MATWIN
MATURATION & ACCELERATING TRANSLATION **WITH INDUSTRY**

TECHNOLOGY OFFER

SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

EPISENS

Sensitization of glioblastoma cells to anticancer treatments via high-resolution epigenetic reprogramming

CONTEXT & BACKGROUND

Epigenetics refers to heritable and reversible changes of gene expression that do not derive from alterations of the nucleotide sequence of DNA. In particular, epigenetic modifications include the DNA methylation and histone post-translational modifications. These different processes (methylation, acetylation and others) are dynamic phenomenon within the cells that involve a high number of proteins in a **network of interactions**. In cancer cells, the description of the **alterations** in this network of epigenetic regulations has started. Currently, pharmaco-epigenomic constitutes a major hope for new strategies in cancer treatment.
To overcome the lack of specificity of wide-spectrum DNMT inhibitors and supported by our basic research, we focused our project on the design of **a new generation of DNMT inhibitor**, that regulate the expression of a limited set of genes. In the glioblastoma indication, we have identified a peptidic molecule that re-sensitizes glioblastoma cells to the current standard-of-care treatment (temozolomide + irradiation) and a mechanistically-related companion diagnostic. The molecular target is also relevant in other cancer types (lung, prostate, oesophagus).

INNOVATIVE COMPONENT & TECHNOLOGY

Our innovation is based on the targeting of precise protein/protein complexes from the epigenetic network that are deregulated in cancer cells.
This approach starts from the identification of the mechanism of action and the drug design and evaluation follow. The main advantages of our approach are:
1) to focus drug-candidate development on the pre-identified target,
2) to limit the off-target effects,
3) to have a companion biomarker available at a early step.

The combination of our drug product and our companion biomarker gives a new and strong rationale for the selection of the most appropriate treatment. In addition, our product position is a potentiator of the standard-of-care (i.e. not a competitor). These two parameters constitute a clear disruption with the current competitors.
The DNMT3A/ISGF3 is the first target, with GBM a primary indication.

SCOPE

SCOPE Innovative approach to increase the efficacy of anti-cancer therapy

KEYWORDS

DNA Methylation, potentiation, drug combination

OBJECTIVES

The objective is to perform the clinical proof-of-concept for a highly-specific DNMT inhibitor, targeting the DNMT3A/ISGF3 molecular complex, primarily in glioblastoma. In parallel, the relevance of the DNMT3A/ISGF3 molecular complex in other cancers

DEVELOPMENT & MATURATION STAGE

Pre-clinical proof-of-concept in vivo is obtained.
Optimization of the drug candidate and formulation is planned

INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S)

European Patent filed (March 2015) and the PCT extension submitted (March 2016), by INSERM-Transfert Exclusive license to EpiDrugs Discovery planned

TARGET POPULATION

The incidence of glioblastoma is estimated to be 115,000 new cases worldwide per year. The target population for our highlyspecific DNMT inhibitor represents 45% of the patients treated with the standard-of-care treatment.

TARGET PROFILE

Route: local delivery
Positioning: synergy with the standard-of-care

STRENGHTS & COMPETITIVE ADVANTAGES

The precise targeting represents the development of a new generation of DNMT inhibitor, with a clear differentiation over the existing inhibitors that display wide-spectrum inhibition.
- The combination of the therapeutic drug and its companion diagnostic allows to guide the rational use of the drug. The expected impact is to increase the efficacy of the current standard-of-care, in a significant fraction of patients (45%).

INDUSTRIAL APPLICATIONS & OPPORTUNITIES

The disruption of the DNMT3A/ISGF3 molecular complex in glioblastoma is the first target. The applicability to other cancers will be questioned in the forthcoming activity.
Beside this first molecular target, the concept of highly specific disruption can be expanded to newly identified complexes.

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