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Human HOX genes are expressed in a spatio-temporal fashion during embryogenesis and early development where they act as master transcriptional regulators. HOX genes are also expressed in normal adult cells, potentially in a tissue specific manner involving maintenance of the normal phenotype. In selected oncogenic transformations, mis-expression of many HOX genes have been shown, indicating an involvement of these transcriptional regulators in carcinogenesis and metastasis. Utilising quantitative real-time RT-PCR assays, the expression of 20 HOX genes and two known HOX co-factors, PBX1B and MEIS1, were analysed in human melanoma and breast cancer cell lines, comparing results against non-malignant cells. Alterations in HOX gene expression were observed for all malignant cells examined, with some dysregulated transcript levels seemingly random, and the expression of other HOX genes apparently following the same patterns in both skin and breast cancer establishment. Furthermore, HOX gene expression was correlated with the invasive capacity of the cells. The expression of the HOX co-factors PBX1B and MEIS1 showed no marked changes from the non-malignant to the malignant phenotypes, further indicating that it is dysregulated HOX gene expression, rather than dysregulated gene expression of HOX co-factors, that potentially commit the cell to re-differentiate and undergo oncogenic transformation.