

**P002** Nanoparticles oligonucleotide complexes for the treatment of EWS/Fli-1 expressing tumours in mice.

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Fli-1 expressing tumours in mice.

Ewing sarcoma is a bone cancer afflicting mostly children.

Relatively good results are obtained using an aggressive therapy but in 30% of patients metastasis are present at the diagnosis and the prognosis is then bad. It is widely recognized that the causal factor is a chromosome translocation creating a fusion oncogene made of the 5' part of EWS and the 3' part of Fli-1. We have used antisense oligonucleotides (ODN) and siRNAs associated to biocompatible polyisobutylcyanoacrylate nanoparticles to target in vivo the EWS/Fli-1 mRNA type 1 junction, present in 50% of patients, which is located only in cancer cells. As a cellular model we have used murine NIH3T3 cells expressing the human EWS/Fli-1 oncogene. These cells induce the formation of tumours after subcutaneous grafting to nude mice. Using nanocapsules, which contain oligonucleotides in their aqueous choir, we have shown that phosphorothioates ODN as well as siRNAs inhibit the tumour growth with specificity. Using nanospheres coated with chitosan where the nucleic acid is externally bound we have shown that ODN are efficient to inhibit tumour growth either by intratumoural or by intravenous injections. When working with the same cells in culture we have observed a cytoplasmic penetration of oligonucleotides when using nanocapsules but not when using nanospheres. We propose that this type of therapy might be used in addition of the classical one to additionally stabilize micro metastasis.