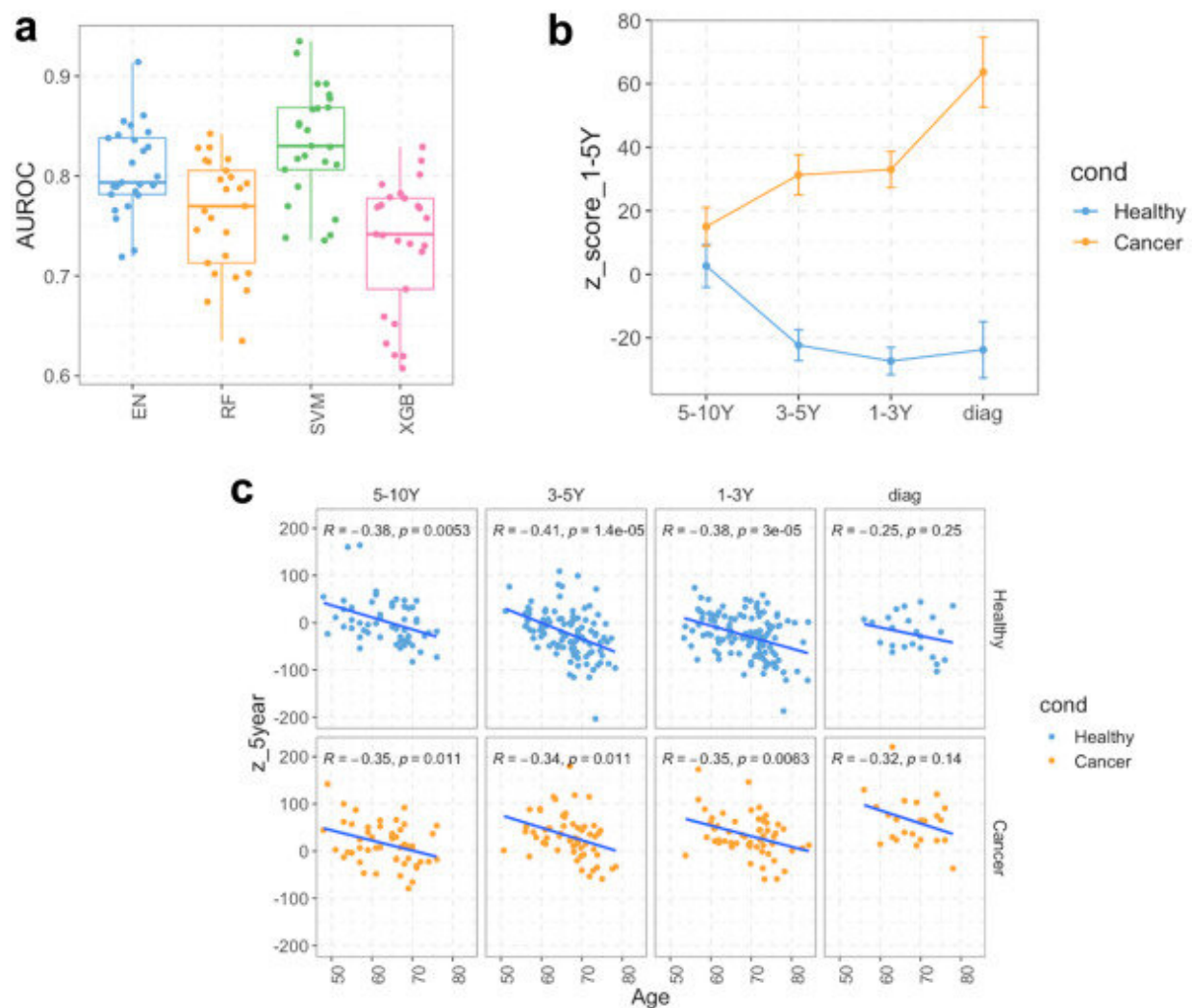# Scientists ever closer to predicting early-stage lung cancer

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Circulating plasma proteins prediction of long-term future lung cancer. (a) A boxplot of training AUC values from four different machine learning models (Elastic Net, Random Forest, Support Vector Machine, XGBoost, five-fold CV

repeated five times) trained on the LLP cohort to predict lung cancer in patients one to five years before diagnosis (110 Cancer, 215 control samples). (b) Protein levels in LLP subjects were transformed using the z-score method and combined to generate one score. Combined z-scores were plotted over time in the LLP cohort for 1-5Y proteins. (c) The z-scores were also correlated with age at time of sample in the same time frame categories; correlation was measured using Pearson correlation coefficient. Credit: *eBioMedicine* (2023). DOI: 10.1016/j.ebiom.2023.104686

Pioneering research led by the University of Liverpool is using molecular biology to analyze blood samples to predict future lung cancer.

The University's Lung Cancer Research Group, in collaboration with Janssen Pharmaceutica NV (Janssen), have demonstrated in a recent publication great potential to use proteins circulating in blood to predict Britain's most common cause of cancer death. While late-stage lung cancer has a poor prognosis, detecting and treating lung cancer at an early stage can save lives.

The long-term study has seen researchers analyze blood samples taken from healthy participants between one and ten years prior to a lung cancer diagnosis. These were compared to control subjects who did not get lung cancer. This comparison demonstrated that proteins in plasma were able to identify those most likely to suffer from lung cancer in the future. Furthermore, they showed that some proteins were related to the presence of undiagnosed tumors.

Over the past three decades, Liverpool has played an essential role in establishing the potential of lung cancer screening for early diagnosis in the U.K. The Roy Castle Lung Cancer Foundation funded the Liverpool Lung Project (LLP), headed by the University of Liverpool's Prof John

Field, Professor of Molecular Oncology (Clinical). This led to the development of the LLP risk model, to help identify individuals at high risk of developing lung cancer, as implemented in the UK Lung Cancer Screening Trial (UKLS) and being used in the NHS Targeted Lung Health Check program.

The LLP Biobank has also accumulated a valuable set of tumor and blood samples used in a wide variety of research. The latest piece of research, recently published in the journal *eBioMedicine*, was led by the University of Liverpool's Dr. Michael Davies, also a Roy Castle Lung Cancer Foundation Senior Research Fellow, in collaboration with scientists at Janssen.

Dr. Michael Davies said, "Lung cancer is Britain's most common cause of cancer death and we are dedicated to the continued understanding of this terrible disease and working with partners to tackle it.

"This latest paper illustrates the importance of our work, as we can potentially look at patterns of proteins in easily obtained blood samples, to help understand the cancer and, significantly, identify who it might affect. This can help us to target those patients for lung cancer screening. We were very fortunate to work with our industrial partners on this project, as they not only supported the ongoing work of the LLP Biobank, but invested in the latest technology to allow us to study more proteins and provided important bioinformatic analysis."

This paper follows the recent Government announcement detailing the continuation of the Targeted Lung Health Checks (TLHC) Program. It will see at-risk patients offered lung cancer screening in order to detect the disease at an earlier stage and improve the chances of successful treatment.

Professor John Field, who also sits as External Advisor on the Cheshire

& Merseyside TLHC Steering Committee added, "Despite great progress towards implementation of lung cancer screening, there is a continued need to better understand early stages of disease, identify biomarkers for early detection and risk stratification and to provide opportunities to intervene to prevent lung cancer, alongside continued efforts to reduce smoking.

"Our latest work complements our international research program, especially with our collaborators on the NIH-funded INTEGRAL project, focusing on use of plasma protein biomarkers for detection of imminent lung cancer and the management of indeterminate nodules detected during screening."

Paula Chadwick, chief executive of Roy Castle Lung Cancer Foundation, said, "We are incredibly proud of our role and the research spearheaded in Liverpool by Prof John Field in the long awaiting announcement of lung cancer screening.

"We funded the Liverpool Lung Project back when no one else was interested in lung cancer, when people dismissed a lung cancer screening program as nothing more than a pipedream. But we knew the potential it had and the lives that could be saved because of it. Many years and a lot of hard work later, that pipedream has become a reality."

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