MedicalXpress

Researchers identify need to sample multiple tumor zones in breast cancer

June 15 2012

Certain short strands of RNA, known as microRNAs (miRNAs), have been linked to the progression and metastasis of breast cancer and may provide information about prognosis. However, studies of miRNA expression profiles often report conflicting findings. While the potential for using miRNAs in breast cancer diagnosis is promising, scientists report in a new study published online today in The *Journal of Molecular Diagnostics* that differences in the amount and types of miRNA within breast tumors can be misleading.

"Personalized medicine will be the future of cancer care," explains lead investigator Stefanie Avril, MD, of the Technical University of Munich. "However, taking a single tumor biopsy for defining individual treatment is probably oversimplified, and we need to take into account the heterogeneity of tumors. "We found considerable differences in the expression of miRNAs associated with breast cancer within a single tumor (referred to as intratumoral heterogeneity). The use of miRNA for diagnosis or prognosis requires sampling at several different tumor locations and of several tumor-involved lymph nodes."

Researchers collected 132 tumor samples from 16 patients who underwent either lumpectomy or mastectomy for large primary invasive breast cancer. Samples were taken from defined tumor zones: the center of the tumor, the periphery, and the area between. Samples were also taken from lymph nodes, if metastases were present. The expression of four miRNAs (miR-31, miR-335, miR-10b, and miR-210) and four control genes (let-7a, miR-16, RNU48, and RNU44) was assessed.

The researchers found significant variation in miRNA expression, from samples both within primary breast cancers and within lymph node metastases from the same patient. The extent of heterogeneity was very similar within the defined tumor zones and between different zones.

To illustrate why intratumoral heterogeneity may produce misleading results if only a single sample is used, the researchers assessed the variation of miRNA expression between different patients. The mean expression of miR31, which is associated with cancer metastasis, from all zones of the primary tumor site in patient 5 was significantly lower than the mean expression from all zones of the primary tumor site of patient 6. However, a sample from a single tumor zone from patient 5 showed a higher expression level than the lowest case from patient 6. "This might in part explain conflicting previous findings regarding miRNA expression profiles," Dr. Avril notes.

"An important strength of this study is the systematic and predefined prospective sampling of tumors in 8 to 10 different areas, whereas previous studies have commonly only analyzed different areas of one tumor section, or core biopsies of the same tumor," says Dr. Avril. "Reliable assessment of breast cancer miRNA profiles should include sampling of the primary tumor in several locations or sampling several tumor-involved lymph nodes when deriving miRNA expression profiles from metastases."

More information: "Intratumoral heterogeneity of microRNA expression in breast cancer," by M. Raychaudhuri, T. Schuster, T. Buchner, K. Malinowsky, H. Bronger, U. Schwarz-Boeger, H. Höfler, S. Avril. DOI: dx.doi.org/10.1016/j.jmoldx.2012.01.016. *The Journal of Molecular Diagnostics*, Volume 14, Issue 4 (July 2012)

Provided by Elsevier