INHIBITION OF A LONG NON-CODING RNA AS A NOVEL THERAPY FOR NEUROBLASTOMA

BIOMARKED, a consortium of research laboratories of Ghent University, member of the Cancer Research Institute Ghent (CRIG), is seeking partners to bring this technology to market, preferable through a licensing strategy.

Introduction

Neuroblastoma is a pediatric cancer, originating from immature sympathetic nervous system cells. Although the incidence is low, the mortality rate of this malignancy is high, accounting for 15% of all children's cancer deaths. To boost the survival rate, patients are stratified in risk groups with different treatment regimes. At present, the stratification is based on age at diagnosis, location of the primary tumor and degree of metastasis. Several genetic markers (*MYCN* amplification, 1p and 11q deletion and DNA ploidy), are also taken into account. While low risk patients have excellent survival rates, patients in the high-risk group have very poor survival rates despite aggressive multimodal treatment. Novel insights in the genetic basis of high-risk neuroblastoma patients is therefore essential in order to better understand the course of the disease and identify novel targets for therapeutic intervention. While only 2% of our genome encodes for proteins, 80-85% of the genome is actively transcribed, resulting in thousands of so-called non- coding RNAs. Long non-coding RNAs form the largest class and have been shown to play key roles in gene expression regulation. Notably, lncRNA expression can be extremely cancer-type specific, suggesting they may play an essential role in cancer cell survival. Therefore, they are considered as novel candidate therapeutic targets. Today, only a handful of lncRNA genes have been implicated in neuroblastoma.

Technology

Researchers at Ghent University identified a particular long non-coding RNA (lncRNA) specifically upregulated in neuroblastoma cells as compared to other cancer cells. High expression of the NESPR lncRNA correlates with a lower survival probability. Perturbation of NESPR was performed through antisense oligonucleotides with an LNA modification. Inhibition of this lncRNA in neuroblastoma cells using ASO therapy leads to a reduction in cell growth and induction of apoptosis and is a novel therapeutic strategy in the treatment of neuroblastoma. In vitro validation on cell lines SKNBE(2c) and NGP, was performed.. Two assays have been set up for pPCR based quantification of the NESPR expression.

Taken together, these findings demonstrate the potential of inhibition of LINC00682 as a new therapy for Neuroblastoma tumors, validation of ASOs targeting this neuroblastoma specific lncRNA were validated in vitro and assays are available for quantification of the lncRNA by qPCR.

Applications

- novel therapy for Neuroblastoma patients using an inhibitor of functional expression of LINC00682. The inhibitor can be an antisense oligomer, a gapmer, a shRNA, a siRNA, a CRISPR, a TALEN, or a Zinc-finger nuclease. Current validations were obtained with a LNA modified ASO.
- in vitro method of identifying neuroblastoma suitable for treatment with an inhibitor of functional expression of LINC00682

Advantages

+ LINC00682 is neuroblastoma specific, less side effects are expected
+ Mechanism of action is identified

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State of development
Pre-clinical validation completed: In vitro and vivo proof-of-concepts were obtained

Partnership
Ghent University is seeking a partner to further bring the technology to market, this can be done in a research and development collaboration, our aim is to license the technology.

Intellectual property
Patent application in PCT phase: “Inhibition of a lncRNA for treatment of neuroblastoma” EP18154813.2
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References
1. Rombaut D et al., Integrative analysis identifies lincRNAs up- and downstream of neuroblastoma driver genes. Sci Rep. 2019 Apr 5;9(1):5685. doi: 10.1038/s41598-019-42107-y

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