

Development and validation of a protein biomarker panel for early lung cancer detection in the INTEGRAL project

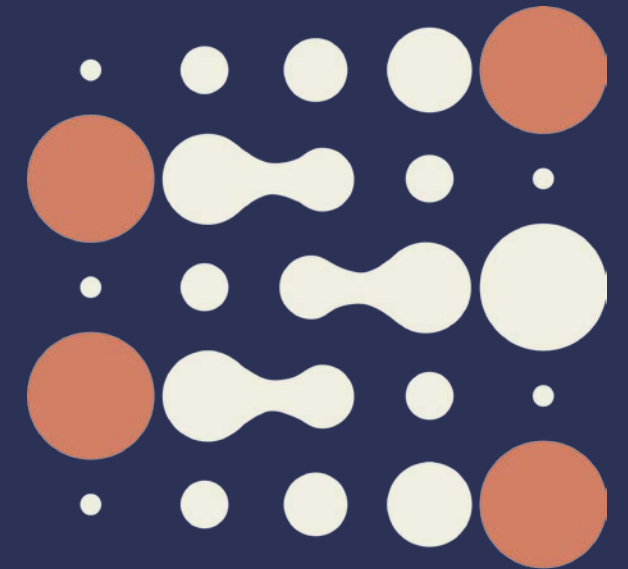
Mattias Johansson,¹ Hana Zahed,¹ Karine Alcala,¹ Xiaoshuang Feng,¹ Florence Guida,¹ Hilary Robbins¹

for the Lung Cancer Cohort Consortium (LC3)

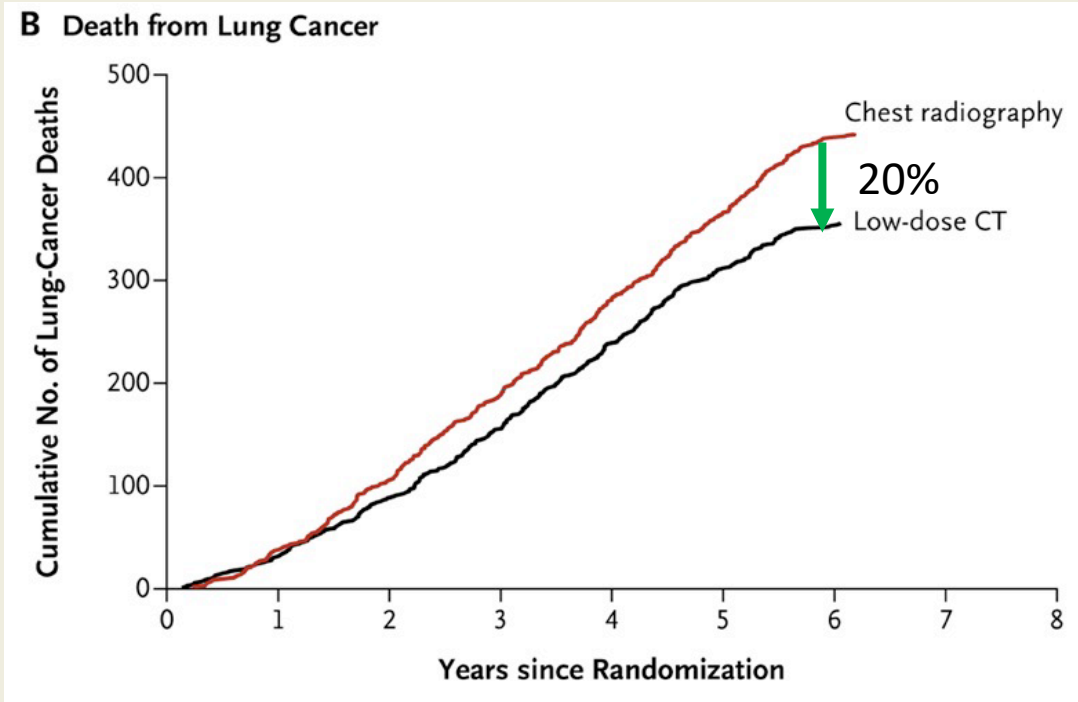
Integrative Epidemiology Team (IET), Genomic Epidemiology Branch (GEM)

JohanssonM@iarc.who.int

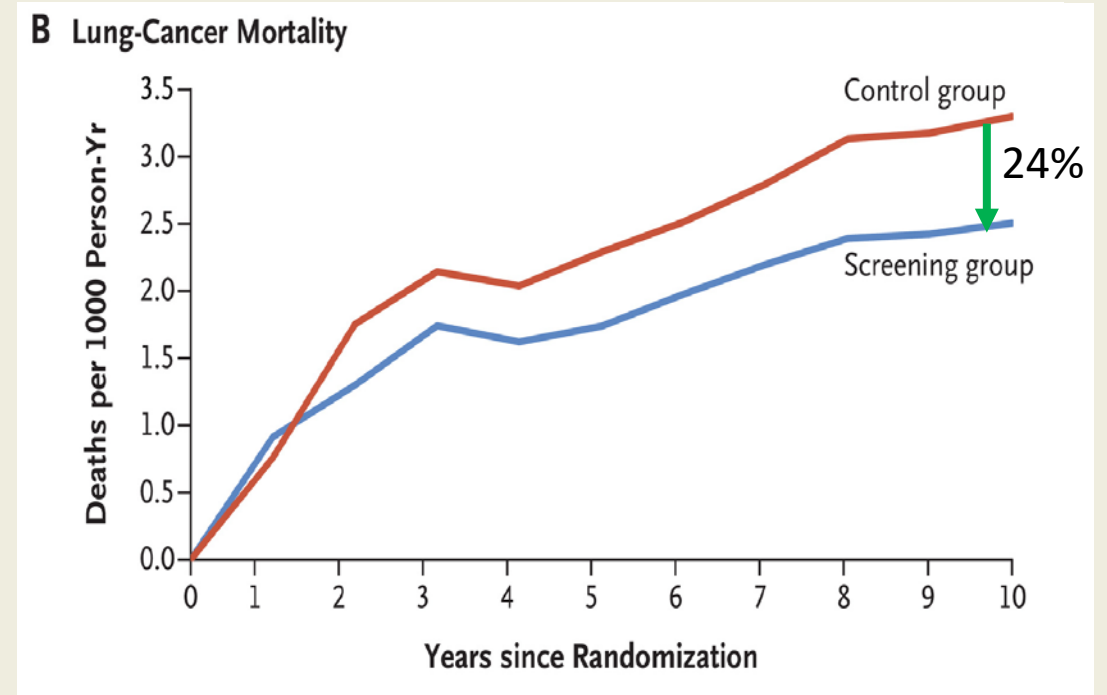
International Agency
for Research on Cancer



Evidence for screening for lung cancer with low-dose CT

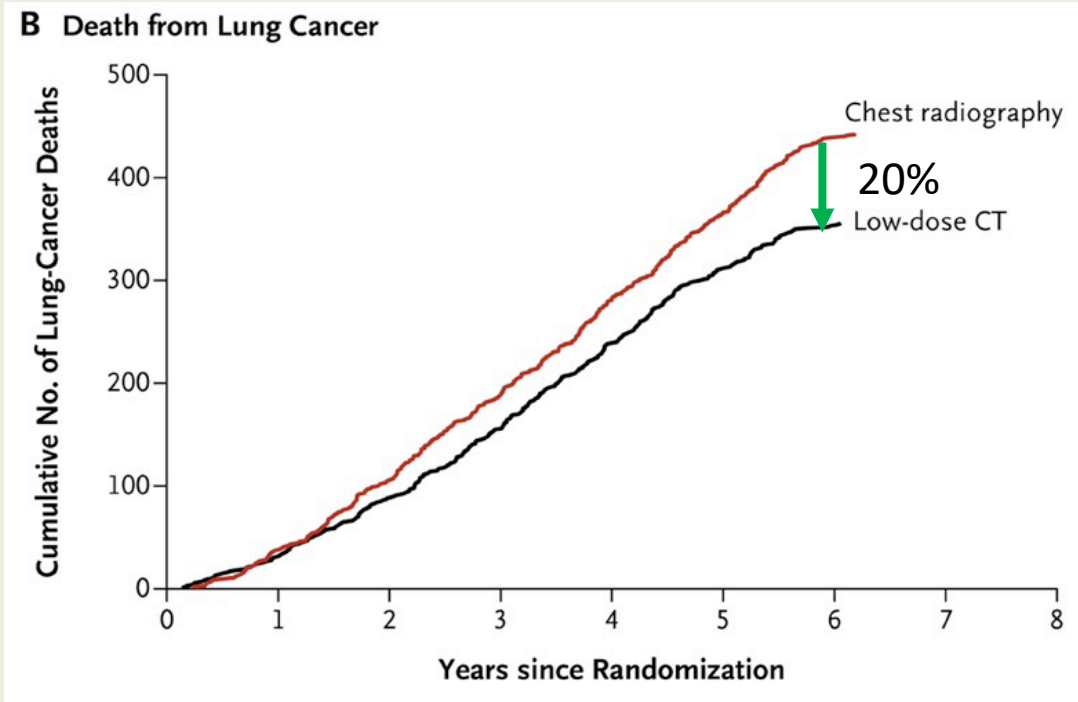


NLST, NEJM, 2011

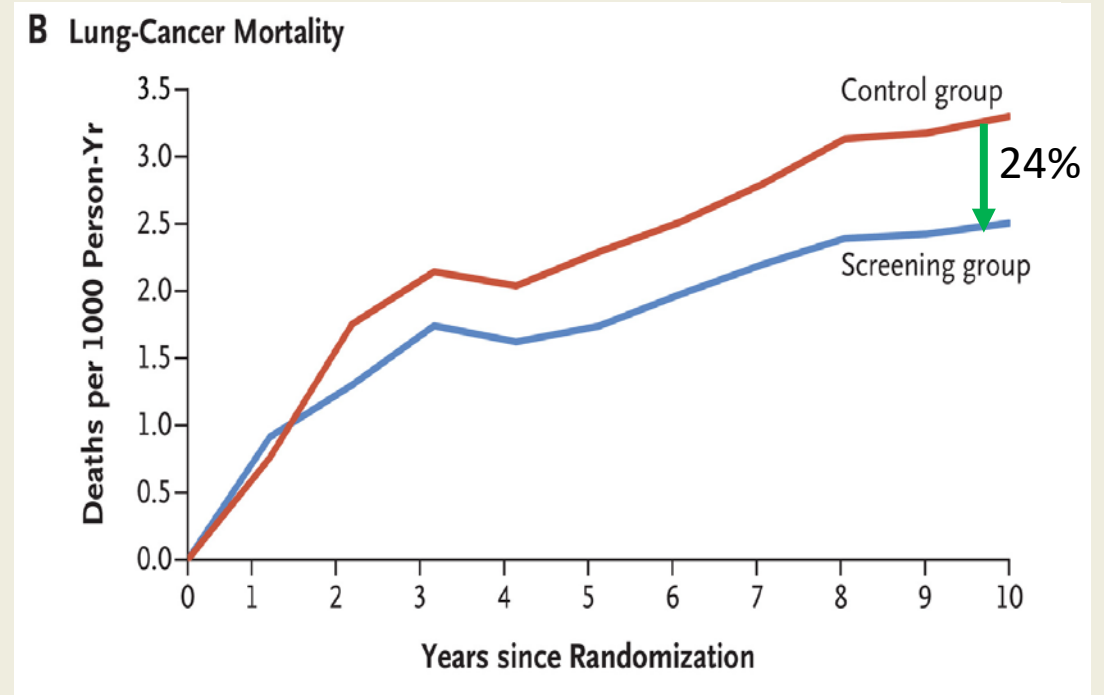


NELSON, NEJM, 2020

Evidence for screening for lung cancer with low-dose CT



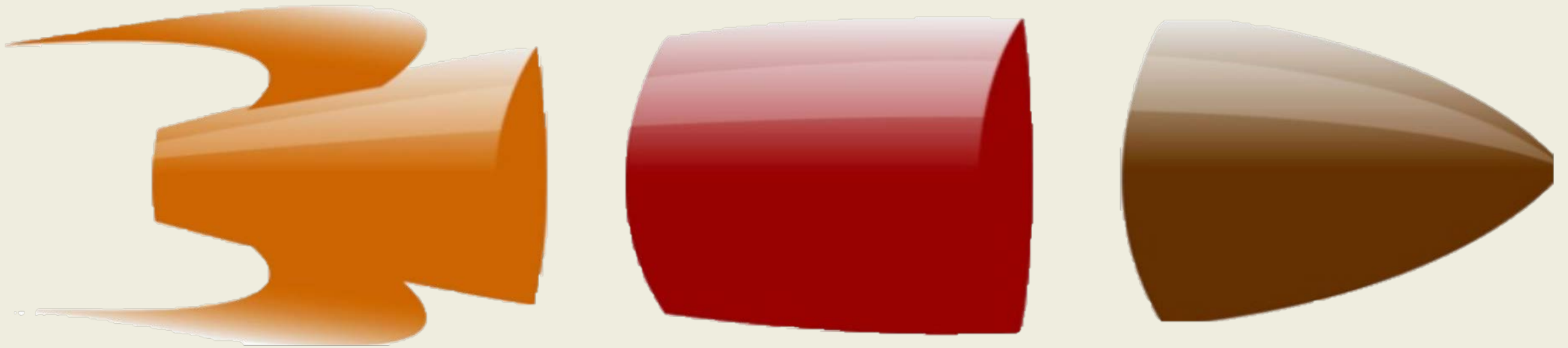
NLST, NEJM, 2011



NELSON, NEJM, 2020

Current eligibility criteria are not sufficiently sensitive in identifying those individuals who will benefit from screening

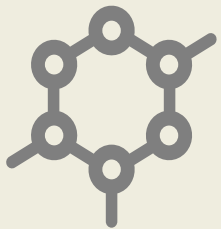
Developing the INTEGRAL protein panel and risk model: *A three-stage rocket*



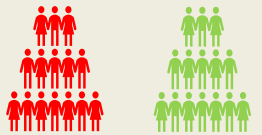
Developing the INTEGRAL protein panel and risk model: *A three-stage rocket*



Discovery
1200 proteins



1163 proteins
Olink Proteomics



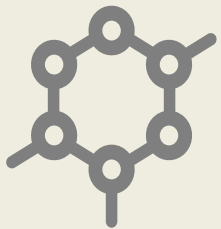
731 case-control
pairs from six cohorts

Developing the INTEGRAL protein panel and risk model: *A three-stage rocket*

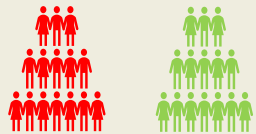
Discovery
1200 proteins

Marker
selection for
clinical
application

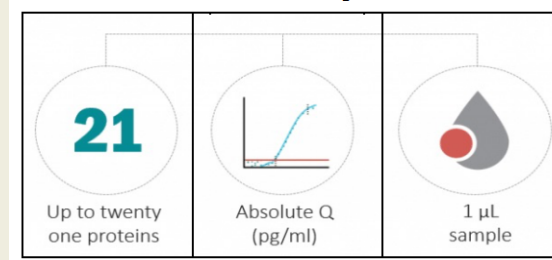
Model training
& validation



1163 proteins
Olink Proteomics



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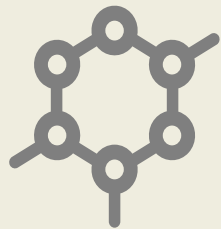
Design of INTEGRAL
custom panel to
quantify 21 proteins

Developing the INTEGRAL protein panel and risk model: *A three-stage rocket*

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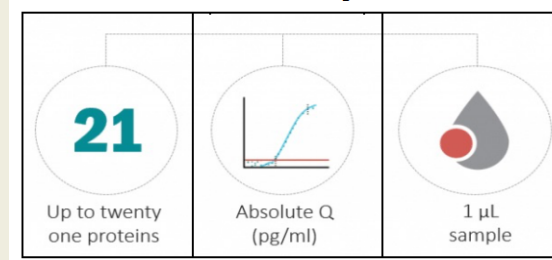
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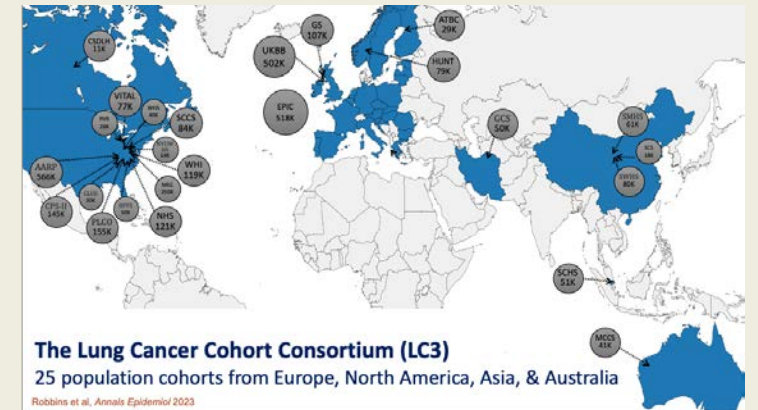
1163 proteins
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731 case-control
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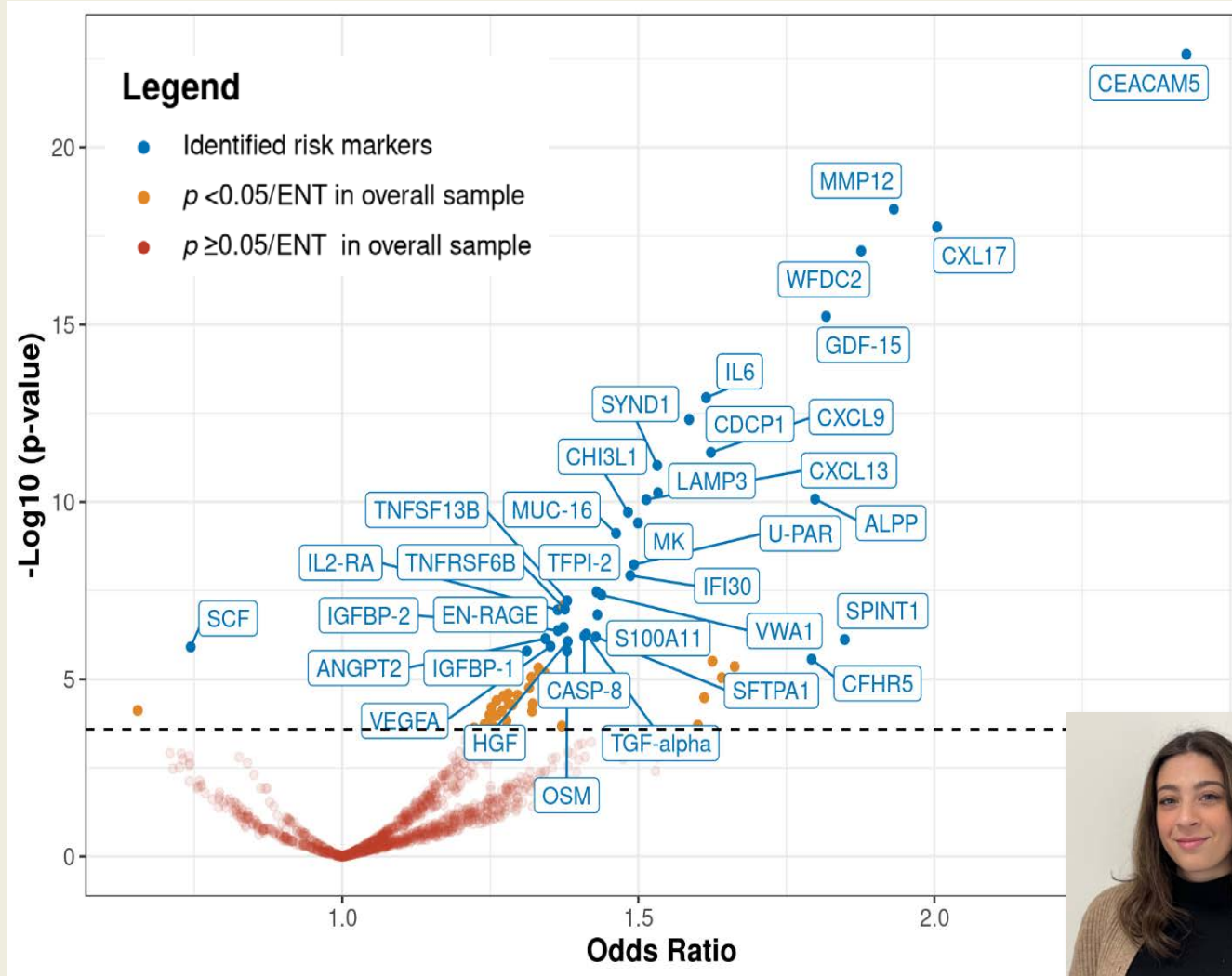


Design of INTEGRAL
custom panel to
quantify 21 proteins



Case-cohort with **1,696 cases**
and **2,926 controls** from the LC3

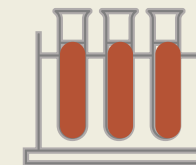
Results from the discovery analysis



731 case-control pairs
from six cohorts



All had a history of
smoking



Pre-diagnostic blood
lead-time < 3 years



1163 proteins
Olink Proteomics

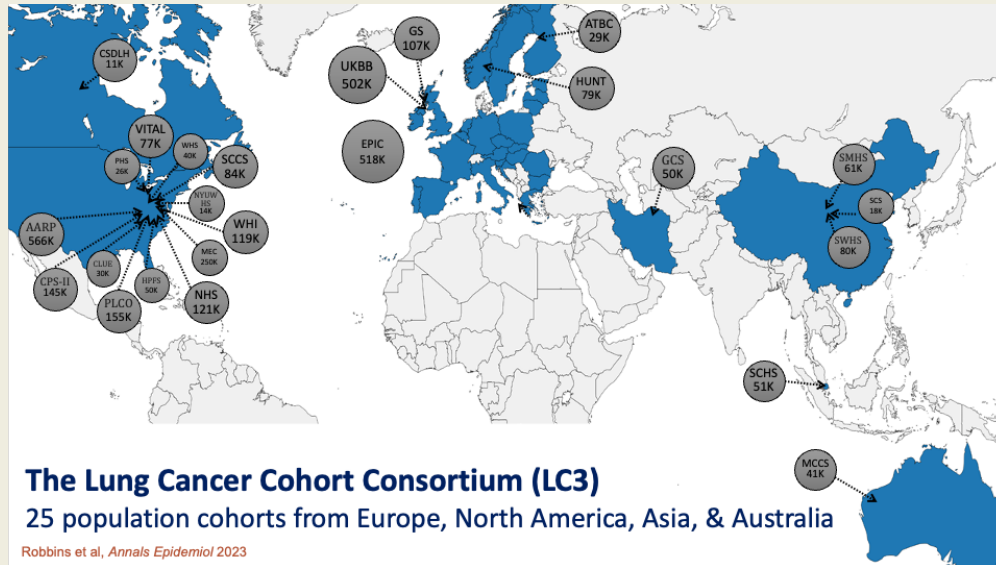


Hana Zahed

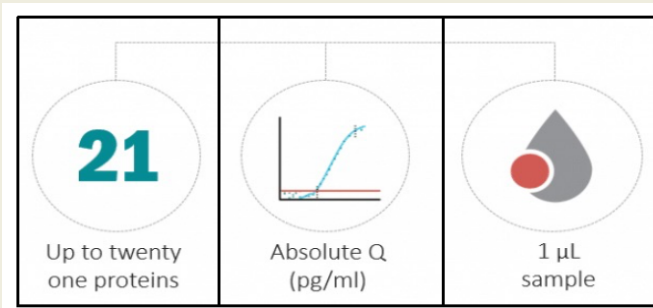
Model training and validation (preliminary)

The Lung Cancer Cohort Consortium (LC3)

25 Cohorts
N: 3,000,000



INTEGRAL panel



LC3 case-cohort
1,696 cases and **2,926 controls** from the LC3

Discussion and Conclusions

- First major exploration for circulating proteins prior to lung cancer diagnosis
- Potential for circulating protein biomarkers to improve risk assessment in LDCT screening
- Related funded initiatives
 - Explore the potential of repeated protein measurements
 - Implementation study in Kentucky, US
 - Expansion to never smokers



Hilary Robbins



Hana Zahed



Karine Alcalá



Xiaoshuang Feng

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Related publications

- Robbins et al. Design and methodological considerations for biomarker discovery and validation in the Integrative Analysis of Lung Cancer Etiology and Risk (INTEGRAL) Program. *Ann Epidemiol.* 2023
- Lung Cancer Cohort Consortium (LC3). The blood proteome of imminent lung cancer diagnosis. *Nat Commun.* 2023.
- Feng et al. Lung cancer risk discrimination of prediagnostic proteomics measurements compared with existing prediction tools. *J Natl Cancer Inst.* 2023
- Khodayari Moez et al. Circulating proteome for pulmonary nodule malignancy. *J Natl Cancer Inst.* 2023



Hilary Robbins



Hana Zahed



Karine Alcalá



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Funding

- INTEGRAL - Integrative Analysis of Lung Cancer Etiology and Risk (U19, 2017-2023), m-PI: Johansson
- LEAP – The Lung EARly Proteins project: A LEAP toward implementing biomarkers in lung cancer screening (R01, 2022-2027), PI: Robbins
- INTEGRAL-AT – Integrative Analysis of Lung Cancer Etiology and Risk – Application and Translation (U19, 2023-2028), m-PI: Johansson



Hilary Robbins



Hana Zahed



Karine Alcalá



Xiaoshuang Feng

Take-home-message: It takes a village....

