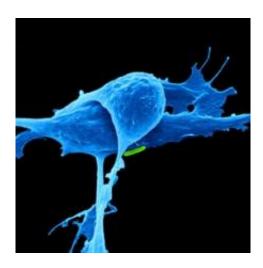


## Tumor RNA in platelets may diagnose and classify cancer, identify treatment strategies

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Analysis of tumor RNA carried in platelets - blood components best known for their role in clotting - may prove to be more useful than other "liquid biopsy" technologies for diagnosing cancer and determining its primary location and potential therapeutic approaches. In a paper published in the journal *Cancer Cell*, an international research team describes finding that the RNA profiles of tumor-educated platelets - those that have taken up molecules shed by tumors - can distinguish among blood samples of healthy individuals and those of patients with six types of cancer, determine the location of the primary tumor and identify tumors carrying mutations that can guide therapeutic decision making.



"By combining next-generation-sequencing gene expression profiles of platelet RNA with computational algorithms we developed, we were able to detect the presence of cancer with 96 percent accuracy," says Bakhos Tannous, PhD, of the MGH Department of Neurology, co-senior author of the *Cancer Cell* paper along with investigators from VU University Medical Center in Amsterdam. "Platelet RNA signatures also provide valuable information on the type of tumor present in the body and can guide selection of the most optimal treatment for individual patients.

In recent years it has become apparent that, in addition to their role in promoting blood clotting, platelets take up protein and RNA molecules from tumors, possibly playing a role in tumor growth and metastasis. The current study was designed to investigate whether tumor RNA carried in platelets could be used to diagnose and classify common types of cancer. The researchers isolated platelets from blood samples taken from 55 healthy donors, 39 individual with early-stage cancer and 189 patients with advanced, metastatic cancer. Patient participants had either non-small-cell lung cancer, colorectal cancer, glioblastoma, pancreatic cancer, hepatobiliary cancer or breast cancer.

After amplifying and sequencing the amount of platelet RNA found in the equivalent of a single drop of blood from each individual, the researchers identified more than 5,000 different platelet RNAs. Comparing RNA profiles of healthy donors with those of cancer patients revealed increased levels of almost 1,500 RNA molecules - many involved in cancer-associated processes - and reductions of almost 800 in samples from cancer patients. Examination of the levels of around 1,000 RNAs from almost 300 individuals with the team's algorithm that classifies whether not they indicated the presence of cancer did so with 96 percent accuracy. All of the patients with localized tumors and 33 of the 39 with tumors of the central nervous system were accurately diagnosed.



Platelet mRNA profiles were able to identify the particular type of cancer in each patient participant, including distinguishing among three types of gastrointestinal adenocarcinoma - colorectal cancer, pancreatic cancer and hepatobiliary cancer. Platelets from patients with tumors driven by mutations in the KRAS or EGFR proteins, biomarkers that can guide the use of drugs targeting those mutations, proved to have unique RNA profiles as well.

While several other approaches are being developed to analyze bloodborne factors such as circulating tumor cells and free DNA in order to characterize and track cancer development and progression, the authors note, none have yet been able to diagnose cancer and pinpoint the location of the primary tumor. "We observed that the mRNA profiles of tumor-educated platelets have the sensitivity and specificity to detect cancer, even in early, non-metastasized tumors," says Tannous, an associate professor of Neurology at Harvard Medical School. "We are further assessing the potential of TEP-based screening for therapeutic decision making and also investigating how non-cancerous diseases may further influence the RNA repertoire of TEPs."

## Provided by Massachusetts General Hospital

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