An Epigenetic Factor, CHD7, Inhibits Migration of Metastatic Breast Cancer Cells

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Breast cancer (BC) is the second leading cause of cancer death for women. BC lethality is mainly caused by metastasis. Identification of factors controlling BC metastasis is crucial for development of new treatments for BC. My project aims to test the role of CHD7 in suppressing BC metastasis using multiple BC cell lines. CHD7 encodes an epigenetic factor that remodels nucleosomes in an ATP-dependent manner. Few studies in the literature have tested the activity of any chromatin remodeling factors, including CHD7, in regulating BC metastasis. First, I find that CHD7 is highly expressed in a low-metastatic BC cell line (Mcf-7), while its expression is much reduced in high-metastatic lines (MDA-MB-468 and MDA-MB-231). Intriguingly, CHD7 is mainly localized in the cytoplasm of MDA-MB-468 and MDA-MB-231 cells, in contrast to its nuclear localization in Mcf-7 cells. A large part of the cytoplasmic CHD7 is localized within lysosomes, and inhibition of lysosomes by chloroquine increases the level of CHD7. These results explain the low expression level of CHD7 in high-metastatic BC cell lines. Next, reducing CHD7 expression by siRNA knockdown significantly increases migration of MDA-MB-468 cells, supporting a role of CHD7 in repressing BC cell metastasis. Finally, treatment of MDA-MB-468 cells with chloroquine, which inhibits lysosomes, significantly reduces cell migration partly through increasing the CHD7 level. In conclusion, my study provides multiple lines of evidence to support the hypothesis that CHD7 is a BC metastasis suppressor. I also showed for the first time that the level of CHD7 can be modulated by a clinical drug, chloroquine. This new action of chloroquine has strong clinical relevance in repressing BC metastasis, warranting further preclinical/clinical tests.

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