

Circulating microRNAs: novel biomarkers in personalized medicine against breast cancer - breakthroughs in cancer research

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To date, several genetic, epigenetic and proteinaceous biomarkers have been found to be associated with breast cancer, but their robustness as indicators of disease remains uncertain. More significantly, most women in the developing countries present with this cancer only when it has reached an advanced stage. The treatment of advanced stage presents several challenges but most important among them is the frequent development of resistance to chemotherapy and hormonal therapy which leads to a high mortality rate. In light of this, there is a need to identify sensitive biomarkers that could be useful in early detection and in following the progression of the disease; these might help to identify new therapeutic targets. MicroRNAs (miRs) form a class of non-coding RNA that regulates post-transcriptional gene expression and thereby cellular processes. In breast cancers, dysregulation of the miRs' expression can result in the progression of cancers. In addition, miRs have been shown to play a role in the development of resistance to drug therapy by regulating signalling cascades. From a cohort of 100 disease-free individuals and 127 breast cancer patients; the levels of these circulating miRNAs are being verified by qRT-PCR. The results of this part have shown over-expression of some types of miRs in the breast tumour patients, while the levels of others remain lower than those in normal individuals. Another interesting pattern emerged when we compared the relative levels of these circulating miRNAs with their expression levels in breast tissue. In addition to intergroup comparisons, plasma miRNA expression levels of all groups were analyzed against cancerous breast tissue (RNA-Seq data from The Cancer Genome Atlas-TCGA). A differential set of miRNAs were identified in the plasma of breast cancer patients and 10 miRNAs were uniquely identified based on ROC analysis. The most striking findings revealed elevated some of the tumor suppressor miRs in luminal breast cancer patients' plasma, irrespective of subtype, and elevated in plasma of TNBC breast cancer patients. We found also that, while most miRNAs in plasma reflected cellular levels, some of them had an inverse pattern, thereby suggesting that they were being selectively secreted into plasma. The circulated miRNA patterns indicate signatures which could be as biomarkers for detection, with potential use in screening and in distinguishing the type of tumour and also could be used as targets for therapies.

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