



Identification of potential prognostic biomarkers for node-negative breast tumours by proteomic analysis: a multicentric 2004 national PHRC study

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Résumé en anglais

We used a 2D-electrophoresis (2-DE) proteomic approach to identify novel biomarkers in node-negative breast cancers. This retrospective study focused on a population of patients with ductal pN0M0 tumours. A subset of patients who developed metastases and in whose tumours were found high levels of uPA and PAI-1 (metastatic relapse, MR: n=20) were compared to another subset in whom no metastatic relapse occurred and whose tumours were found to have low levels of uPA and PAI-1 (no relapse, NR: n=21). We used a 2-DE coupled with MS approach to screen cytosol fractions using two pH-gradient scales, a broad scale (3.0-11.0) and a narrower scale focussing in on a protein rich region (5.0-8.0). This study was conducted on 41 cytosol specimens analyzed in duplicate on two platforms. The differential analysis of more than 2,000 spots in 2-DE gels, obtained on the two platforms, allowed the identification of 13 proteins which were confirmed by western blotting. Two proteins, GPDA and FABP4 were down-regulated in the MR subset whereas all the others were up-regulated. An in silico analysis revealed that GMPS (GUAA), GAPDH (G3P), CFL1 (COF1) and FTL (FRIL), the most informative genes, displayed a proliferation profile (high expression in basal-like, HER2+ and luminal B molecular subtypes). Inversely, similar to FABP4, GPD1 [GPDA] displayed a high expression in luminal A subtype, a profile characteristic of tumour suppressor genes. Despite the small size of our cohort, the 2-DE analysis gave interesting results which were confirmed by the in silico analysis showing that some of the corresponding genes had a strong prognostic impact in breast cancer, mostly because of their link with proliferation: GMPS, GAPDH, FTL and GPD1. A validation phase on a larger cohort is now needed before these biomarkers could be considered for use in clinical practice.

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