MADRID 2023 ESMO congress

Differentiation of Malignant and Benign Lung Nodules using Epigenetically Modified Nucleosomes in Plasma

Pei-Hsing Chen, MD
National Taiwan University Hospital, Taiwan

October 22nd, 2023

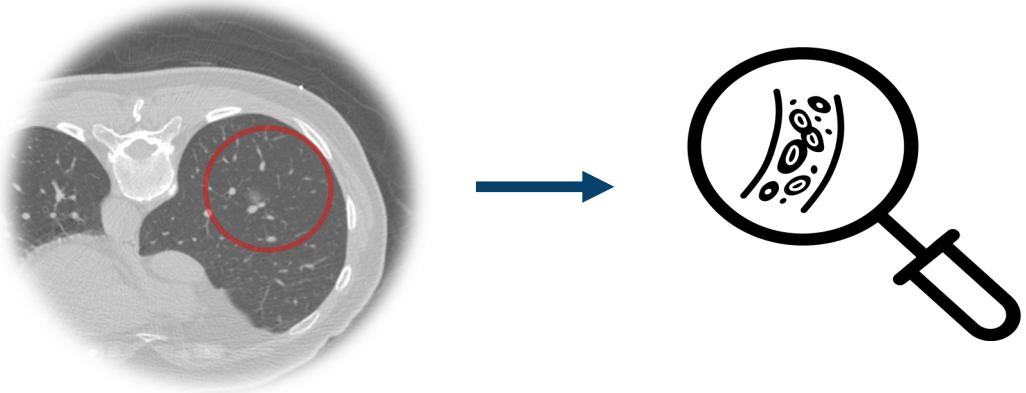
DECLARATION OF INTERESTS

Pei-Hsing Chen

This research was conducted in collaboration with Belgian Volition SRL.
The results presented here were partially funded by a research grant from Belgian Volition SRL.

Introduction

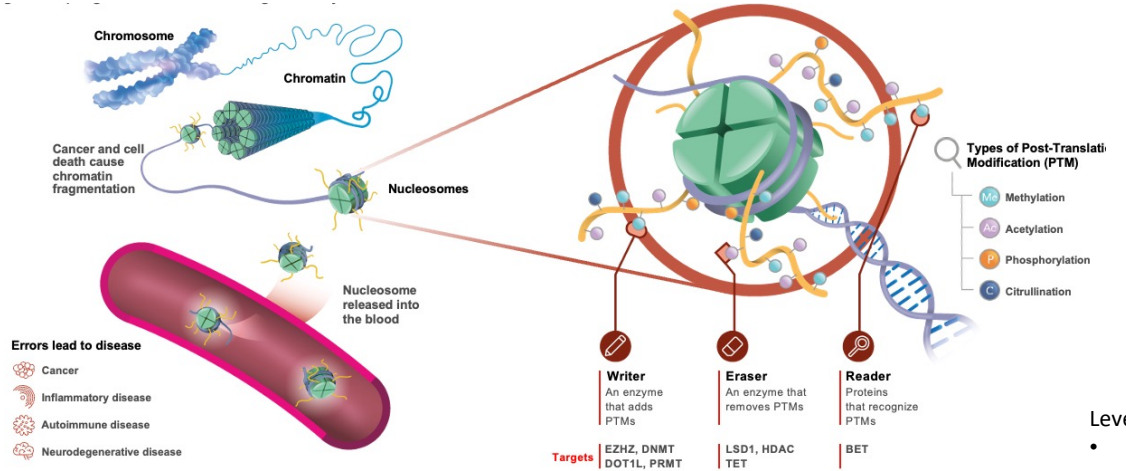
- In Taiwan, the initiation of the LDCT screening program led to an increase in the detection of nodules.
- An unmet clinical need for accurate noninvasive tests to differentiate between malignant and benign nodules following LDCT screening.
- Novel blood-based tests could provide a straightforward distinction between lung cancer and non-malignant nodules.

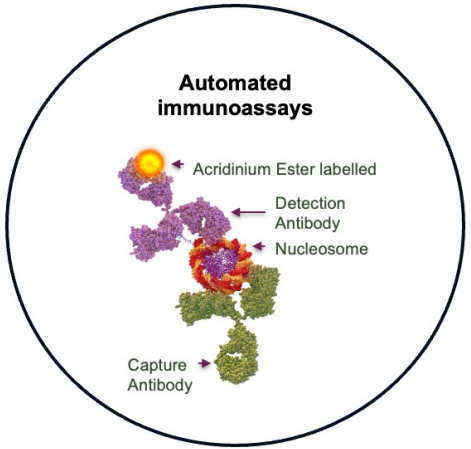


Tsai et al., Ann Transl Med 2019;7(2):31

Epigenetic biomarkers: a valuable tool from target identification to validation in clinical studies

Measuring and monitoring nucleosome levels and modifications in circulating blood has the potential to aid diagnosis, prognosis and monitoring of lung cancer

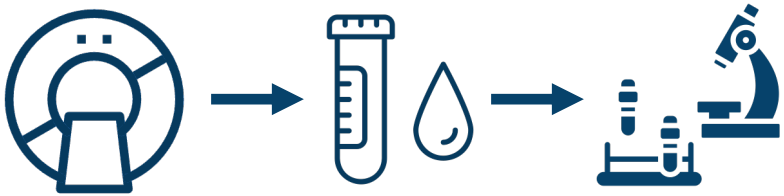




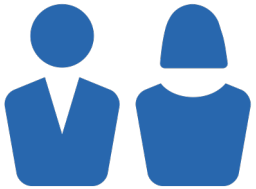
Levels of circulating nucleosome were evaluated

- Histone isoform H3.1 (Nu.Q® H3.1)
- Methylated lysine 27 of histone H3 (Nu.Q® H3K27Me3)
- Methylated lysine 36 of histone H3 (Nu.Q® H3K36Me3)

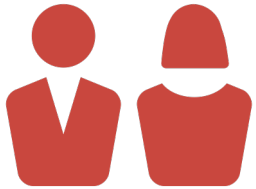
Study Design



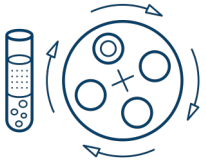
Pathology confirmed (94.4 %) or lesion disappeared in the follow-up image.



Benign nodule (BN, n=158)

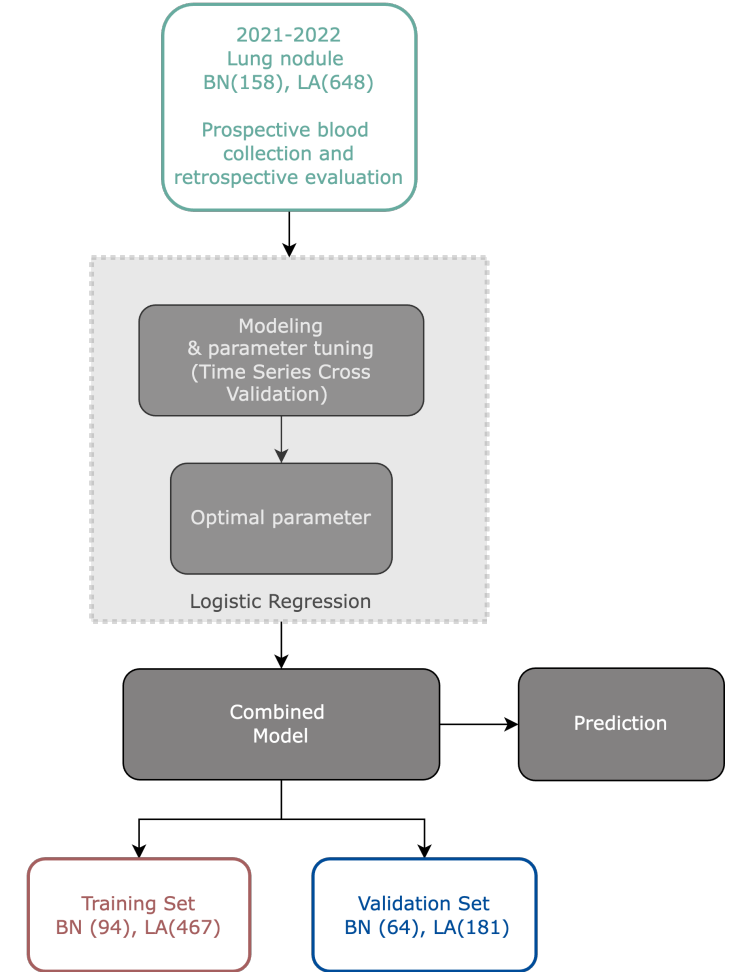


Cancer / Pre-cancer (LA, n=648)



K2-EDTA Plasma samples

Circulating Nucleosomes and their histone modifications (Nu.Q® immunoassay, Volition SRL).

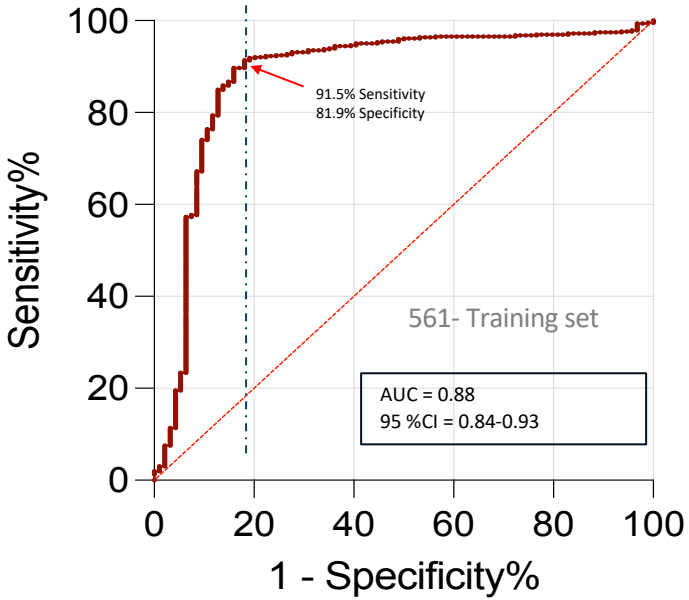


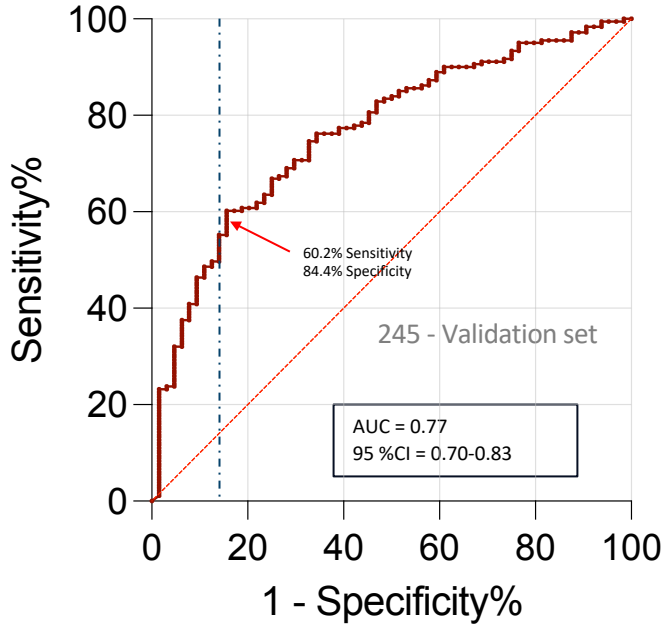
MADRID 2023 ESMO congress

Pei-Hsing Chen, MD

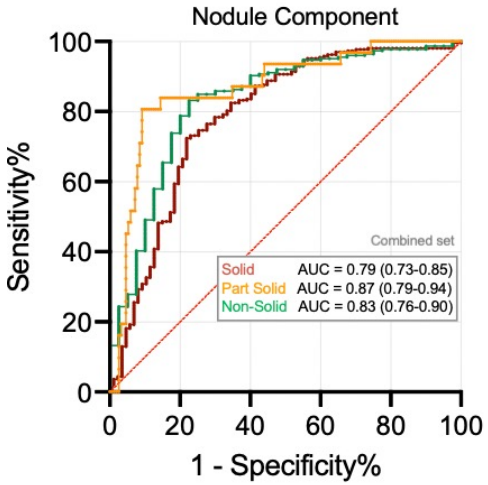
Statistical model for differentiation

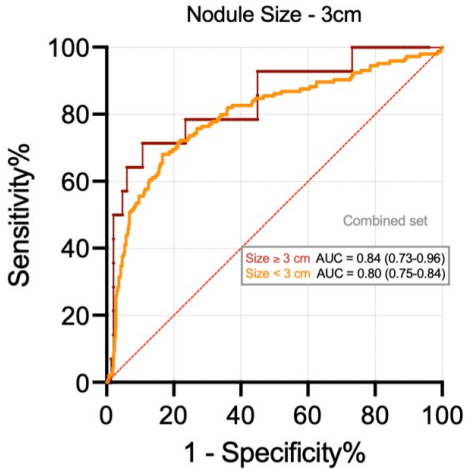
Logistic regression model for simple algorithm
Based on histone modifications, Including H3K27Me3/H3K36Me3 and the H3.1 histone isoform
561 (70%) training / 245 (30%) validation

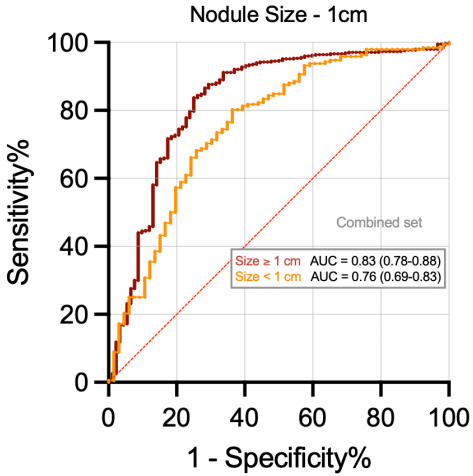


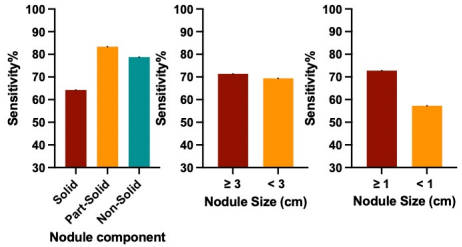


Combined model from training set : subgroup analysis









Sensitivity at 80% Specificity

- Component

  Performance is superior in part-solid and non-solid lesions

- Size

  Performance was maintained with a cutoff of 3 cm, but diminished with a cutoff of 1 cm, though it remained satisfactory for differentiating small nodules.

Conclusions

- **Epigenetic features of nucleosomes in blood plasma offer potential for identifying cancer/pre-cancer, potentially reducing the false-positive rates of LDCT.**

- **Epigenetic features of nucleosomes allow for precise differentiation between cancer/pre-cancer and benign nodules using a combined logistic model, particularly for tumors with non-solid components.**

- **Epigenetic features of nucleosomes demonstrated superior performance in larger tumors, yet maintained satisfactory results for nodules smaller than 1cm.**

Pei-Hsing Chen, MD

Acknowledgment

Research Team Members and Co-authors

Tung-Ming Tsai, Dorian Pamart, Tom Bygott, Marielle Herzog, Jake Micallef, Jin-Shing Chen

Pei-Hsing Chen

b96401034@ntu.edu.tw

MADRID 2023 ESMO congress