



2020 World Conference
on Lung Cancer Singapore

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CONQUERING THORACIC CANCERS WORLDWIDE

Cell-Free DNA (cfDNA) Methylation Assay Allows for Early Detection and Identification of Lung Cancer

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JANUARY 28-31, 2021 | WORLDWIDE VIRTUAL EVENT



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DISCLOSURES

Commercial Interest	Relationship(s)
Universal Diagnostics S.L.	employee

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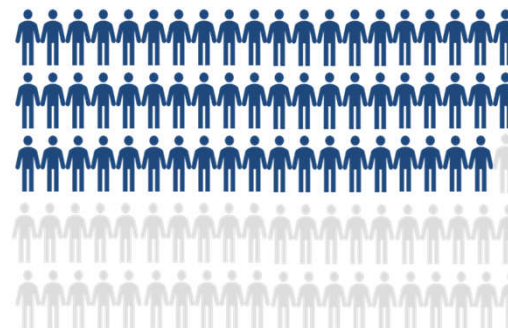
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Lung cancer problem

Distant: ~6% survival 5 years*



Localized: 59% survival 5 years*



**Early detection saves lives. Current screening struggles with low accuracy
Current screening only for high risk patients – while low risk cases are rising**

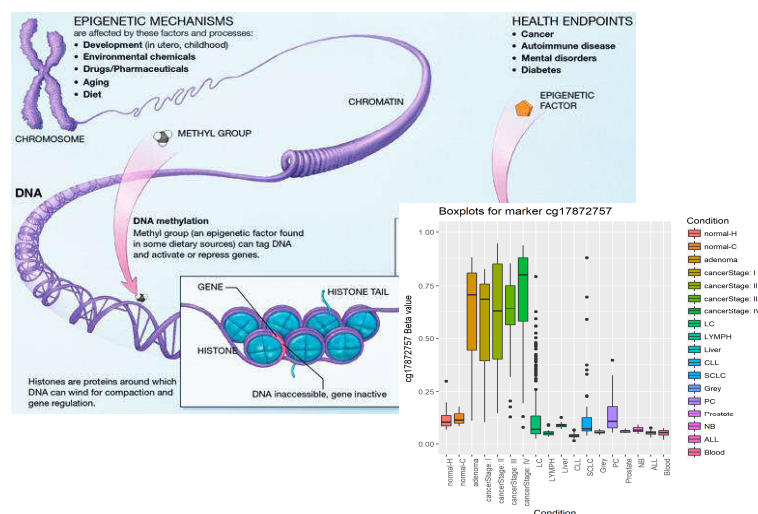
*Source: SEER 18 2010-2016

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DNA methylation = „ideal“ biomarker

Examples



Comment

- mC- changes = early event in cancerogenesis /complex disease development
- influence course of illness, response to drugs
- tissue specific (cancer specific)
- heritable pattern
- chemically as stable as DNA
- detectable and stable in blood plasma (e.g. plasma cfDNA (ctDNA))

Early indicator for cancerogenesis



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Sample set description

Overview

Characteristics	Control	Lung cancer
Age (average (min-max))	60(32-78)	59(42-75)
Gender Male (%)	35(49%)	25(68%)
Stage		
Stage I		11
Stage II		4
Stage III		7
Histology		
Adenocarcinoma		11
Squamous cell carcinoma		11
SCLC		9
Other		6
Smoking history		
Current or ex	19	14
Never	33	13
Unknown	19	10

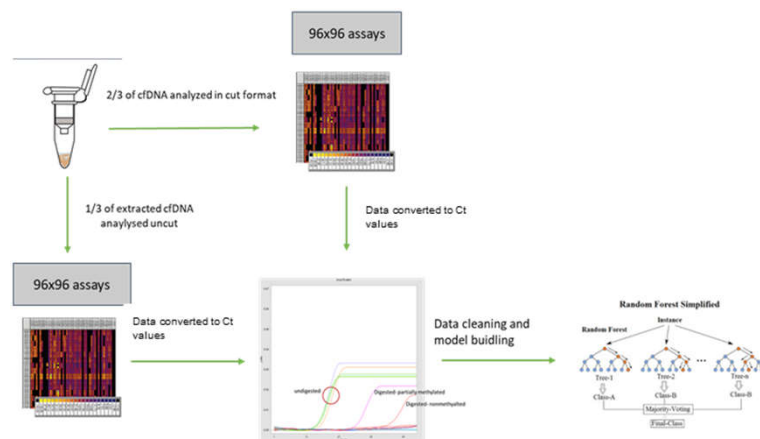
Comment

- 8 ml of plasma collected from 108 patients attending general check up or oncology units in Spain and USA was used
- Lung cancer patients had to have a confirmed cancer diagnosis with histology and stage information included
- Control patients were asymptomatic patients with no known cancer diagnosis or history



Analysis description

Overview



Comment

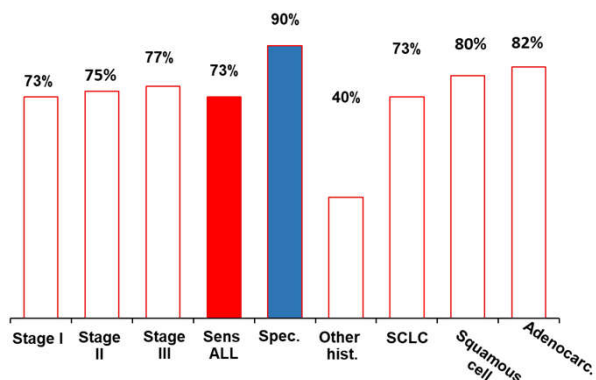
- Human Methylation 450K data available from The Cancer Genome Atlas (TCGA) consortium was used for initial biomarker selection*
- Methylation-sensitive restriction enzyme–qPCR approach was used to target regions of interest in plasma cfDNA
- dCt (delta cycle threshold) values were used for further analysis
- Random forest feature selection algorithm utilizing Monte-Carlo cross-validation over 50 sub-setting was utilized for building and testing marker panel
- Accuracy was defined as the fraction of correct calls

*<https://www.cancer.gov/about-nci/organization/ccg/research/structural-genomics/tcga>

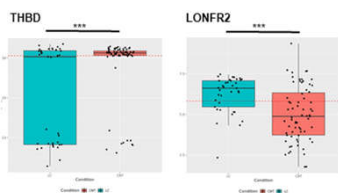


Results

Overview



	Panel Prediction (Pearsons correlation p-value)
Sex	0.70
Smoking history	0.51
Histology	0.64
Age	0.32



Comment

- 10 methylation marker panel:
 - Overall sensitivity 73% at 90% specificity
 - Stage I sensitivity of 73%
 - Good sensitivity for main histological subtypes
- According to Preasons correaltion test panel prediction was not correlated to main clinical/physiological features- $p > 0.05$
- Single markers** with singificant discriminative power $p < 0.05$ (***)
- Biological relevance of the **10 markers** checked: E.g.- **THBD** promotes **angiogenesis** by enhancing **cell adhesion, migration**, and FAK activation through interaction with fibronectin



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Conclusions

- Targeted methylation marker panels have potential for early blood-based detection of lung cancer with high sensitivity and specificity
- Methylation marker panel has good accuracy for detection of main histological subtypes
- Methylation panel performance is not connected to the smoking history of the patient
- This method could serve as the basis for further development of a highly accurate and minimally invasive blood-based screening test for wider population.