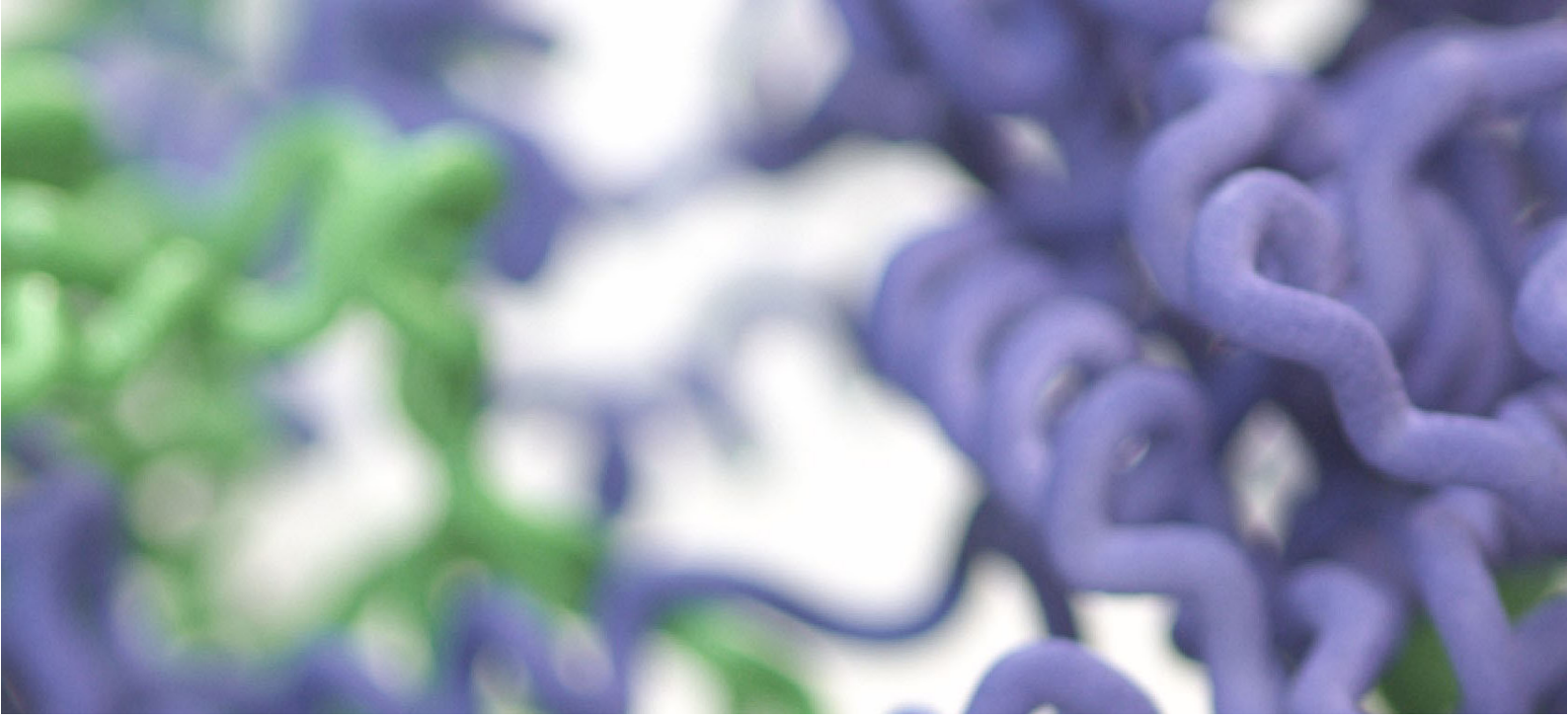


IRB BARCELONA

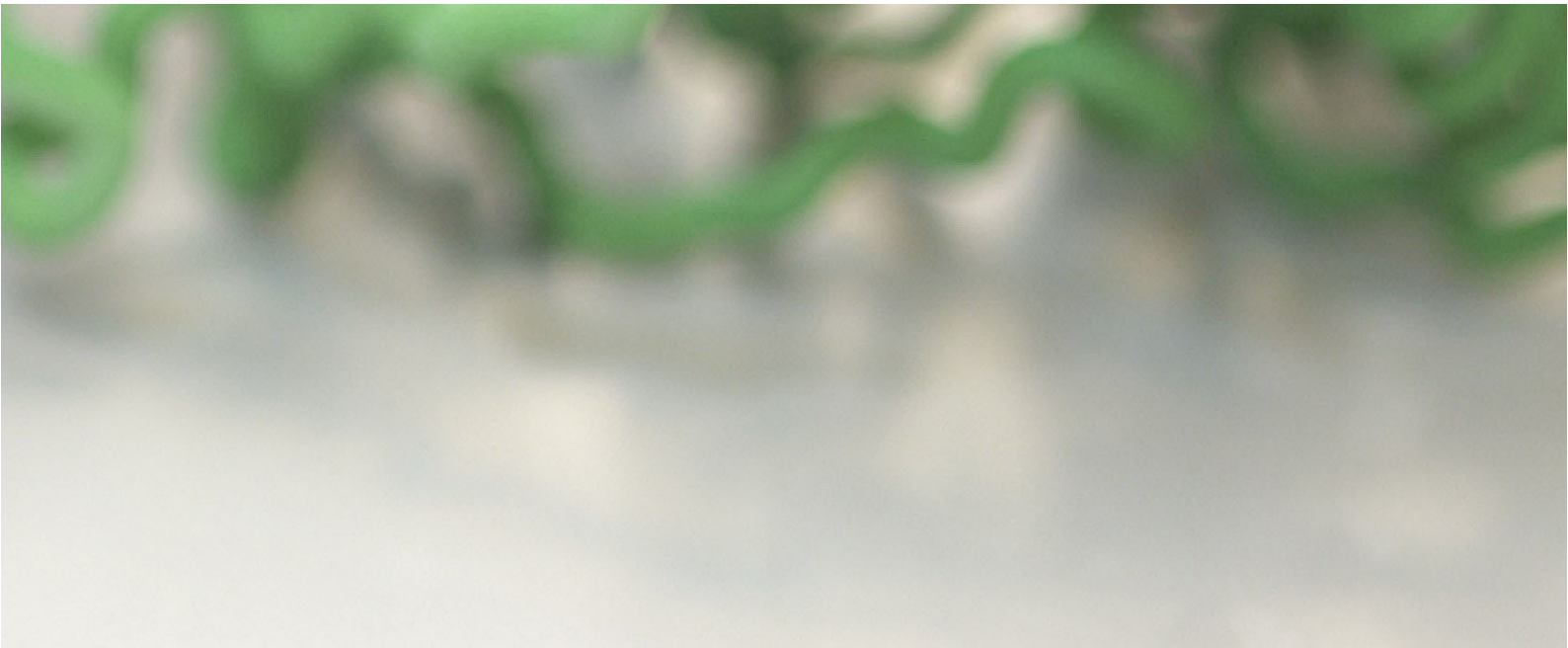
INSTITUTE FOR RESEARCH IN BIOMEDICINE

Advancing the frontiers of biomedical research

The Institute for Research in Biomedicine (IRB Barcelona) is an independent, non for-profit research center engaged in basic and applied biomedical science. The convergence of biology, chemistry, medicine, physics and computer science at IRB Barcelona provides a unique opportunity for the translation of basic biomedical research into innovation.

2shRNA

THERAPEUTIC BIFUNCTIONAL shRNAs



2shRNA
THERAPEUTIC BIFUNCTIONAL shRNAs

2shRNA is a novel nanobinder capable of delivering a complete set of therapeutic agents to specific tissues: two different shRNAs and up to three other molecules (imaging probes, cell-targeting or penetrating peptides, drugs, etc.), multiplying the possible therapeutic applications.

TECHNOLOGY

In the search of **innovative and efficient shRNA-based therapeutic approaches**, IRB Barcelona has recently created *2shRNA*, a n**ovel nanobinder structure with innovative chemical and structural characteristics** that could be exploited to develop new RNA pro-drugs. Its main features are:

- **High degree of conformational flexibility** allows adapting to differently shaped RNA structures.
- **Free chemical groups** offer the possibility to conjugate biomolecules or fluorescent probes to the RNA structure in a selective manner and via click chemistry.
- **Compatibility with non-natural nucleotides** for shRNAs (such as LNAs) allowing the increase of half-life in serum.
- The structural characteristics of the branched scaffold allow **combining an unlimited number of sequences** in the same molecule.

CURRENT STAGE OF DEVELOPMENT

The proof-of-concept for **2shRNA** has been *in-vitro* validated by targeting simultaneously a variety of gene combinations against the HER2+ resistance mechanisms.

Results were very positive as the selected combinations were able to reduce the proliferation of HER2+ breast cancer cells significantly higher than using classical shRNAs.

Moreover, molecules such as a fluorescent tag has been bound to 2shRNA allowing the visual tracking or tissue targeting of the structure uptake in cells.

RESEARCH TEAM

Prof. Modesto Orozco (IRB Barcelona / University of Barcelona)

Dr. Montserrat Terrazas (IRB Barcelona)

MOLECULAR MODELLING AND BIOINFORMATICS RESEARCH GROUP

MORE INFORMATION

Efficient siRNA-peptide conjugation for specific targeted delivery into tumor cells.
Gandioso et *al.* Chem Commun 2017 Mar PMID: 28218319

Rational design of novel N-alkyl-N capped biostable RNA nanostructures for efficient long-term inhibition of gene expression.
Terrazas et *al.* Nucleic Acids Res. 2016 PMID: 26975656

COMPETITIVE ADVANTAGE

The prototype of 2shRNA has been designed as a **therapeutic strategy to overcome resistance in HER2+ breast cancer** patients treated with anti-HER2+ drugs.

Given the plasticity of the system given by the possibility of joining any shRNA of interest, the different linkers, ability to additionally bind, in the same structure, other molecules such as imaging probes, cell-targeting peptides, drugs, etc., converts 2shRNA in a valuable tool applicable to any pathology to which siRNAs can be designed and double genetic inhibition can be a relevant mechanism of action.

A patent application has been filed on **2shRNA** and the **technology is available for licensing**.

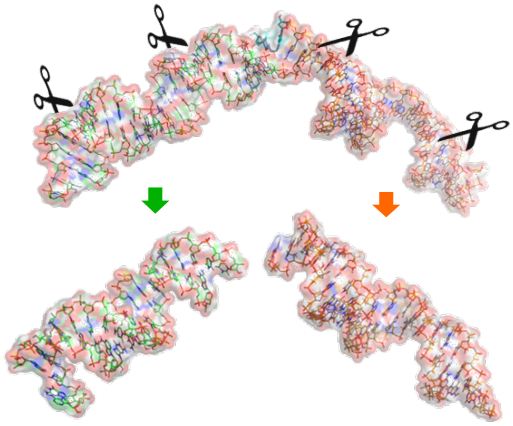


Figure - Scheme of the intracellular processing of the 2shRNAs by the activity of Dicer enzyme, producing two independent fragments of shRNA (one against each target).

CONTACT

Dr. TIAGO BOTELHO

Innovation Department - IRB Barcelona

+34 93 402 0962

tiago.botelho@irbbarcelona.org

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