Abstract

Extracellular signal regulated kinase (ERK) is a key molecule located in the Mitogen activated protein kinase (MAPK) pathway responsible for several cell process in cancer including cell invasiveness which primarily involved breakdown of extracellular matrix. Matrix metalloproteinase facilities cell invasiveness by degrading Gelatinase which are again differentially regulated by Integrins, a family of receptors. Our study analyses the role of ERK in modulating cell invasiveness in Cancer. The study is divided into 3 parts where role of ERK1/2 has been analysed in Breast and Melanoma cancer cell lines, Mice model and clinical specimens. There is an additional part where the role of ERK 1 and ERK 2 has been analyzed separately in modulating cancer cells. The study involves downregulation of ERK through potent inhibitors and ERK1/2 siRNA and its effect on MMP2 and MMP9 and Integrin alpha 5 and beta 1 molecules in breast and melanoma cancer cell lines. The mice model includes the same downregulation with only the clinically proven potent inhibitor U0126. ERK1/2 expression and activity were checked in the clinical specimens and correlated with MMP2 and MMP9 along with other clinic-pathological inhibitors. There was a considerable change in MMP 9 and MMP 2 after ERK1/2 inhibition which was also reflected in the downstream process of the MAP kinase pathway both in the breast and melanoma cancer cell line which was supported by the mice model. In all three cell lines there is a possible interdependency between the isoform ERK1 and ERK2 and both the isoforms has distinguishable individual role with respect to cell invasiveness. Combinatorial inhibition of ERK1 and ERK2 has more effect than individual inhibition of ERK1 or ERK 2 separately. There might be a direct correlation of ERK activity and MMP2 and MMP 9 activity with targeted modulation of ERK. The results in the clinical specimens from Eastern India supported our hypothesis of possible role of overexpression of ERK1/2 in breast cancer progression. Over all our studies with ERK 1/2 if properly interpreted can be used in clinical and therapeutic management of Cancer.