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Area tematica

Breast cancer

Titolo

Differential gene expression patterns in HER2 positive metastatic breast cancer patients according to hormone receptor status

Testo

Background: HER2 positive breast cancer (HER2+ BC) is a heterogeneous disease. Presenting features, patterns of recurrence and survival of HER2+ BC can differ according to hormone receptors (HR) status. The purpose of this study is to highlight different gene profile and molecular pathways between HR+ and HR- metastatic HER2+ BCs.

Material and Methods: 34 HER2+ metastatic BC patients were included: 18 patients with HR+/HER2+ and 14 with HR-/HER2+. Data regarding tumor characteristics, treatment information and clinical outcomes were collected. The expression of 770 genes and 13 molecular pathways were evaluated by means of *Nanostring PanCancer pathway panel* performed on BC formalin-fixed paraffin-embedded tissues from diagnostic core biopsy or surgical resection specimen.

Results: Gene expression analysis identified 118 genes with significantly different expression in the two cohorts. All but one of these genes were over-expressed; only the gene CACNG6 was down-regulated in HR+/HER2+ group. In particular, 93 genes were over-expressed in HR-/HER2+ while 24 were overexpressed in HR+/HER2+. Most of these genes encoded growth factors, pro- or anti-inflammatory interleukins and DNA repair factors. 62% of these genes were involved in PI3K, MAPK and RAS pathways (32, 22 and 18, respectively). PI3K, MAPK and NOTCH pathways were differently expressed between HR+/HER2+ and HR-/HER2+ ($p=0.003$, $p=0.0018$, $p=0.02$, respectively). All these three pathways were overexpressed in HR-/HER2+ BC. In particular, all the significantly different expression

genes in NOTCH pathways were overexpressed in HR-/HER2+ group.

Conclusions: This genome expression analysis identified a gene expression profile able to differentiate HR+ versus HR- HER2+ metastatic BC. The overexpression of PI3K, MAPK and NOTCH pathways in HR-/HER2+ BC could justify its more aggressive behaviour. The validation of this HER2+ BC profile needs further investigation.

Parole Chiave

1. HER2 positive metastatic breast cancer
2. gene expression profile
3. PanCancer

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