Epigenetic Nucleosomes in Plasma for Pulmonary Nodule Differentiation

290 eTiP

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- *Clinical Trial identification:* NCT06838806

INTRODUCTION

Recent trials confirm that low-dose CT (LDCT) screening lowers lung-cancer mortality in high-risk populations; however, its high false-positive rate inflates costs and exposes patients to unnecessary procedures, underscoring the need for adjunct biomarkers. Given most nodules detected on LDCT measure less than 20 mm, obtaining tissue for biopsy is challenging. We previously developed a plasma-based immunoassay that quantifies lung-cancer-specific, epigenetically modified nucleosomes with robust performance. The assay is rapid, fully automatable, and cost-effective — features well suited for routine clinical use. After demonstrating strong performance in a retrospective cohort, we are now conducting an external, prospective validation to confirm its accuracy in distinguishing malignant from benign pulmonary nodules.

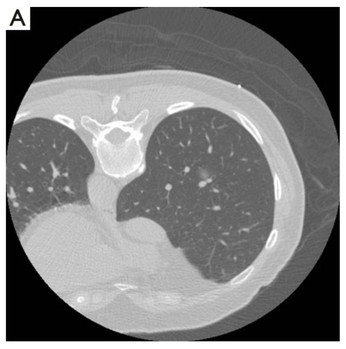

Figure 1. Central undiagnosed GGO nodule

STUDY HYPOTHESIS

The objectives of this study are to validate the diagnostic accuracy of the Nu.Q® blood test for lung cancer in the Taiwanese population, compare its diagnostic performance with LDCT, and explore its potential role in lung cancer prevention and improved survival outcomes.

DESIGN & KEY CRITERIA

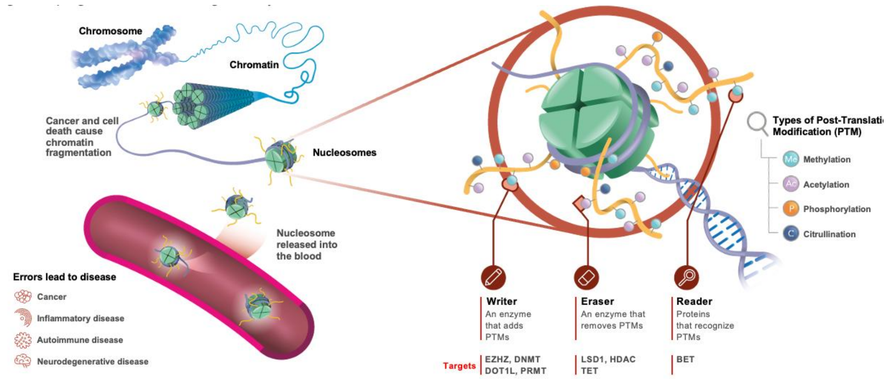

Figure 2. Nucleosomes and Epigenetic Modifications

Inclusion Criteria:

- Aged 20 or older
- Underwent a low-dose chest CT scan or a standard chest CT scan, showing lung nodules ≥ 6mm
- Individuals understand the content of the consent form and are willing to participate in this study
- The lung nodule is assessed by a physician as high-risk, requiring thoracic surgery or biopsy for diagnosis

PROCEDURE

- We are conducting a **single-arm, prospective, specimen-collection, blinded-evaluation trial.**
- 20 mL of peripheral blood will be drawn from individuals undergoing chest LDCT or CT who have pulmonary nodules ≥ 6 mm — the threshold warranting clinical management in Asia. Plasma will be isolated and analysed on the Nu.Q® platform, and results will be compared with all participant's histopathological diagnoses.
- All specimens are processed with Nu.Q® H3.1 and Nu.Q® H3K27Me3 chemiluminescent sandwich immunoassays (Belgian Volition SRL, Isnes, Belgium) on the IDS-i10 automated analyser, following the manufacturer's instructions.

SAMPLE SIZE

Designed for a cancer-screening outpatient context, the study is powered for a disease prevalence of ≥ 70 %. The study aims for a performance of 70 % sensitivity and specificity; and allows for a 18 % attrition rate.
A total of 500 participants will be enrolled.

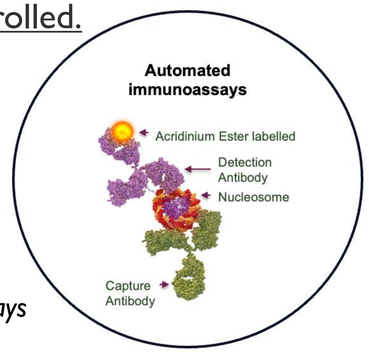

Figure 3. Nu.Q® Immunoassays

STUDY STATUS

- The study is intended to recruit 500 patients from 2 centers in Taiwan (NTUH, NTUCC). Patient enrolment is in progress, the first patient was enrolled in March, 2025.
- There are currently 295 patients recruited and 260 patients with pathology result at the end of Sep 2025. Patient recruitment is expected to be completed by March 2026.

CONCLUSION

The study is currently on time and anticipated to complete by the end of 2025. We expect to provide evidence for a new method to aid in diagnosis of undiagnosed nodules, especially small nodules.

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Reference::
Accurate Diagnosis of High-Risk Pulmonary Nodules Using a Non-Invasive Epigenetic Biomarker Test
Chen, P.-.H., Tsai, T.-.M., Lu, T.-.P., Lu, H.-.H., Pamart, D., Kotronoulas, A., Herzog, M., Micallef, J.V., Hsu, H.-.H. & Chen, J.-.S. Cancers 2025