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Performance of a Nu.Q™ H3.1 assay for lung cancer detection.

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Abstract Disclosures

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Background:
Lung cancer diagnosis relies on invasive methods and often occurs at a late stage of disease, explaining its poor outcome. Nucleosomes are DNA fragments wrapped around histones. They may constitute a non-invasive and early diagnostic method for lung cancer. We investigated the clinical and statistical performance of nucleosome assay levels alone and in combination with cytokines in plasma from untreated lung cancer (LC) patients and what their discriminant power was towards chronic obstructive pulmonary disease (COPD) and healthy (H) subjects.

Methods:
142 plasma samples were prospectively collected: H, n = 45; LC, n = 44 and COPD, n = 53. The circulating level of intact nucleosomes containing the histone H3.1 isoform (Nu.Q^a-H3.1) was individually tested and in combination with cytokines for its performance in discriminating subjects for their underlying condition. Then, statistical performance of each model was tested with binary logistic regression models for the best combination of biomarkers for the following groups: cancer vs control (group A), cancer vs COPD+control (group B) and for cancer vs COPD (group C). The best model for each group was then applied to two independent biobank cohorts for validation.

Results:

Results for Nu.Q-H3.1 was an area under the curve (AUC) of 0.79, for group A, B and C; a sensitivity of 68%, 66% and 66% for group A, B and C, respectively, for 80% specificity. For group A the H3.1+IL-10 model achieved a sensitivity of 77% for 80% specificity with an AUC of 0.88 (R^2 = 55.8%). For group B the H3.1+IL-6+IL-10 model achieved a sensitivity of 70% with an AUC of 0.85 (R^2 = 40.6%). For group C the H3.1+IL-6+IL-10 model achieved a sensitivity of 79% with an AUC of 0.85 (R^2 = 46.1%). The validation cohort performed similarly. Results for the 3 cohorts taken together were: AUC of 0.83, 0.87 and 0.90 for group A, B and C, respectively; sensitivity of 75%, 76 % and 84% for group A, B and C, respectively, for 80% specificity.

Conclusions:

Nucleosomes are detected in the plasma of H, LC and COPD patients. Combination with cytokines as described in these models allows for a good power ofdiscrimination between the three groups. Based on these encouraging results, we believe further studies with larger numbers of patients should be performed to confirm and validate the usefulness of these biomarkers and models.

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