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Meeting abstract

Signaling induced by PAR1 on breast cancer cell lines is correlating with its invasive potential

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Background

PAR1 (Protease-Activated Receptor 1) is an oncogene that has long been proposed to be involved in the invasive and metastatic process of breast cancer. PAR1 activates Mitogen-Activated Protein Kinases (p44 and p42 also called ERK1/2) leading to cell proliferation. It has been suggested hyperexpression of the MAP Kinases may be a key process in the metastatic potential of breast cancer. PAR1 signaling mechanisms are not completely understood. The aim of this study was to determinate ERKs activation in relation to PAR1 expression leading to tumor progression on breast cancer cell lines.

Materials and methods

We assayed by immunoblot PAR-1 and ERKs expression and activation on a highly invasive MDA-MB-231 and minimally invasive MCF-7 breast cancer cell lines. We also determined PAR1-induced cell proliferation and invasion. To determine ERKs specific contribution to tested activities, we used U0126 MEK inhibitor. Additionally we evaluate their ability to growth on 3D cultures. Two tailed Student's test was used to compare data. P values ≤ 0.05 were considered significant.

Results

We found invasive cells overexpressed PAR1, and when stimulated with thrombin (1 nM), we observed a selective and time independent ERK1 activation ($P < 0.05$). Cell proliferation and invasion were also significantly increased (83% ± 0.05% stimulation above media control, $P < 0.02$; and 87% ± 0.05% cell invasion compared with media control, $P < 0.05$ respectively). All activities were blocked significantly when assayed in the presence of U0126 ($P < 0.0001$). Spheroid's size was elevated upon thrombin stimulation and elongated in shape. In contrast in the low invasive cell line we found very low levels of PAR1. We observed thrombin-induced an up-modulation of ERKs activation. ERK1 showed a maximal activation at 30 minutes, while ERK2 was barely activated in a time independent way. No significant increase was found on cell proliferation or invasion. Neither between spheroid's sizes, and they were all round.

Conclusion

Our data suggest different modulation of signaling pathways induced by PAR1 leading to tumor progression in breast cancer.

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