Researchers develop tool that could improve liquid biopsy

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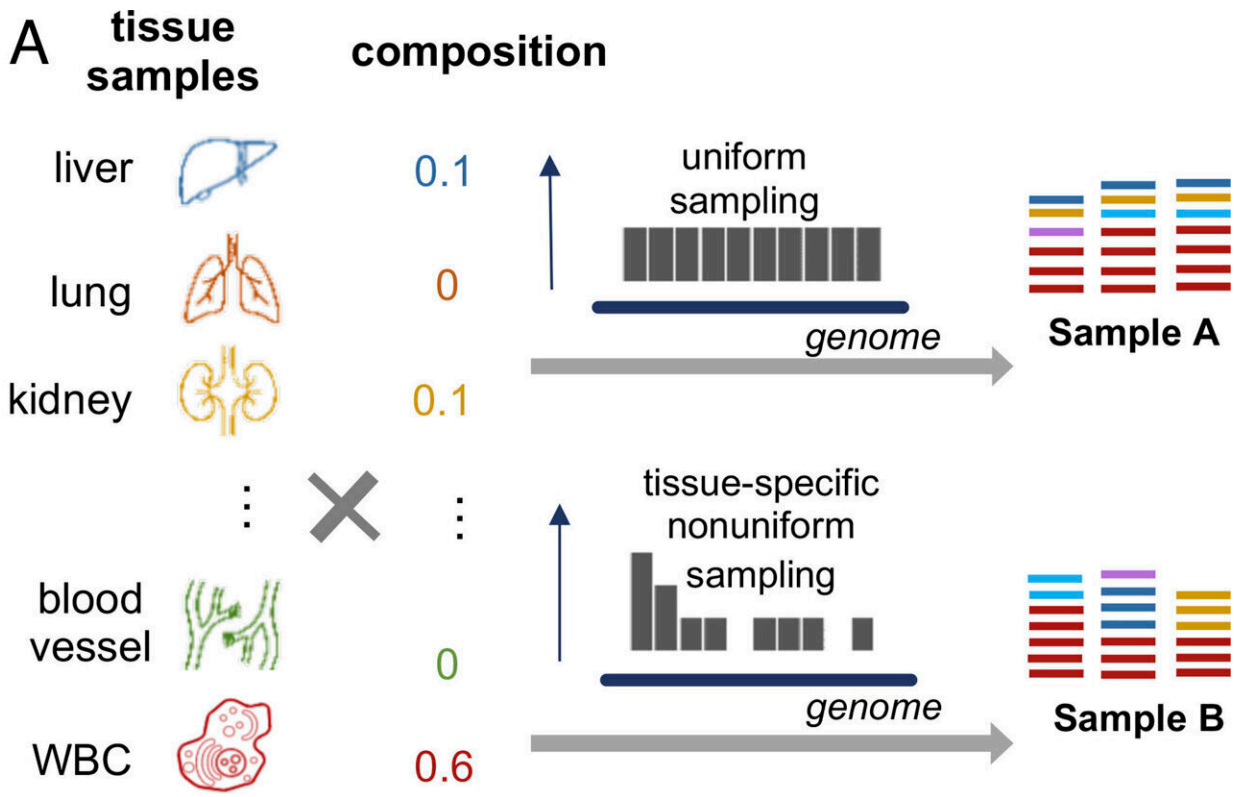

Evaluation of robustness of the cfSort. (A) Generation of the simulated testing sample pairs for the evaluation of robustness. We generated a testing sample pair (A and B) using the same tissue composition and the same original tissue samples but with different sequencing read sampling distributions. For sample A, we randomly sampled DNA fragments from the original tissue samples following a uniform distribution. For sample B, we used a nonuniform distribution to sample DNA fragments from the original tissue samples. The non-uniform distribution was randomly generated for each tissue type, and the distribution was different

for different tissue types. (B) Robustness of the cfSort. The robustness was evaluated by the intercept, slope, and R^2 of the fitted linear regression model between the tissue fractions estimated from the testing sample pairs. Credit: *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2305236120

A research team led by Xianghong Jasmine Zhou, Ph.D., professor of Pathology and Laboratory Medicine at the David Geffen School of Medicine at UCLA, has made an important advancement to address one of the major challenges in cell-free DNA (cfDNA) testing, also known as liquid biopsy.

They've identified specific methylation patterns unique to each tissue, potentially helping to Identify the specific tissue or organ associated with cfDNA alterations picked up by testing, a critical challenge for accurate diagnosis and monitoring of diseases.

Cell-free DNA has significant potential in disease detection and monitoring. However, accurately quantifying tissue-derived cfDNA has proven challenging with current methods, among them determining the tissue origin of cfDNA fragments detected in these tests.

In a new study, published in *Proceedings of the National Academy of Sciences*, the team developed a comprehensive and high-resolution methylation atlas based on a vast dataset of 521 noncancerous tissue samples representing 29 major types of human tissues.

They call the approach cfSort, and showed it successfully identified specific methylation patterns unique to each tissue at the fragment level and validated these findings using additional datasets.

Going further, the team illustrated the clinical applications of cfSort through two potential uses: aiding in disease diagnosis and monitoring treatment side effects. By estimating the tissue-derived cfDNA fraction using cfSort, they were able to assess and predict clinical outcomes in patients.

"We have shown that the cfSort outperformed the existing methods in terms of accuracy and detection limit: making more accurate tissue fraction estimation and distinguishing a lower level of tissue-derived cfDNA," said first author Shuo Li.

"In addition, the cfSort demonstrated nearly perfect robustness toward the unseen local fluctuations of tissue compositions, indicating its wide applicability to diverse individuals."

More information: Shuo Li et al, Comprehensive tissue deconvolution of cell-free DNA by deep learning for disease diagnosis and monitoring, *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2305236120

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