DNA microarrays reveal relationship of Ewing family tumors to both endothelial and fetal neural crest-derived cells and define novel targets.

Abstract:
Ewing family tumors (EFTs) are small round blue cell tumors that show features of neuroectodermal differentiation. However, the histogenetic origin of EFTs is still a matter of debate. We used high-density DNA microarrays for the identification of EFT-specific gene expression profiles in comparison with normal tissues of diverse origin. We identified 37 genes that are up-regulated in EFTs compared with normal tissues and validated expression of these genes in EFTs by both conventional and quantitative reverse transcription-polymerase chain reaction. The expression pattern of EFT-associated genes in normal tissues indicated a high similarity between EFTs and fetal and neuronal as well as endothelial tissues and supports the concept that a primitive neural crest-derived progenitor at the transition to mesenchymal and endothelial differentiation is transformed in EFTs. EFT-associated genes could be used for molecular discrimination between EFTs and other small round blue cell tumors and clearly identified a cell line (SK-N-MC) that was initially established as neuroblastoma as being an EFT. Ectopic expression of the EFT-specific EWS-FLI1 fusion protein in human embryonic kidney (HEK293) cells was not sufficient to induce the complete EFT-specific gene expression signature, suggesting that the
EFT-specific gene expression profile is not just a consequence of EWS-FLI1 expression but depends on the histogenetic background of the EFT stem cell.