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On the relevance of a complete characterisation of miRNAs, isomiRs and miRNA-mRNA interaction sites through miRNA-specific alignment tools

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The advent of NGS dramatically changed the characterisation of multifactorial pathologies such as cancer. The high molecular variability of cancer makes essential the identification of biomarkers able to explain the differences among cancer sub-types, allowing physicians to provide patients with suitable therapies. In this context, miRNAs are considered adequate biomarkers and miRNAs profiling from miRNA-sequencing is widely used. However, state of the art tools performing miRNAs reads mapping rely on general-purpose alignment algorithms. On the other side, researches carried out in the last decade led to the identification of many miRNAs specific features that are not exploited by miRNAs aligner. Moreover, the role of miRNAs variants called 'isomiRs' is still an open issue. IsomiRs impact miRNA targets affinity characterization and their analysis enables a more accurate evaluation of miRNA expression profiles.

In light of these considerations, there is need of algorithmic methodologies able to provide users with a complete and accurate picture of the whole miRNAs, isomiRs and interaction sites spectrum. We report the impact of the application of such methodology on 23 human miRNA-Seq datasets from GEO, for which the overall isomiRs expression level and the characteristics of the interaction sites has been evaluated. As a result, 40% of the 189M miRNAs mapped reads showed a miRNA exact sequence, whereas 50% are characterized by a sequence accounting for 3' isomiRs and the remaining reads possess sequences compatible with 5' and SNP isomiRs or combinations of them. Furthermore, in the 2% of the cases some interaction sites are missed. Two other samples (hESCs and NSCs), recently analysed to confirm isomiRs importance, have been also studied in terms of isomiRs and interaction sites profiles, pointing out that such characteristics require a suitable methodology for miRNA sequences analysis because they cannot be appreciated from the overall miRNAs expression profile.

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