteins.

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