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Using machine-learning to leverage variations in DNA methylation for early lung cancer detection

Stanford scientists have discovered that differentially methylated regions (DMRs) in circulating tumor DNA (ctDNA) can be used as a blood-based biomarker for early cancer detection. Using machine-learning to detect DMRs in blood-based tests could increase cancer screening uptake in high-risk adults and reduce lung-cancer-related mortality

Image-based screening of high-risk adults, such as individuals with a history of smoking, reduces lung-cancer-related mortality; however, uptake of screening has been relatively low. Only around 5% of eligible individuals undergo screening due to factors such as high costs, limited access, and concerns for false positives. Genomic blood tests for cancer screening could be an effective alternative to increase the total number of patients screened and the number of lives saved annually from lung-cancer-related mortality. But current methods suffer from low sensitivity or have focused on diseases other than lung cancer. Interestingly, aberrant DNA methylation has been shown to be associated with lung ctDNA, suggesting that the use of DMRs as a biomarker in blood-based lung cancer screening could increase its sensitivity and utility in early cancer detection.

Including DNA methylation in a machine-learning enabled molecular method for lung cancer screening resulted in a positive correlation between DMR detection and the fraction of ctDNA in the sample. Importantly, the novel, blood-based method for early cancer detection has a 15% increase in sensitivity relative to the leading published method. Consequently, including DNA methylation in blood-based tests for early cancer detection has the potential to drastically improve screening sensitivity, increase cancer screening uptake in high-risk adults, and reduce lung-cancer-related mortality.

Stage of Development:
Clinical - Initial validation

Applications

- Early lung cancer detection in high-risk adults
- Initial blood-based screening for lung cancer for potential recommendation for image-based screening
- Increasing cancer screening uptake and reducing lung-cancer-related mortality

Advantages

- Uses a blood-based molecular method as opposed to radiologic
- Non-invasive relative to image-based screening
- Adjustable thresholds enable use as a method for stand-alone screening or initial screening prior to follow-up

Publications

- Chabon, J. J., Hamilton, E. G., Kurtz, D. M., Esfahani, M. S., Moding, E. J., Stehr, H., ... & Diehn, M. (2020). Integrating genomic features for non-invasive early lung cancer detection. Nature, 580(7802), 245-251.

Patents

- Published Application: WO2024124207

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