Molecular markers for early detection

miR-Test: A Blood Test for Lung Cancer Early Detection

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Disclosure slide

- Our department is the recipient of a sponsored research fund from a privately held molecular diagnostic company (Gensignia Life Sciences, Inc.). The research fund in object was conferred after the termination of the experimental work herein described.

- I am a co-inventor on a patent application regarding the diagnostic miRNA-based blood signatures described herein (WO2012089630 A1).
Outline

• Introduction on microRNA

• Development of a microRNA-based blood test (miR-Test) for lung cancer early detection.

• Validation of miR-Test in a LDCT screening trial.
Biogenesis and diverse functions of miRNAs

Mechanisms of release of extracellular miRNAs
Circulating miRNA screening to select high-risk individuals

At-risk Individual

Serum miRNAs Test

LD-CT Screening

High-Risk Individual

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**miR-Test Development**

**Global Serum miRNA Expression Profile**

**IEO serum miRNA-test**

34-miRNA signature

Risk-Index = \( \sum x_iw_i \)

-20
-10
0
10
20
30

-4.2 + 7.7 + ... samples

Low
High

Normal
Adenocarcinoma (AC)
Squamous Cell Carcinoma (SCC)

Bianchi et al. EMBO Mol Med 3(8) 2011

**DISCOVERY PHASE**

Serum <0.5ml

365 miRNAs

253 samples

**Organisers**

**Partners**

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miR-Test Development

1. Overall study design:

- **N=1115**
  - COSMOS screening trial (asymptomatic cohort)

- **N=74**
  - IEO thoracic surgery

   **Calibration Set**
   - N12/T12

   **miR-Test**

   **Validation Set**
   - N972/T36

   **Specificity Set**
   - 38 NOD
   - 16 COPD
   - 24 PN
   - 5 Benign

   **Clinical Set**
   - T74

   **Additional clinical validation**

2. miR-Test simplification (from 34 to 13 miRNAs)

- Calibration set
- Validation set
- Specificity set
- Clinical set

3. **miR-Test validation (LDCT screening trial):**

- **COSMOS trial**
  - >50 years
  - >20 packs/year

- **972 w/o Lung Cancer**

- **36 with Lung Cancer**

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Summary

miR-Test performance in all CT screened individuals (N=1115):

- 820 individuals were miR-Test negative (NPV>99%).
- Of the 295 miR-Test positive, 38 out of 48 had cancer (SE, 79%).

Outlook:

- Today: 10,000 CT exams to detect 100 tumors in a high-risk population.
- Tomorrow: 2455 CT exams in miR-Test positive subjects to detect 79 tumors or 3108 CT exams to detect 100 tumors in a high-risk population.
High-risk individuals screened by LDCT and miR-Test: the COSMOS-II trial (results expected in 2017)

Multicentric Study

- **Italy**
  - COSMOSII
    - 10,000 HIGH RISK SUBJECTS SCREENED BY LD-CT (AIRC-FUV)
  - Recalibrated Bach model
    - 6000 BACH-HIGH SUBJECTS (AIRC-FUV)
      - 6000 SCREENED FOR SERUM MIRNAS (AIRC-FUV)
    - 4000 BACH-LOW SUBJECTS
      - 1000 SCREENED FOR SERUM MIRNAS (LCRP)

- **U.S.**
  - MSSM
    - 1000 HIGH RISK SUBJECTS SCREENED BY LD-CT (LCRP)
      - 1000 SCREENED FOR SERUM MIRNAS (LCRP)
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