Clinic and therapeutic potential of non-coding RNAs in cancer

Since the early beginning of the 21th century, the research in molecular and translational oncology has been going deeper and deeper in the exploration of the non-coding human transcriptome (1,2). A simple comparison of the number of publications in PubMed containing the "non-coding RNA" and "cancer" words between the years 2000 and 2019 reveals an increase fold of 29.8 in the number of matches. This data highlights the weight and interest that non-coding RNAs (ncRNAs) has reached in the last years.

The ncRNAs comprises a vast family of different RNA molecules, mainly divided according to its size in small non-coding RNAs (sncRNAs) and long non-coding RNAs (lncRNAs) (3). Both families, has been related to all hallmarks of cancer (4,5). Within the sncRNA, microRNAs have been extensively studied and are well known players in tumorigenesis, acting as both oncogenes and tumor suppressors (6,7). MicroRNAs are key players in gene expression regulation, mainly at post-transcriptional level avoiding the translation of their target mRNAs (8). Several microRNAs identified across different cancer types acts as oncogenes by targeting the expression of different tumor suppressor genes such as RB1 or TGFBR2 (9). Other sncRNAs types such as piwiRNAs has identified as regulators of the genomic stability in germ line (10). However, their role in cancer initiation remains poorly understood , and further characterization is needed (11).

LncRNAs plays a plethora of roles in cancer progression related to different key events for tumorigenesis such as epithelial-to-mesenchymal transition (12), angiogenesis (13) or tumor metabolism (14). They can act according to four different functional archetypes as: signals, relating its differential expression to a concrete cellular process or context; scaffolds, allowing different protein component of a complex to spatially join; decoys, disrupting the interaction between two different cellular components; or guides, recruiting transcription factors or protein complexes to the genomic locations where they act (15). Additionally, they has been proposed as an ideal source of biomarkers, due to its highly specific expression pattern across different cancer types and between normal and tumor tissue (16). LncRNAs includes different members such as long intergenic non-coding RNAs (lincRNAs) or antisense lncRNAS (AS-lncRNAs) well characterized in the last years (17), and other members that begin to be explored such as circular RNAs (circRNAs) (18).

The potential of ncRNAS has been studied from the basis of the molecular oncology, dissecting its biological function, to the translational research, demonstrating its high applicability as biomarkers (19). Furthermore, their potential use as biomarkers in clinics is enhanced by the field of liquid biopsy. It has been proved that, the detection of ncRNAs in different biofluids, as free-circulating RNAs or as part of extracellular vesicles cargo, is an ideal source of diagnostic, prognostic and response-monitoring biomarkers (20).

In summary, even though the efforts made to date in the exploration of ncRNA's role in cancer, there is still further research needed about their utility not only as biomarkers, but also as therapeutic targets. The present special series will explore todays knowledge about the potential role of ncRNAs in the clinic, especially in the liquid biopsy field, and intends to shed light into the future questions to be raised on this matter.

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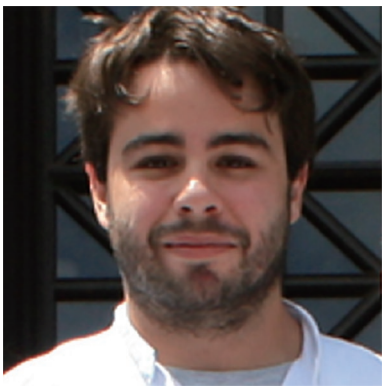

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