Use of Serum Autoantibodies to Identify Early-Stage Lung Cancer: A Significant Step Forward in Early Detection

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BACKGROUND

***Early*CDT-Lung**™ is a commercially-available blood test offered in the United States by Oncimmune USA LLC to aid in the early detection of lung cancer in a high-risk, asymptomatic population. The test measures autoantibodies (AAbs) to a panel of six cancer-associated antigens (p53, NY-ESO-1, CAGE, GBU4-5, Annexin 1 and SOX2). Previous studies in our laboratory have confirmed the value of a panel for detecting AAbs in cancer.[1-4] Validation studies (*n*=1310) demonstrated the ability of the panel to detect nearly 40% lung cancers while maintaining 90% specificity.[4] Separating these data according to lung cancer type revealed a sensitivity of 45% for SCLC and 34% for NSCLC with 90% specificity. We report confirmatory data for clinical sensitivity and specificity determined in an independent, prospective, post-validation dataset.

METHODS

PATIENTS

Four separate and unique groups of patients with newly-diagnosed lung cancer are reported and compared to published validation data.[4] Samples were collected from multiple locations in the USA, Canada, and Europe. All samples were collected under ethical approval and full patient consent.

Cancers:

- All cancer specimens were drawn post-diagnosis and prior to any treatment.

Controls:

- Controls were matched to cancers by risk, matching gender, age and smoking history, for three of the four post-validation studies reported.
- Two of the three sets run with controls were matched 2:1 (controls:cancers) while the third was matched 1:1.
- All controls were taken from the general population.

Table 1. Demographic summary of sample sets.

	Gender		Age			
	Male	Female	Min	Max	Mean	Median
Validation set[4]	199	70	38	87	64.4	65
Midlands SCLC	68	54	43	86	65.3	65
122K Post-Val set	201	48	23	82	61.9	62
Vancouver	50	71	45	90	69.0	70
Nott/Seralab/MO	43	38	50	86	69.3	70

ASSAY PROCEDURE

Patient sera were diluted and evaluated using ***Early*CDT-Lung**, a quality-controlled semi-automated indirect enzyme-linked immunosorbent assay (ELISA) based method, as described elsewhere.[4] Briefly, plates are coated with the six cancer-associated antigens (as well as two control antigens), each diluted to create a six-point titration curve and incubated overnight. Plates are washed and blocked for 1 hr before addition of diluted serum. After a 90 min incubation, an anti-human IgG-HRP secondary antibody is added to washed plates and allowed to react for 1 hr. Substrate is then added to the plates, and 15 min later the OD at 650 nm is measured. Following calibration of the OD signal to a log reference unit (RU), the values at the two highest antigen concentrations for each AAb are compared to previously established cut-offs. A result is considered positive when two criteria are met: 1) the RU must exceed the cut-off for any one of the six AAbs and 2) a dose response must be observed with respect to the antigen titration series.

RESULTS

Table 2. Calculated ***Early*CDT-Lung** performance for each of four unique sample sets compared to a validation study.

	Study	Number Ca / N	NSCLC %	Overall Sens/Spec (%)	Sensitivity (95% CI) NSCLC	Sensitivity (95% CI) SCLC	Specificity (95% CI)
VALIDATION STUDIES: Antigens: p53, NY-ESO-1, CAGE, GBU4-5, Annexin I, SOX2							
1	*Validation set* [4]	*269/269*	*76%*	*37 / 90*	***34*** *(27, 41)*	***45*** *(34, 57)*	***90*** *(86, 93)*
POST-VALIDATION STUDIES: Antigens: p53, NY-ESO-1, CAGE, GBU4-5, Annexin I, SOX2							
2	Midlands SCLC	122/0	0%	57 / NA	-	**57**	-
3	122K Post-Val set	249/497	97%	34 / 87	**34**	N/D	**87**
4	Vancouver	121/115	100%	31 / 84	**31**	-	**84**
5	Nott/Seralab/MO	81/206	62%	38 / 89	**35**	**43**	**89**
POST-VALIDATION STUDIES TOTAL: Antigens: p53, NY-ESO-1, CAGE, GBU4-5, Annexin I, SOX2							
1-5	Totals *	842/1087	-	38 / 88	**34** (30, 37)	**50** (44, 57)	**88** (86, 90)
2-5	Totals	573/818	-	39 / 87	**33** (29, 38)	**53** (45, 61)	**87** (84, 89)
3-5	Totals	451/818	-	34 / 87	**33** (29, 38)	**41** (25, 58)	**87** (84, 89)

**Note: Data from the Validation set are included here.*

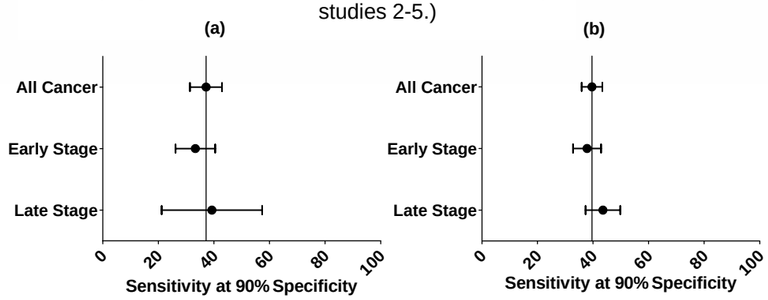
Table 3. Sample numbers by stage of disease for all studies 1-5. (Stage was not available for 110 cancers.)

	Number of Samples	Total
EARLY-STAGE DISEASE		
Stage I NSCLC	307	502
Stage II NSCLC	114	
Limited SCLC	81	
LATE-STAGE DISEASE		
Stage III NSCLC	85	230
Stage IV NSCLC	32	
Extensive SCLC	113	

Table 4. Positivity rate of ***Early*CDT-Lung** for early-stage disease from post-validation studies 2-5. (Stage was not available for 63 cancers.)

	Positivity Rate for Early-Stage Disease
Stage I & II NSCLC	34.5%
Limited SCLC	53.2%

Figure 1. Sensitivity of ***Early*CDT-Lung** for both early and late-stage lung cancers evaluated a) in the validation study compared to b) post-validation studies. (Stage was not available for 47 cancers in study 1 and 63 cancers in studies 2-5.)



DISCUSSION

Four unique datasets comprised of patients from five different countries revealed very similar sensitivities and specificities and also agreed well with the results from the validation study. High-risk controls were matched to cancers in 3 of the 4 studies for specificity comparison; controls were obtained from the general population and matched for gender, age and smoking history, ensuring a comparable control group.

***Early*CDT-Lung** detects autoantibodies in both early- and late-stage lung cancer and also across all types of lung cancer, with a higher sensitivity for SCLC compared to NSCLC.

The authors would like to point out that some numbers reported here vary from the submitted abstract due to the recent availability of additional data.

CONCLUSIONS

- This large dataset further shows that up to 40% of lung cancer, including early-stage disease, can be identified through a blood test.
- ***Early*CDT-Lung** is able to detect both early- and late-stage lung cancer. The positivity rate for early-stage disease was found to be 34.5% for NSCLC and 53.2% for SCLC.
- ***Early*CDT-Lung** is a valuable tool for physicians providing an aid to early detection of lung cancer in high-risk, asymptomatic patients, namely long-term smokers and individuals with exposure to environmental carcinogens such as radon and asbestos.

REFERENCES

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