

様式 8

論 文 内 容 要 旨

題目

BIG3 Inhibits the Estrogen-Dependent Nuclear Translocation of PHB2 via Multiple Karyopherin-Alpha Proteins in Breast Cancer Cells

エストロゲン受容体陽性乳がん細胞において、BIG3は複数のKaryopherin- α を介したPHB2のエストロゲン依存性核移行を阻害する

著者

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内容要旨

We recently reported that brefeldin A-inhibited guanine nucleotide-exchange protein 3 (BIG3) binds Prohibitin 2 (PHB2) in cytoplasm, thereby causing a loss of function of the PHB2 tumor suppressor in the nuclei of breast cancer cells. However, little is known regarding the mechanism by which BIG3 inhibits the nuclear translocation of PHB2 into breast cancer cells. Here, we report that BIG3 blocks the estrogen (E2)-dependent nuclear import of PHB2 via the karyopherin alpha (KPNA) family in breast cancer cells. We found that overexpressed PHB2 interacted with KPNA1, KPNA5, and KPNA6, thereby leading to the E2-dependent translocation of PHB2 into the nuclei of breast cancer cells. More importantly, knockdown of each endogenous KPNA by siRNA caused a significant inhibition of E2-dependent translocation of PHB2 in BIG3-depleted breast cancer cells, thereby enhancing activation of estrogen receptor alpha (ER α). These data indicated that BIG3 may block the KPNAs (KPNA1, KPNA5, and KPNA6) binding region(s) of PHB2, thereby leading to inhibition of KPNAs-mediated PHB2 nuclear translocation in the presence of E2 in breast cancer cells. Understanding this regulation of PHB2 nuclear import may provide therapeutic strategies for controlling E2/ER α signals in breast cancer cells.