

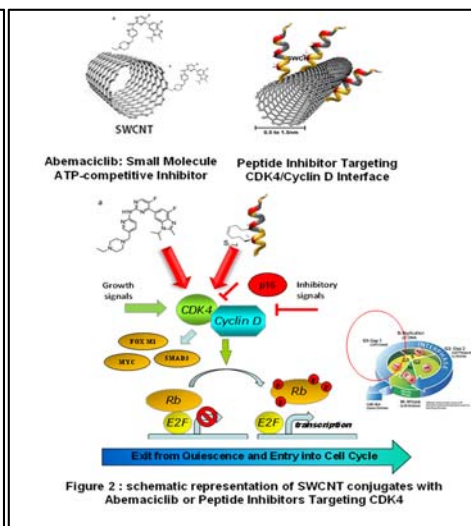
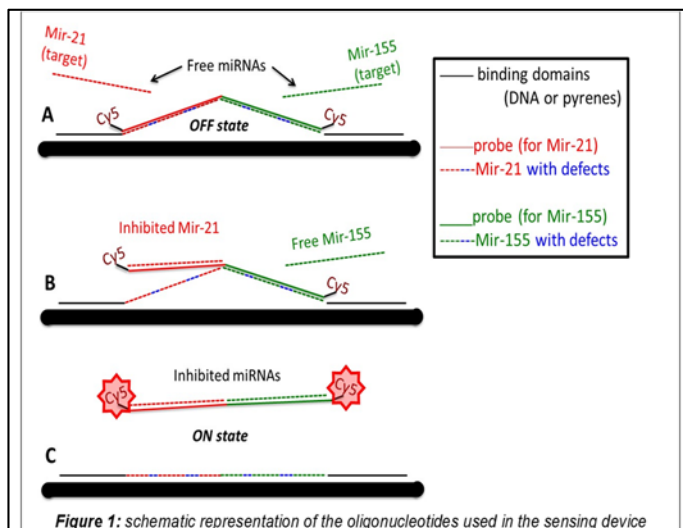
Topic for Master Thesis

February – August 2021

Title of the research topic	MicroRNA detection and therapeutic targeting of CDK4 kinase in pancreatic cancer with functionalized single-walled carbon nanotubes
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Scientific Project :

We propose to design and develop SWNT conjugates able to detect 2 miRNAs that are overexpressed in pancreatic cancer (PC), and deliver therapeutic peptides and small molecule inhibitors for targeted inhibition of CDK4 kinase biomarker of PC. The project will involve chemical synthesis, photophysical, chemical and biological characterization of SWNT conjugates in vitro and in cultured cells. To detect simultaneously the 2 miRNA, we will use singlewall carbon nanotubes (SWNTs), modified with a construction made of oligonucleotides (Fig. 1) : i) a probe, modified at both ends with a dye emitting light in the biological window, ii) two sequences containing domains that recognize the targeted miRNAs and recognize the probe partially, and iii) two additional domains that bind the SWNT (in black in fig. 1). In this design dye fluorescence (FL) will be quenched, until target miRNAs are detected through release of the probe from the SWNT, leading to a strong and specific FL signal of the dyes and a modulation of the FL signal of the SWNT in the near infrared. A second set of functionalized SWNT will be prepared for therapeutic purposes, through adsorption or conjugation of peptides or small molecule inhibitors targeting CDK4 through photo- or thermos-sensitive linkers (Fig. 2). Therapeutic peptides and small molecules will be selectively released when SWNTs are heated under resonant laser irradiation. The outcome of this project will enable to establish a proof-of-concept for theragnostics of pancreatic cancer targeting two different sets of relevant biomarkers thanks to combined and complementary sensing and targeting approaches.



Techniques used : DNA synthesizer, MALDI-TOF, sonication/centrifugation, UV-visible and near infrared optical spectroscopy (absorption, Raman, fluorescence)

Recent publications related to the topic :

M. Peyressatre M et al., *Biotechnology J.* 1900474 (2020) ; M. Pellerano M., M.C. Morris, *ChemBioChem* 4, 605 (2019) ; G. Bepete et al, *ACS Nano* 12, 8606 (2018)