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A contemporary approach in treating pancreatic cancer with therapeutic MicroRNAs identified using computational appraoch.

Jasjit K Banwait and Dhundy R Bastola
College of Information Science &Technology, University of Nebraska, USA

Cancer research has generated valuable body of knowledge about the mutations that play significant role in cell proliferation. These mutations have led to gain of function in oncogenes whereas detrimental loss of function in tumor suppressor genes. Pancreatic ductal adenocarcinoma (PDAC) is an aggressive and exceptionally fatal cancer. Only 6% of patients survive more than 5 years after diagnosis. Gemcitabine is the primary drug used to treat PDAC with a mere 6.8 month survival rate as monotherapy, and up to 11.1 months as combination therapy. A major barrier to PDAC treatment is that chemoresistance eventually renders conventional drug therapy ineffective. Hence, new, therapies are urgently needed to combat this deadly disease. Use of microRNA (miRNA) has recently emerged as a promising alternative therapeutic approach. These miRNAs are ~21 nucleotides long non-protein-coding RNAs that post-transcriptionally regulate gene expression through translational repression and/or mRNA degradation mechanism. Numerous studies support the role of miRNA dysregulation in the poor prognosis, resistance, invasion, metastasis, and epithelial–mesenchymal transition in PDAC. However, identifying new miRNAs that can treat PDAC and the mRNA(s) which are regulated to provide the therapeutic benefit remains a challenge. Several computational studies have been conducted to identify miRNAs and genes involved in PDAC. In this study, we developed a computational framework to integrate knowledgebases (miRNA-mRNA interaction, gene expression, biological process and metabolic pathway data) and identify candidate therapeutic miRNA(s). Our long-term goal is to facilitate the efficient discovery of novel therapeutic miRNA through computational approaches that build on biological insights and data.

jbanwait@unomaha.edu

Post-PCR DNA modification using metal-free click chemistry and its applications in cancer cell recognition

Ke Wang, Kaili Ji, Danzhu Wang, Weixuan Chen, Yueqin Zheng, Chaofeng Dai, and Binghe Wang
Department of Chemistry and Center for Diagnostics and Therapeutics, Georgia State University, USA

DNA molecules endowed with extra functional groups are very useful in a wide variety of applications including sensing, developing new therapeutics and in vitro aptamer selection. Conceivably, such DNA modifications can be achieved by first incorporating a functional group handle, which allows further manipulations, on a natural nucleotide base and then conduct synthesis using either chemical methods or a DNA polymerase. In the latter case, it requires that a sidechain handle be tolerated by the DNA polymerase used. Herein we describe polymerase-mediated incorporation of trans-cyclooctene modified thymidine triphosphate. Subsequently, the trans-cyclooctene group was reacted with a tetrazine tethered to other functional groups through a fast copper-free click reaction. The utility of this DNA functionalization method was demonstrated with the incorporation of a boronic acid group and a fluorophore. Boronic acid modified DNA molecules were further applied in aptamer selection targeting cancer cells.

kwang10@gsu.edu