Aptámeros con actividad anti-metastásica

Seminaris Tecnològics de la Facultat de Farmàcia

21 de Noviembre 2024, Barcelona

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aptadel therapeutics

PROBLEM: Cancer therapeutics are unspecific and highly toxic

- The primary cause of cancer death is metastatic disease
- Metastasis management is performed by chemotherapeutics that kills both cancer cells and healthy cells

TRADITIONAL APPROACH

CHEMOTHERAPY

RADIATION THERAPY

- Poor efficacy
- Non-specific
- Serious side-effects
- Low quality of life

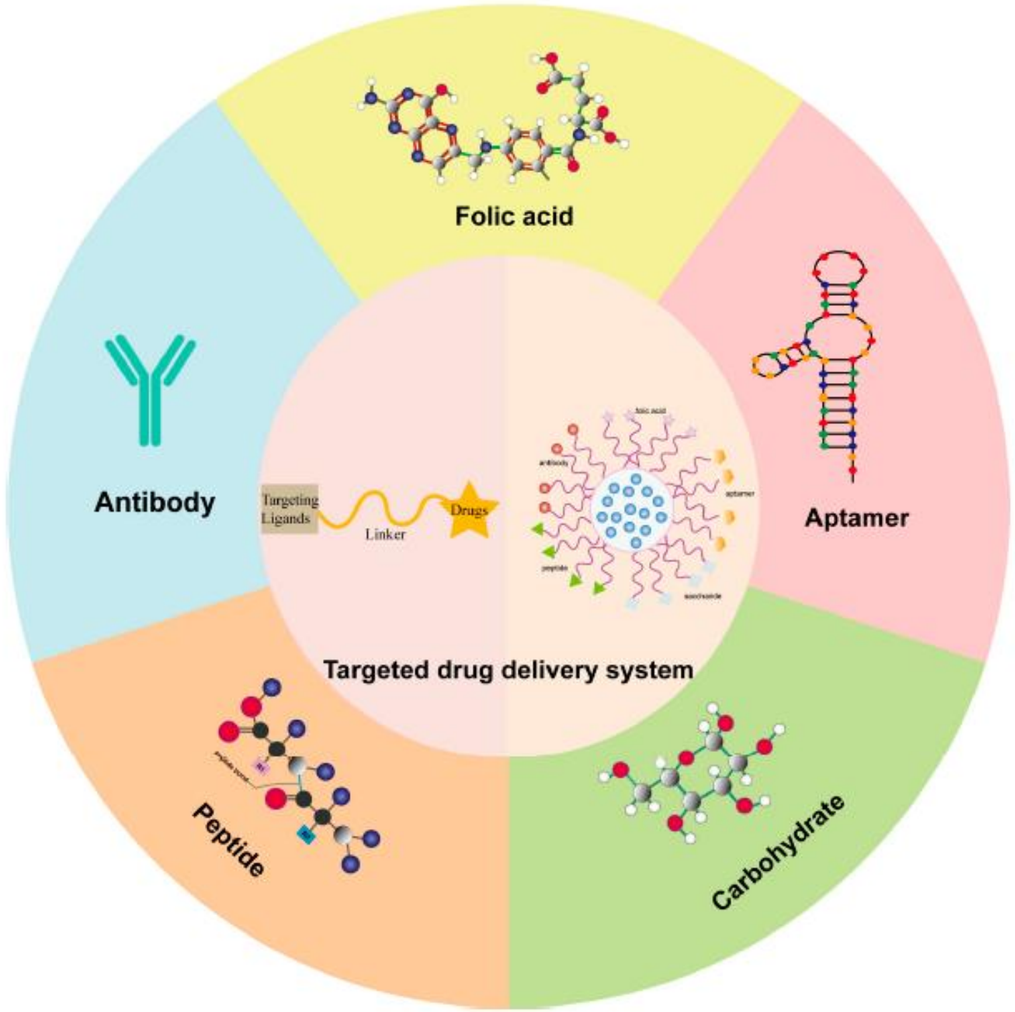
FUTURE OF CANCER TREATMENT: TARGETED THERAPIES

- ANTITUMORAL DRUGS CONJUGATED TO DELIVERY AGENTS THAT TAKES THEM SPECIFICALLY TO CANCER CELLS.
- PERSONALIZED: TAILORED FOR SPECIFIC CANCER TYPES AND PATIENT SUBGROUPS

- More efficacious
- Highly specific
- Minimal side-effects
- Minimal effect on quality of life

ptadel therapeutics

Modalities for targeted delivery of drugs



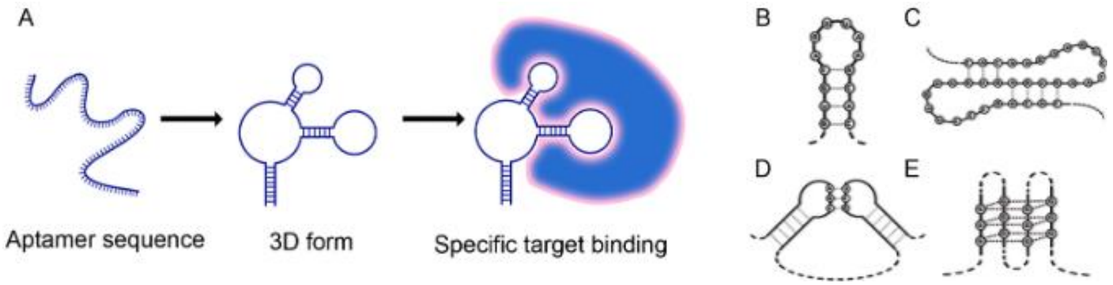
Yan, S. et al (2024). Different Targeting Ligands-Mediated Drug Delivery Systems for Tumor Therapy. Pharmaceuticals, 16: 248.

KEY PARAMETERS

- TARGET AFFINITY
- TARGET SPECIFICITY
- STABILITY
- TISSUE PENETRATION
- BIOCOMPATIBILITY
- CHEMICAL SIMPLICITY
- PURITY AND SYNTHESIS REPRODUCIBILITY
- DRUG LOADING CAPACITY
- TAILORING CAPACITY

Aptamers: “chemical antibodies”

RNA APTAMERS ARE RNA OLIGONULCEOTIDES CAPABLE OF BINDING TO SPECIFIC TARGETS WITH **HIGH AFFINITY AND SPECIFICITY**.



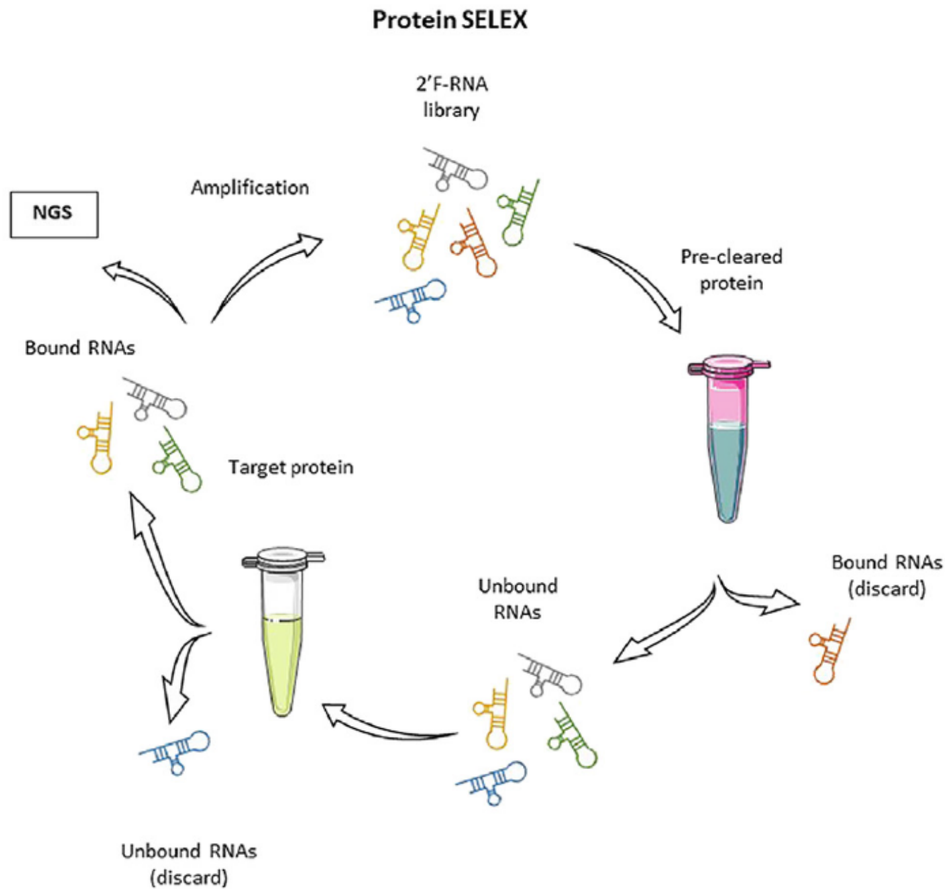
Domsicova, M. et al (2024). New Insights into Aptamers: An Alternative to Antibodies in the Detection of Molecular Biomarkers. Int J Mol Sci, 25: 6833.

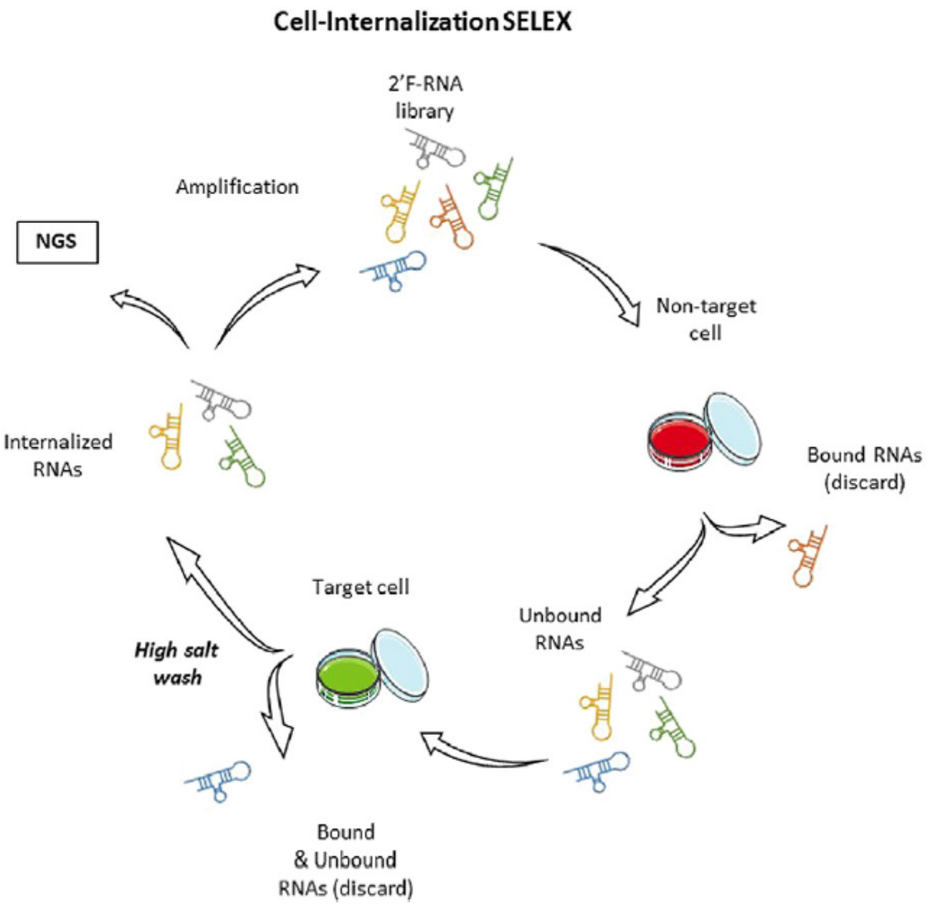
OFTEN COMPARED TO ANTIBODIES, THEY PRESENT SEVERAL **MANUFACTURING AND APPLICABILITY ADVANTAGES** OVER THESE.

	Antibodies	Aptamers
HIGHT TARGET AFFINITY / SPECIFICITY	✓✓	✓✓
LACK OF TOXICITY	✓	✓
LACK OF IMMUNOGENICITY	✗	✓
HIGHT TISSUE PENETRATION	✗	✓
COST-EFFECTIVE MANUFACTURING	✗	✓
STABILITY	✗	✓
AGAINST ANY TARGET TYPE (NOT ONLY PROTEINS)	✗	✓✓

Aptamer discovery

APTAMERS ARE IDENTIFIED THROUGH “SYSTEMATIC EVOLUTION OF LIGANDS BY EXPONENTIAL ENRICHMENT” (**SELEX**).





OTHER VARIANTS

- IN VIVO-SELEX
- CE-SELEX
- M-SELEX
- CAPTURE-SELEX
- GO-SELEX
- FACS-SELEX
- PHOTO-SELEX
- AFM-SELEX
- HTS-SELEX
- ST-SELEX
- …

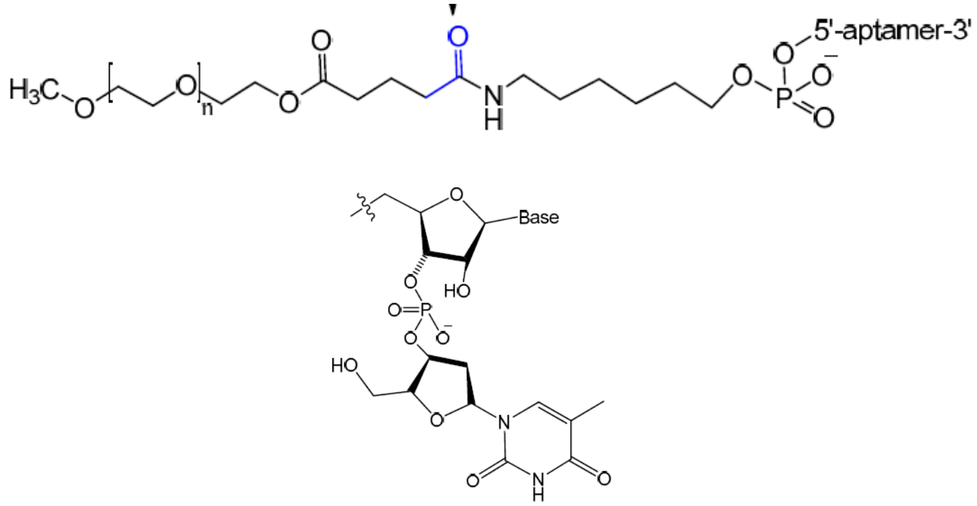
L.Santana-Vera et al. (2023) Combination of protein and cell internalization SELEX identifies a potential RNA therapeutic and delivery platform to treat EphA2-expressing tumors. Mol Ther Nucleic Acids. 32:758-772.

Aptamer optimization

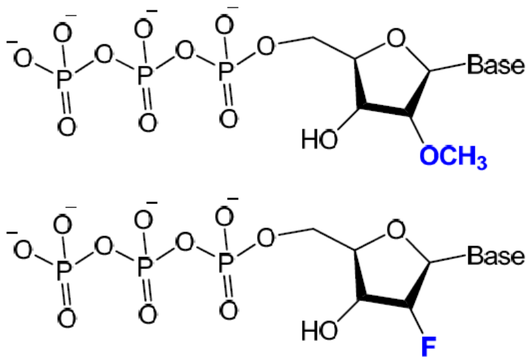
APTAMER CAN BE **CHEMICALLY SYNTHESIZED** AND **SITE-SPECIFICALLY MODIFIED.**

- Reduce size
- Improve stability
- Modulate bioavailability
- Reduce toxicity

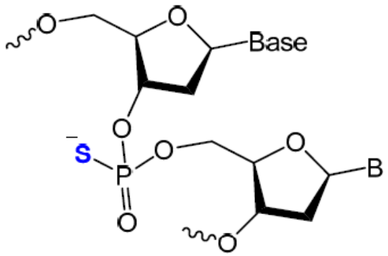
Terminal modifications: increase size, protect from exonucleases



2'-Substitutions: protect from nucleases, reduce toxicity



Backbone modifications: protect from nucleases, improve biodistribution



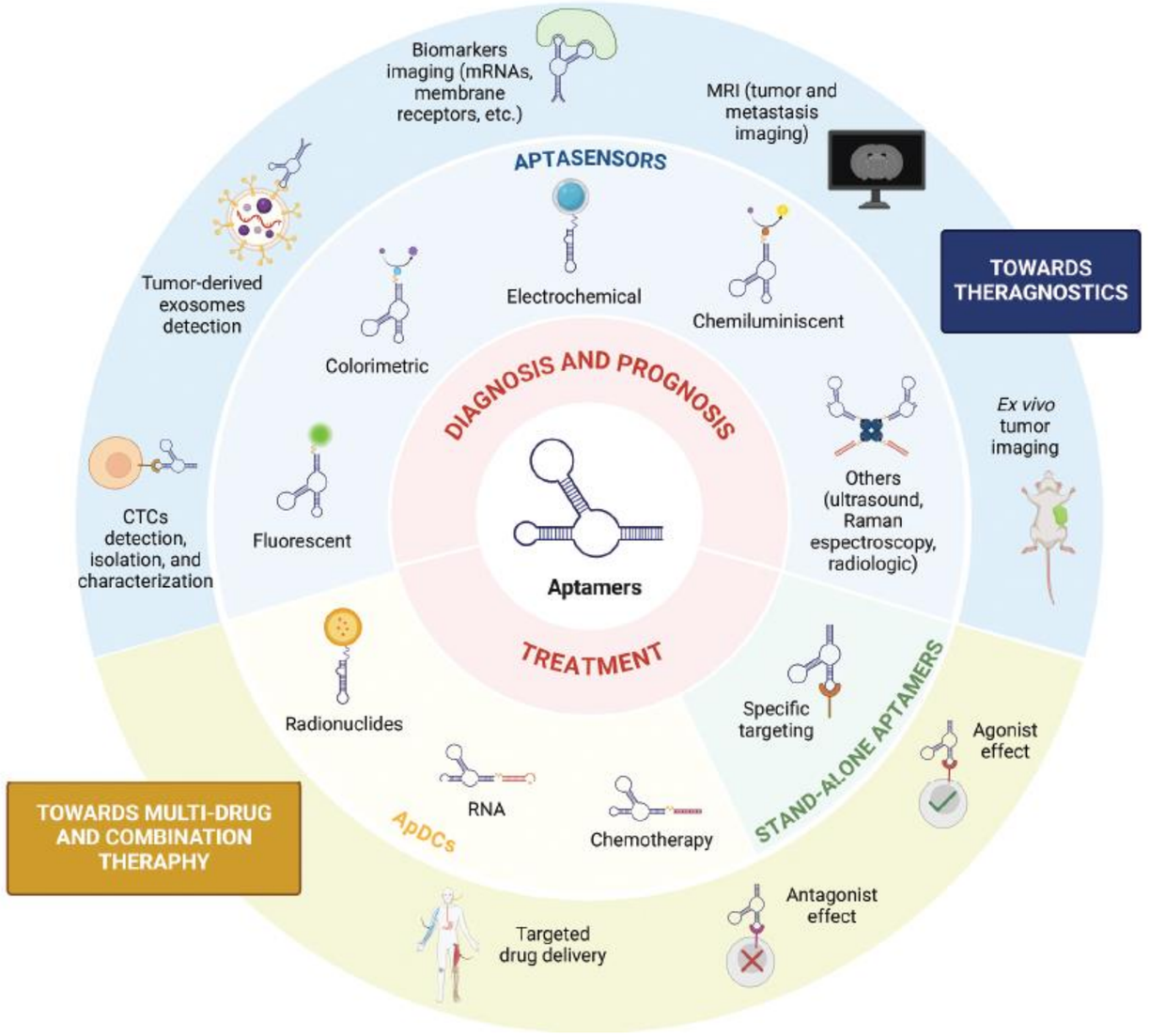
Odeh, F. et al. (2019) Aptamers Chemistry: Chemical Modifications and Conjugation Strategies. Molecules 25: 3.

Aptamers as a versatile modality

APTAMERS CAN ACT UPON **INTRACELLULAR AND EXTRACELLULAR TARGETS** TO INHIBIT OR ACTIVATE THEIR FUNCTIONS.

THEY CAN BE FURTHER **CONJUGATED** TO REPORTERS (**APTASENSORS**) OR THERAPEUTIC AGENTS (**APTAMER-DRUG CONJUGATES; ApDC**).

Aptamers are emerging as a powerful technology for diagnostics and therapeutics



Arévalo, J. and Torres, AG. (2024). The future of aptamers in cancer diagnosis, prognosis and treatment. Expert Opin Biol Ther. 24:873-877.