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Sample parameters affecting the clinical relevance of RNA biomarkers in translational breast cancer research.

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Source

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Abstract

In the frame of translational breast cancer research, eligibility criteria for formalin-fixed paraffin-embedded tissue (FFPE) material processing for gene expression studies include tumor cell content (TCC) and sample site (primary vs metastatic tumors). Herein we asked whether the observed differences in gene expression between paired samples with respect to TCC and sample site also have different clinical significance. We assessed ESR1, ERBB2, MAPT, MMP7, and RACGAP1 mRNA expression with real time PCR in paired samples before (NMD) and after macrodissection (MD) from 98 primary tumors (P(MD), P(NMD)) and 72 metastatic lymph nodes (LN(MD), LN(NMD)), as well as from 93 matched P (mP) and LN (mLN). TCC range was 2.5-75 % in the NMD series and 28-98 % in the MD and in the mP/mLN series. The prognostic effect of these markers, individually or in clusters, remained stable between paired P(MD/NMD). In comparison, cluster classification failed in the LN(NMD) group with lower TCC. In the mP/mLN cohort, RACGAP1 mRNA expression was of prognostic significance when tested in mLN samples ($p < 0.001$). Similarly, luminal B, HER2, and triple negative tumors were of dismal prognosis when classified in the LN component of the same series (mLN, overall survival: $p = 0.013$, $p = 0.034$, and $p = 0.007$, respectively). In conclusion, the clinical relevance of the RNA markers examined may be affected by TCC in metastatic LN samples but not in primary tumors, while it differs between primary tumors and matched metastases. These data will facilitate the design of translational studies involving FFPE sample series.