Contribution ID : **257** Type : **Poster Presentation**

Advancing RNA Aptamer Therapeutics for Glioblastoma: Structural Characterization of the A40s Aptamer Targeting EphA2

Advancing RNA Aptamer Therapeutics for Glioblastoma: Structural Characterization of the A40s Aptamer Targeting EphA2

Vincenzo Maria D'Amore1, Isidora Diakogiannaki1, Alessandra Affinito2, Cristina Quintavalle2, Mario Mörl3, Gerolama Condorelli4, Luciana Marinelli1 and Francesco Saverio Di Leva1

1 Department of Pharmacy, University of Naples Federico II, Naples, 80131, Italy 2 Institute of Experimental Endocrinology and Oncology (IEOS) "G. Salvatore", National Research Council (CNR), Naples, 80131, Italy 3 Institute of Biochemistry, Leipzig University, Leipzig, 04103, Germany. 4 Department of Molecular Medicine and Medical Biotechnology, University of Naples Federico II, Naples, 80131, Italy.

vincenzomaria.damore@unina.it

Glioblastoma (GBM) is a highly aggressive and lethal brain tumor, with GBM stem cells (GSCs) playing a central role in drug resistance and tumor relapse. The ephrin type-A receptor 2 (EphA2), which is overexpressed in both GBM and GSCs, has emerged as a promising target for innovative therapeutic strategies. [1] Previous studies identified the RNA aptamer A40s—a 30-nucleotide molecule selected via SELEX—as a selective EphA2 binder capable of impairing GSC proliferation, stemness, and migration.[2,3] To further refine A40s as a therapeutic candidate, we combined computational and experimental approaches. We predicted its secondary structure and explored its three-dimensional conformation using all-atom molecular dynamics (MD) simulations. Detailed analysis of the A40s–EphA2 interaction revealed key binding regions and structural determinants critical for specificity and stability. These results lay the groundwork for enhancing A40s' therapeutic potential and support its development as a next-generation EphA2-targeted treatment for glioblastoma.

Figure 1. EphA2/A40s complex.

References [1] S. Bao et al., Nature 444 (2006), 756. [2] A. Affinito et al., Mol. Ther. Nucleic Acids, 18 (2019), 99. [3] A. Affinito et al., Mol. Ther. Nucleic Acids, 20 (2020), 176.

Primary author(s) : D'AMORE, Vincenzo Maria

Presenter(s) : D'AMORE, Vincenzo Maria