A-to-I RNA editing in cancer

Post-transcriptional modifications, such as RNA editing, are developing as important players in RNA/protein diversification, microRNA modulation, cell differentiation and are involved in the onset/progression of several human cancer. A-to-I RNA editing is a molecular process that changes nucleotide sequences of double-stranded RNAs (dsRNAs) by the deamination of the canonical Adenosine (A) base to the Inosine (I). A-to-I editing occurs in both coding and non-coding RNA molecules in all human tissues and targets adenosines at different levels diversifying and increasing RNA/protein isoforms. In mammals, this molecular mechanism is mediated by the Adenosine Deaminases Acting on dsRNA enzymes (ADAR 1-3). Inosine is recognized as Guanosine by splicing and translational machineries so it can alter splicing, mRNA sequence, protein–RNA and miRNA–RNA interactions. Thanks to these properties, RNA editing is a common phenomenon in cancer helping to drive transcriptomic and proteomic diversity.

In the last years I worked with Dr. Angela Gallo (ORCID 0000-0003-0297-1807) at Bambino Gesù Pediatric Hospital (Rome) and I focused my attention on the role played by RNA editing in cancer and in particular in Glioblastoma, one of the most aggressive and lethal brain tumors.

We systematically characterized miRNA editing in healthy brain and glioblastomas and found some miRNAs differentially edited in human brain compared to glioblastoma tissues, one in particular (miR-589–3p) is completely edited in brain while this editing is lost in glioblastomas. The edited version of the miRNA, when restored in cancer cells, is indeed able to inhibits glioblastoma cell proliferation, migration and invasion, thus being a potential therapeutic agent for glioblastoma treatment.

We also studied the editing signature (inosinome) of Glioblastoma providing the first evidence that RNA editing plays an important role in patients' outcome. We found that specific RNA editing events, particularly enriched in cancer samples compared to healthy brain, are pro-tumoral in glioblastoma cells promoting proliferation and migration. Furthermore, the editing level at these sites is associated to patients' survival making them possible prognostic factors and indicating RNA editing signature as a possible novel method for glioblastoma patients’ stratification.

References:
ADAR2/miR-589-3p axis controls glioblastoma cell migration/invasion.


Keywords:
RNA editing, post-transcriptional modifications, glioblastoma therapy

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