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Dysregulated protease activated receptor 1 (PAR-1) promotes metastatic phenotype in breast cancer through HMGA2

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As the majority of patients with basal-like breast carcinoma present with invasive, metastatic disease that do not respond to available therapies, it is essential to identify new therapeutic targets that impact invasion and metastasis. Protease-activated receptor 1 (PAR1), a G-protein coupled receptor has been shown to act as an oncogene, but underlying mechanisms are not well understood. Here, we show that ectopic expression of functionally-active PAR1 in MCF-7 cells induced a hormone-refractory, invasive phenotype representative of advanced basal-like breast carcinoma that readily formed metastatic lesions in lungs of mice. PAR1 was found to globally upregulate mesenchymal markers, including vimentin a direct target of PAR1 and down-regulate the epithelial markers including E-cadherin, as well as estrogen receptor. In contrast, non-signaling PAR1 mutant receptor did not lead to invasive phenotype. PAR1 expression increased spheroid formation and the level of stemness markers and self-renewal capacity in human breast cancer cells. Here, we identified HMGA2 (high mobility group A2) as important regulator of PAR1-mediated invasion. Inhibition of PAR1 signaling suppresses HMGA2 driven invasion in breast cancer cells. HMGA2 gene and protein are highly expressed in metastatic breast cancer cells. Overall, our results show that PAR1/HMGA2 pathway may present a novel therapeutic target.

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Indicating patients with breast cancer using infrared thermography

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Early detection of breast cancer involves two questions: The early diagnosis and screening. In early diagnosis, the first signs and symptoms of cancer are recognized by the patient or health professional before the advance of the disease. On the other hand, in screening, tests are performed in asymptomatic individuals in order to identify those with abnormalities suggestive of breast cancer before any symptoms and/or sign of this disease. Screening is divided into two types: The opportunistic and the organized. In opportunistic screening, tests are requested unsystematically in routine consultations. Differently happens in organized screening, where tests are ordered systematically to a population at risk-the target population-within a structured program. One of the tests used in screening is mammography. Considered the gold standard, mammography reduces by approximately 30% mortality rate. But mammography equipment forms the image by radiation of the breast, and each time the breast is exposed to X-rays, the risk of cancer increases by 2% and premenopausal breast is even more sensitive to radiation. Because of the difficulty to obtain access to the most appropriate screening test for breast cancer, the mammography, especially for women with low levels of education and socioeconomic status, it is necessary to define precisely the target population for an organized screening program. In this sense, the thermography has been considered a promising method of screening for the detection of breast cancer, for generating images which reveal the distribution of temperature on the surface of both breasts.

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