TITLE

Development of multifunctional RNA-based therapeutics to selectively target the stem-like glioblastoma cancer cells

DESCRIPTION

Glioblastoma (GBM) is the most frequent and aggressive primary brain tumor in adults and despite advances in surgical and medical neuro-oncology, the prognosis for patients remains dismal. A minor cell population, constituted of multipotent tumor-initiating stem-like cells (GSCs), has been recently implicated in GBM recurrence and resistance to conventional treatments. Small non coding RNAs and transcription factors governing tumor spreading, proliferation and escape from immune-surveillance have been reported to play crucial role in the maintenance of the malignant phenotype. Among transcription factors, the signal transducer and activator of transcription-3 (STAT3) has been reported as a master gene in the highly aggressive mesenchymal glioblastoma subtype. Thus, small oligonucleotides or peptides inhibiting STAT3 phosphorylation and dimerization, revealed a great potential as anti-cancer therapeutics. In addition, microRNA (miRNA) mimics or miRNA inhibitors (antimiRs) are emerging as promising tools to inhibit cancer development and progression.

However, the development of safe, effective and selective approaches for the delivery of these therapeutic molecules remains a challenge.

In this regard, a highly promising class of molecules is represented by aptamers. These are short, single-stranded RNAs or DNAs that provide high affinity ligands and potential antagonists of disease-associated proteins. Thanks to their unique specificity, they hold as well great advantages as delivery agents. We have recently characterize two aptamers (GL21.T and Gint4.T) against receptor tyrosine kinase Axl and PDGFRβ that are overexpressed in several cancers including GBM. These aptamers are able to inhibit their proper target receptor, thus hampering the extracellular signaling and the tumor growth. In addition, they are rapidly internalized into target cells and provide interesting carriers for targeted delivery of secondary reagents. Here we want to develop GL21.T and Gint4.T for selective targeting of small interfering RNA antagonizing STAT3, miRNAs or antimiRs into glioblastoma stem like cells. Novel RNA-based conjugates will be generated and characterized both *in vitro* and *in vivo*.

The proposed molecules will provide promising therapeutic tools able to increase the therapeutic effectiveness, simultaneously reducing the occurrence of unwanted side effects due to the action on normal cells, thus ultimately improving GBM clinical outcome.

SELECTION CRITERIA

Eligibility Criteria

- Academic degree: Applicants shall have a master degree in **Biology Biochemistry, Biotechnology and related fields such as Molecular Biology, Immunology, Cell Biology etc**, corresponding to the second level of studies.
- Mobility rule: There will be no nationality restrictions. Applicants can be from any Country. However, according to the mobility rule, at the time of the application deadline researchers should not have resided or carried out their main activity (work, studies, etc.) in Italy for more than 12 months in the 3 years immediately prior to the reference date. Compulsory national service and/or short stays such as holidays will not be taken into account.

- Research experience: Applicants shall, at the time of the application deadline, be in the first four years (full-time equivalent research experience) of their research careers and not yet awarded a doctoral degree.

Full-Time Equivalent (FTE) Research Experience will be determined from the date when a researcher obtained the degree which would formally entitle her/him to embark on a doctorate, either in the country in which the degree was obtained or in Italy, irrespective of whether or not a doctorate is or was ever envisaged.

Evaluation Criteria

Step 1 -Evaluation of documentation provided by the candidate: a) Academic record and training b) Research activities c) CV/motivation letter; d) Level of English; e) Reference letters.

Step 2 - Interview: a) Scientific knowledge in the field of interest; b) Research experience in the field of interest c), Motivation; d) English proficiency.

Supervisor

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