Microarray analysis of Ewing's sarcoma family of tumours reveals characteristic gene expression signatures associated with metastasis and resistance to chemotherapy.

Abstract:
In Ewing's sarcoma family of tumours (ESFT), the clinically most adverse prognostic parameters are the presence of tumour metastasis at time of diagnosis and poor response to neoadjuvant chemotherapy. To identify genes differentially regulated between metastatic and localised tumours, we analysed 27 ESFT specimens using Affymetrix microarrays. Functional annotation of differentially regulated genes revealed 29 over-represented pathways including PDGF, TP53, NOTCH, and WNT1-signalling. Regression of primary tumours (n=20) induced by polychemotherapy was found to be correlated with the expression of genes involved in angiogenesis, apoptosis, ubiquitin proteasome pathway, and PI3 kinase and p53 pathways. These findings could be confirmed by in vitro cytotoxicity assays. A set of 46 marker genes correctly classifies these 20 tumours as responding versus non-responding. We conclude that expression signatures of initial tumour biopsies can help to identify ESFT patients at high risk to develop tumour metastasis or to suffer from a therapy refractory cancer.