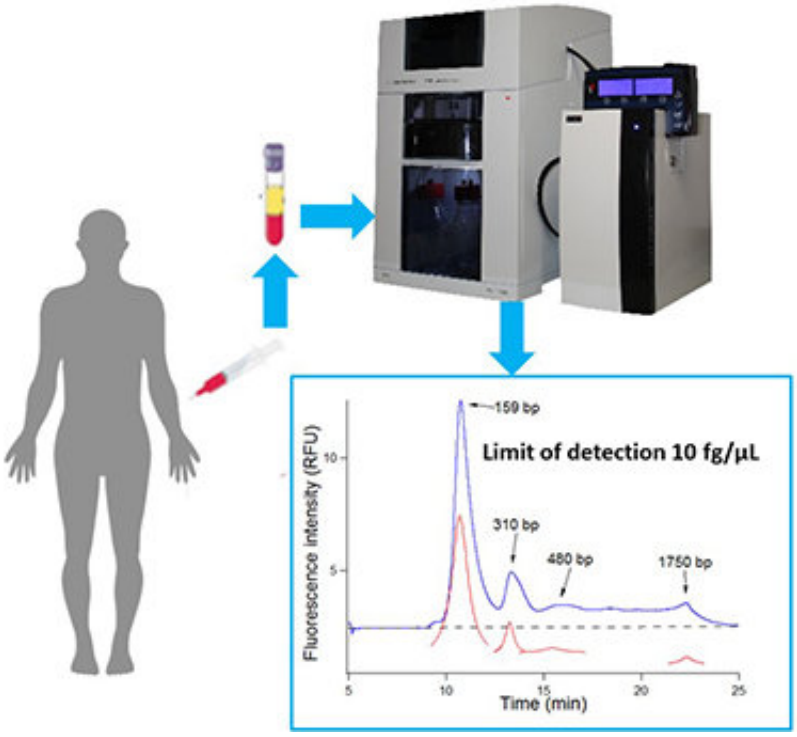
A more sensitive device for characterizing DNA in blood circulation

March 28 2018



Principle of the BIABooster analytical system. From a purified plasma sample, 1 µL is analyzed with the BIABooster device, which concentrates, separates and detects the size profile of the circulating DNA. The bottom right graph represents a "typical" size profile with a succession of low molecular weight peaks in the 100-300 base pair (bp) range and a high molecular weight residue of about 1700 bp. The device's sensitivity limit is 10 fg/µL. Credit: © Aurélien Bancaud, LAAS-CNRS. Human silhouette (on the left): icon made by Freepik from flaticon.com

Developed and patented in 2012 and 2014 in the Laboratoire d'Analyse et d'Architecture des Systèmes (LAAS-CNRS) and implemented industrially by Picometrics-Technologies, BIABooster technology characterizes DNA with new precision and sensitivity. When used to analyze residual DNA circulating in the blood, it has identified promising signatures for monitoring patients with cancer. These signatures, presented in the March 20, 2018 issue of *Analytical Chemistry*, could be confirmed by a larger study led by teams at the Université Paris Descartes, INSERM, AP-HM and AP-HP (Hôpital Européen Georges-Pompidou).

In the human body, occasional cell death translates into degradation and release of DNA, which then circulates in the blood before being eliminated. Prior studies have shown that cancer patients have high levels of DNA fragments in their blood. However, factors such as a rich diet or physical effort may also be responsible for high levels of DNA fragments. BIABooster achieves sensitive and fast analysis on DNA molecules, opening new avenues for improved characterization of the composition of this residual DNA fraction in the blood and therefore specification of its origin.

To analyze DNA, the BIABooster device operates in two in-line concentration and separation steps. First, the DNA is concentrated via a system of capillaries formed from the junction of a small capillary and another with a larger cross-section. The researchers make a solution containing the DNA flow into the large capillary and use an electric field with low amplitude to slow migration. The change in flow rate and electric field in the constriction stop the DNA and concentrate it like a "wafer." This wafer is then released through the progressive drop in the electric field, which also separates the fragments according to size.

The researchers have been using BIABooster since 2016 and have defined a protocol presented in Analytical Chemistry. In about twenty

minutes, the tool detects DNA up to a concentration of 10 fg/µL. It determines the concentration and size of a sample with, respectively, precisions of 20% and 3%. It has been shown to be particularly suited to tackling the profile of DNA in the blood circulation for healthy volunteers or patients with cancer, both in terms of concentration and size profile.

Beyond the technical prowess, the researchers decided to use this device to analyze about one hundred clinical samples from patients with cancer that came from the Hôpital Européen Georges-Pompidou AP-HP and AP-HM hospitals. Their first results confirm that the presence of low molecular weight DNA in high quantities may be relevant clinical information for patient monitoring.

More information: Comtet-Louis Andriamanampisoa et al, BIABooster: Online DNA Concentration and Size Profiling with a Limit of Detection of 10 fg/µL and Application to High-Sensitivity Characterization of Circulating Cell-Free DNA, *Analytical Chemistry* (2018). DOI: 10.1021/acs.analchem.7b04034

Provided by CNRS