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Biological effects of therapeutic siRNA against TMPRSS2-ERG fusion oncogene for the treatment of prostate cancer

Giorgia Urbinati
National Research Scientific Centre, France

Prostate cancer is one of the most common tumors in men worldwide and the second leading cause of death among all cancer types in western countries.

Combined with surgery, hormone therapy is the first line treatment administrated for hormone-dependent prostate cancers, however when the pathology turns into a castration independent phase, the treatments become less specific. New specific molecular targets would then be highly useful to develop innovative personalized medicines. Among these targets Tomlins *et al.* decrypted in 2005 a chromosomal rearrangement resulting in the fusion of TMPRSS2 gene with members of the E26 Transformation-Specific (ETS) family and in particular E26 related gene (ERG). The TMPRSS2-ERG genomic fusion is found in 50% of localized and 30% of metastatic prostate cancers and this particular chromosomal rearrangement lead to more aggressive cancer phenotypes and worst cancer-specific survival rate.

Because TMPRSS2-ERG fusions were found to be involved in carcinogenesis and tumor development, we conceived new possible therapeutic siRNAs specifically directed against TMPRSS2-ERG oncogene. ERG mRNA and protein levels were dramatically down-regulated after siRNA transfection in TMPRSS2-ERG positive cell line. Microarray analysis showed regulation of apoptosis related genes by TMPRSS2-ERG siRNA which was confirmed by Western blot and fluorescent kit assays and regulation of other genes involved in intracellular protein trafficking. In addition, cell viability was compromised and angiogenesis appeared to be affected. The siRNAs are now bioconjugated with lipids to obtain nanoparticles in order to evaluate their potential antitumor effects *in vivo*.

Biography

Giorgia Urbinati obtained the Pharm.D diploma in 2006 from the faculty of Pharmacy in Turin (Italy). She obtained her Ph.D. degree in 2010 working in the research unit of Couvreur (UMR CNRS 8612- Faculty of Pharmacy- Paris XI) developing new liposomal formulations encapsulating anticancer drugs for the treatment of breast cancer and multiple myeloma. She worked in Mader's laboratory (IRIC- University of Montreal-Canada) investigating the role of Raldh3 in the development of breast cancer and she is actually working on new methods delivering siRNAs *in vivo* at Gustave Roussy's Institute.

Giorgia.URBINATI@igr.fr