Biography

Cimona Vaughn Hinton received her B.S. in Chemistry from the University of Maryland Eastern Shore in 2000 and her Ph.D. in Biochemistry in 2005 from Meharry Medical College studying BRCA1 tumor suppressor localization, which was funded by a Ruth L. Kirschstein National Research Service Award (F31). She completed postdoctoral training at Beth Israel Deaconess Medical Center and Harvard Medical School in tumor biology and experimental medicine in 2008. Dr. Hinton is jointly appointed as Associate Professor in the Department of Biological Sciences and the Center for Cancer Research and Therapeutic Development at Clark Atlanta University, a member institution of the historically black consortium Atlanta University Center. Dr. Hinton’s research bridges biochemistry and cancer biology, and the lab studies two major overarching projects: cannabinoid antagonism of cancer movement and migration; and (ii) inflammatory signaling in cancer progression. Dr. Hinton’s work is funded by the National Institute of General Medical Sciences (NIGMS), and has been previously supported by Research Centers for Minority Institutions (RCMI), the United Negro College Fund (UNCF), the American Association for the Advancement of Science (AAAS), and the National Science Foundation.

Abstract

“Heterodimerization of G-protein coupled receptors: A novel mechanism for targeting cancer progression”

Upon activation by stromal cell derived factor 1 alpha (SDF1α), the G-protein-coupled chemokine receptor, CXCR4, generates signals that eventually lead to the metastatic spread and survival of primary tumor cells in distal organs. Indeed, elevated expression of CXCR4 protein in tumor tissues correlates with the propensity to metastasize, and an overall prediction of poor survival. CXCR4 can form homodimers with CXCR4 or can heterodimerize with unrelated G-protein coupled receptors. As a result, individual receptors that are heterodimerizing can result in a dimer that amplifies signaling, or is unable to signal, although each receptor binds its respective ligand. Therefore, heterodimerization causes functional desensitization; in the context of cancer therapeutics, CXCR4 signaling and subsequent functions can be reduced via desensitization through heterodimeric association with other receptors, thereby inhibiting CXCR4-generated signals that would otherwise lead to metastasis. Thus, antagonizing the function of CXCR4 through heterodimerization could be a rational approach to the prevention and management of metastatic cancer, and could be an effective alternative to current therapeutics involving neutralizing antibodies or antagonists against CXCR4, both of which have undesirable consequences. Considering that cannabinoid receptor CB2, a GPCR, reduces cancer proliferation and metastatic spread, a heterodimer of CXCR4/CB2R could potentially attenuate responses triggered individually by CXCR4 or CB2R, without the side effects experienced with the use of receptor antibodies or antagonists, especially in situations where both receptors are expressed on the same tumor cells. We will demonstrate that receptor heterodimerization could form the molecular basis for decreasing CXCR4-mediated signaling, and therefore, cell migration.