Franck Tirode, Karine Laud-Duval, Alexandre Prieur, Bruno Delorme, Pierre Charbord, Olivier Delattre (2007 May 8)

**Mesenchymal stem cell features of Ewing tumors.**
*Cancer cell* : 421-9

**Summary**

The cellular origin of Ewing tumor (ET), a tumor of bone or soft tissues characterized by specific fusions between EWS and ETS genes, is highly debated. Through gene expression analysis comparing ETs with a variety of normal tissues, we show that the profiles of different EWS-FLI1-silenced Ewing cell lines converge toward that of mesenchymal stem cells (MSC). Moreover, upon EWS-FLI1 silencing, two different Ewing cell lines can differentiate along the adipogenic lineage when incubated in appropriate differentiation cocktails. In addition, Ewing cells can also differentiate along the osteogenic lineage upon long-term inhibition of EWS-FLI1. These in silico and experimental data strongly suggest that the inhibition of EWS-FLI1 may allow Ewing cells to recover the phenotype of their MSC progenitor.

Odette Mariani, Caroline Brennetot, Jean-Michel Coindre, Nadège Gruel, Carine Ganem, Olivier Delattre, Marc-Henri Stern, Alain Aurias (2007 Apr 10)

**JUN oncogene amplification and overexpression block adipocytic differentiation in highly aggressive sarcomas.**
*Cancer cell* : 361-74

**Summary**

The human oncogene JUN encodes a component of the AP-1 complex and is consequently involved in a wide range of pivotal cellular processes, including cell proliferation, transformation, and apoptosis. Nevertheless, despite extensive analyses of its functions, it has never been directly involved in a human cancer. We demonstrate here that it is highly amplified and overexpressed in undifferentiated and aggressive human sarcomas, which are blocked at an early step of adipocyte differentiation. We confirm by cellular and xenograft mouse models recapitulating these sarcoma genetics that the failure to differentiate is dependent upon JUN amplification/overexpression.


**Identification of typical medullary breast carcinoma as a genomic sub-group of**
basal-like carcinomas, a heterogeneous new molecular entity.

*Breast cancer research : BCR : R24*

**Summary**

Typical medullary breast carcinoma (MBC) has recently been recognized to be part of the basal-like carcinoma spectrum, a feature in agreement with the high rate of TP53 mutations previously reported in MBCs. The present study was therefore designed to identify phenotypic and genetic alterations that distinguish MBCs from basal-like carcinomas (BLC).

**Year of publication 2006**

Patricia Albanese, Marie-France Belin, Olivier Delattre (2006 Aug 16)

**The tumour suppressor hSNF5/INI1 controls the differentiation potential of malignant rhabdoid cells.**


**Summary**

Malignant rhabdoid tumours (MRT) are highly aggressive cancers of early childhood that arise in different organs or tissues. The unifying criterion for these tumours is the presence of inactivating mutations of the hSNF5/INI1 tumour suppressor gene which encodes a core subunit of the chromatin remodelling SWI/SNF complex. Using a variety of markers we analysed the phenotypic traits of MON and DEV cell lines derived respectively from an undifferentiated abdominal MRT and from a brain MRT. DEV cells express spontaneously a wide range of neural and glial markers. It can be induced to differentiate into the neural lineage following hSNF5/INI1 expression with appearance of neurite processes, strong increase of neural markers and decrease of glial markers. A less pronounced neural differentiation is also observed with MON cells, which possess more primitive polyphenotypic features with positivity for markers from the three embryonic layers. Finally, we show that the neural differentiation of rat PC12 cells in the presence of nerve growth factor (NGF) is strongly impaired when hSNF5/INI1 expression is inhibited by RNA interference. Altogether these results indicate that hSNF5/INI1 is an essential subunit for SWI/SNF-dependant induction of neural differentiation programs. Further experiments should enable documentation of whether it provides instructive or permissive signals for differentiation.