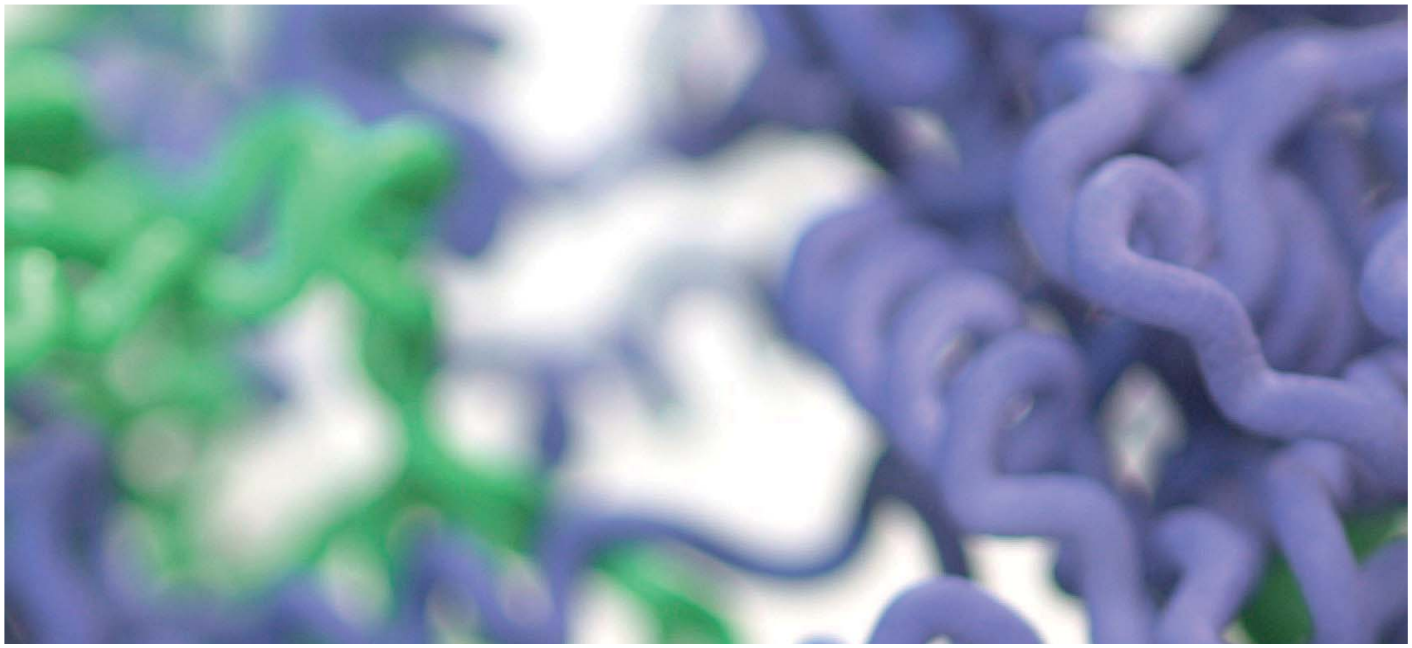


IRB BARCELONA

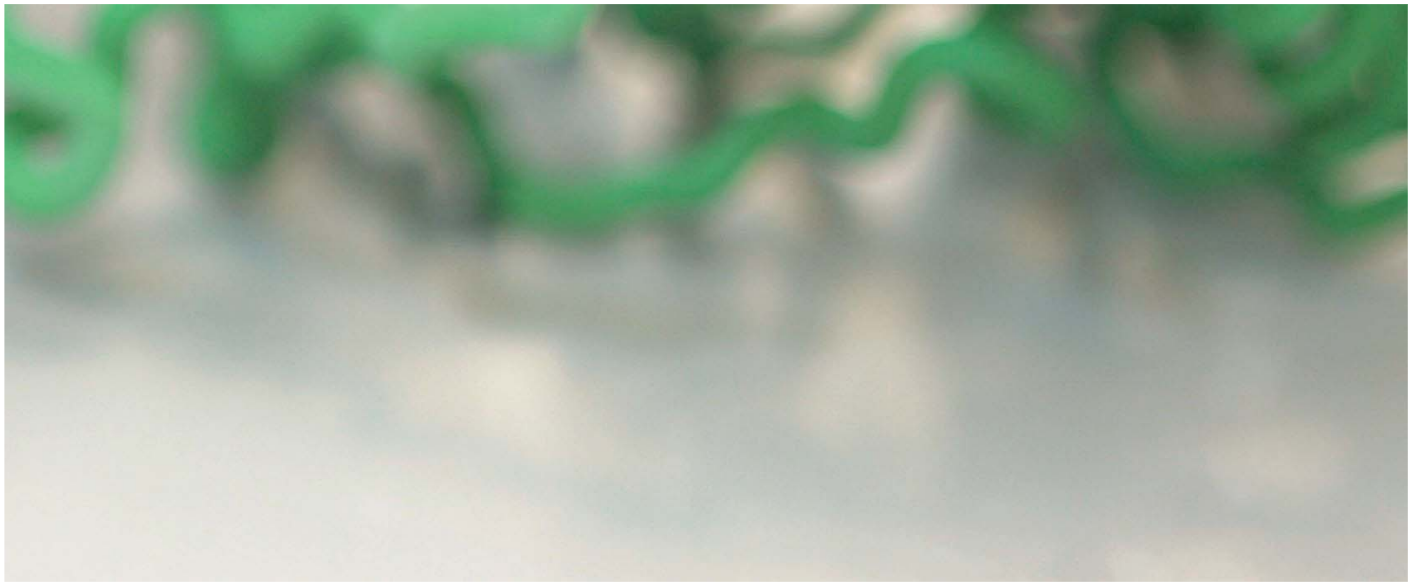
INSTITUTE FOR RESEARCH IN BIOMEDICINE

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.

ONCO-SELEC

ONCOSELECTIVE MECHANISM FOR GENE OR VIRAL THERAPY



ONCO-SELEC

ONCOSELECTIVE MECHANISM FOR GENE OR VIRAL THERAPY

ONCO-SELEC is a new tool designed to fight cancer.

It is based on a novel mechanism that may be applyed in optimising the efficacy of genetic therapies.

It works by providing full oncolytic potency of the cytotoxic gene when in cancer cells and, at the same time, producing attenuation of the same cytotoxic gene, in normal ones.

This system will improve both safety and efficacy of gene and viral based therapies.

CHALLENGE

One of the main unmet needs in oncology treatments is avoiding the strong side-effects. Ideally, this should be achieved by specifically targeting tumor cells preserving normal ones.

Recent advances in gene modification and viral therapy have provided a diversity of new vectors able to replicate with certain specificity but it is still difficult to reduce the number of normal cells affected.

Moreover, due to the high safety risks, current available treatments involving oncolytic viruses require local administration.

Doing so, **new strategies able to increase tumor selectivity while preserving healthy tissue are highly needed** to overcome this strong limitation of these powerful tools to fight against cancer.

TECHNOLOGY

ONOC-SELEC is a mechanism that can be implemented in almost any gene or virus-based therapy, both existing or in development, providing higher selectivity of cancerous tissues.

This selectivity is mainly due to a dual regulation: **in tumor cells our mechanism acts as an activator** and in **non-tumor cells it acts as a repressor**. This mechanism is regulated through a protein expression pattern observed in different cancer models and therefore it might be applied against a broad range of tumors such as liver, pancreas, kidney, glioma, colorectal and breast ductal carcinomas.

Moreover, **ONCO-SELEC** mechanism is able to be combined with transcriptional regulation system (currently more broadly used), in order to enhance the robustness of the oncoselectivity of the vector and, due to ONCO-SELEC's small size, it does not affect therapy vector fitness and/or delivery.

COMMERCIAL OPPORTUNITY

ONCO-SELECT main competitive advantages are:

-High tumor selectivity: activator in tumoral cells and repressor in non-tumoral cells.

-Does not affect vector fitness and/or delivery.

-It can be combined with transcriptional regulation systems.

-Proven stability (20 cycles of replication).

European patent application. Looking for a licensing out partner.

CURRENT STAGE OF DEVELOPMENT

For viral therapy we have been able to demonstrate that our system included in adenovirus has full lytic activity in several human pancreatic tumors and synergic effects with complementary oncoselective systems. Validation results obtained in animal model.

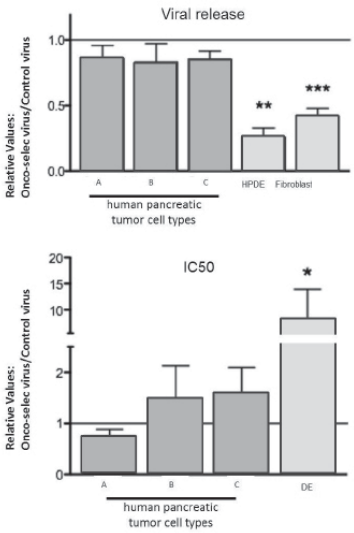


Fig 1 - Strong reduction in viral genome copy number and decreased cytotoxicity in normal cells as compared to control virus. Cytotoxicity assay in human pancreatic tumor cell types and non-tumoral cells (HPDE and fibroblast). Half growth inhibitory concentration (IC50) was calculated for each cell line from dose-response curves. Data is shown as mean ±SEM of five independent experiments. * $p<0.05$.

CONTACT

Innovation Department - IRB Barcelona

+34 93 402 0962

innovation@irbbarcelona.org

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