

PROPOSITIONS

belonging to the thesis

MicroRNAs in the Tumor Biology of Soft Tissue Sarcomas

1. MiRNA expression profiling of soft tissue sarcomas can aid in the diagnostic decision making and lead to the identification of novel therapeutic targets. (*this thesis*)
2. Myxoid/round cell liposarcomas have a miRNA expression profile distinct from other liposarcoma subtypes, lipomas and normal fat. (*this thesis*)
3. The myxoid/round cell specific FUS-DDIT3 fusion protein induces miR-497 and miR-30a expression, which in turn regulate the IGF1R pathway. (*this thesis*)
4. Overexpression of miR-17, miR-20a and miR-222 in GIST cell lines strongly inhibits cell proliferation, interferes with cell cycle progression, induces apoptosis and downregulates both *KIT* and *ETV1*, two essential GIST oncogenes. (*this thesis*)
5. In soft tissue sarcomas, hypoxia responsive miR-210 and miR-485-5p regulate HIF3 α , thereby fine-tuning its expression. (*this thesis*)
6. MicroRNA expression profiling holds many advantages over mRNA expression profiling in human cancers. (Lu J et al. *Nature*. 2005;435:834-8. Rosenfeld N et al. *Nat Biotechnol*. 2008;26:462-9)
7. MiRNA expression profiles correlate with clinical and biological characteristics of tumors, including tissue type, differentiation status, aggressiveness and response to therapy. (Calin GA and Croce CM. *Nat Rev Cancer* 2006;6:857-66)
8. An increased understanding of fundamental miRNA biology, improved bioinformatics, and directed *in vivo* targeting while minimizing off-target effects and toxicity will be required for successful translational application. (Nana-Sinkam SP and Croce CM. *Clin Pharmacol Ther* 2013;93:98-104)
9. Combining multiple targeted drugs that have distinct mechanisms of action is more effective than sequential treatment at preventing therapy resistance in cancer. (Komarova NL and Boland CR. *Nature* 2013;499:291-92; Bozic I. et al. *eLIFE* 2013; e00747)
10. MicroRNAs: What they lack in size, they make up for in attitude.
11. Nobody makes a greater mistake than he who did nothing because he could do only a little. (Edmund Burke)