



# A New Gold Standard for Detection of Theranostic Gene Rearrangements and *MET* exon 14 splicing in Thoracic Oncology is Born!

## *One-Year Prospective Routine LD-RTPCR in 413 Newly Diagnosed Lung Tumors*

Nicolas Piton<sup>1</sup>, Marie-Delphine Lanic<sup>2</sup>, Florent Marguet<sup>1</sup>,  
Aude Lamy<sup>1</sup>, France Blanchard<sup>1</sup>, Florian Guisier<sup>3</sup>, Mathieu Salaün<sup>3</sup>,  
Luc Thiberville<sup>3</sup>, Fabrice Jardin<sup>2</sup>, Philippe Ruminy<sup>2</sup>, Jean-Christophe Sabourin<sup>1</sup>

<sup>1</sup> Rouen University Hospital, Department of Pathology, Rouen, France

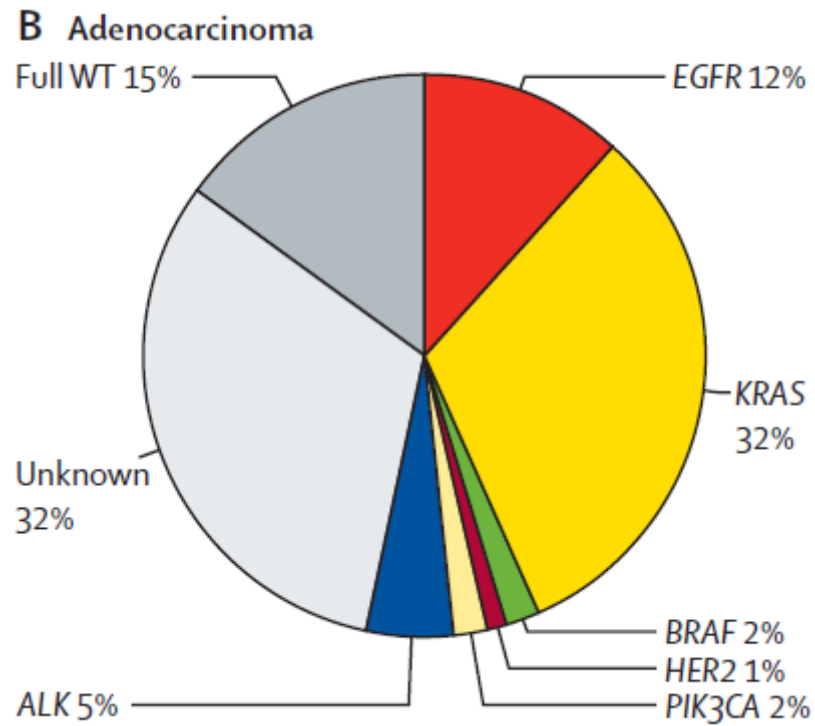
<sup>2</sup> Henri Becquerel Cancer Centre, Rouen, France

<sup>3</sup> Rouen University Hospital, Clinique Pneumologique, Rouen, France

This work was mainly funded by Normandie Valorisation.

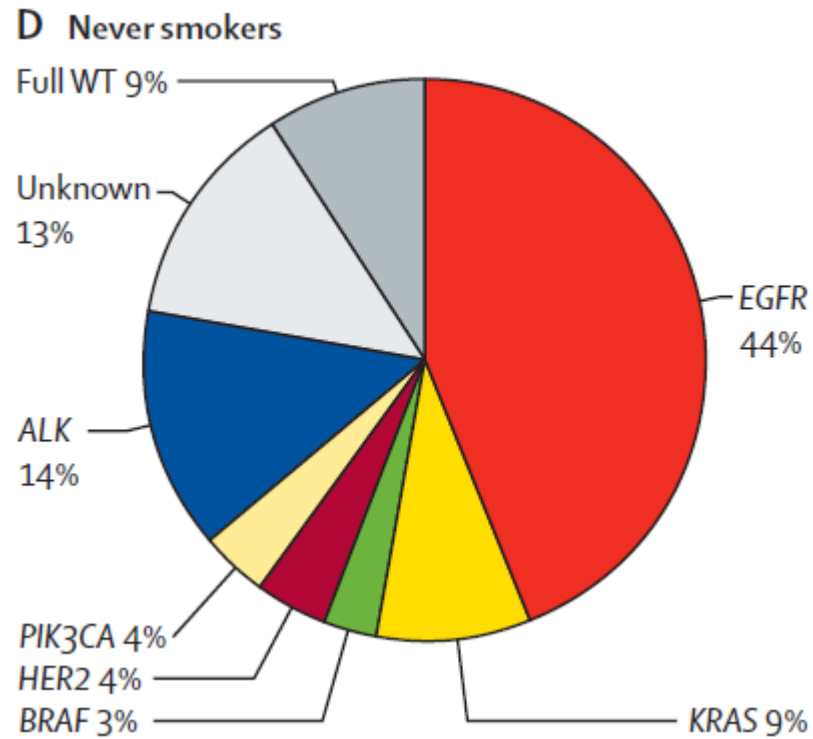
NP received additional funding from  
Boehringer (“Bourse Régionale Profil Onco 2017”) and  
Rouen University Hospital (AOJC n°2017-12)

# Background



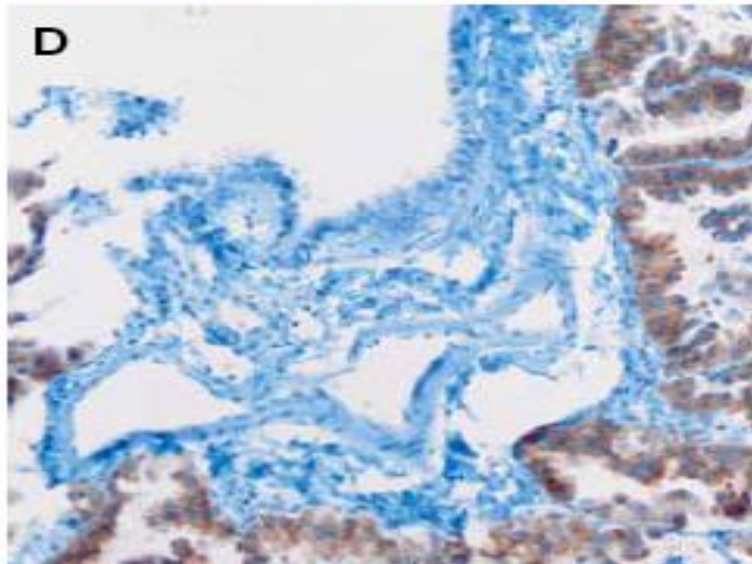
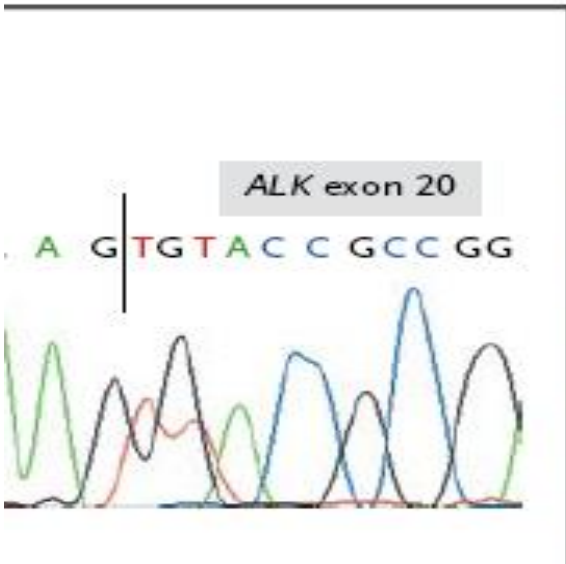
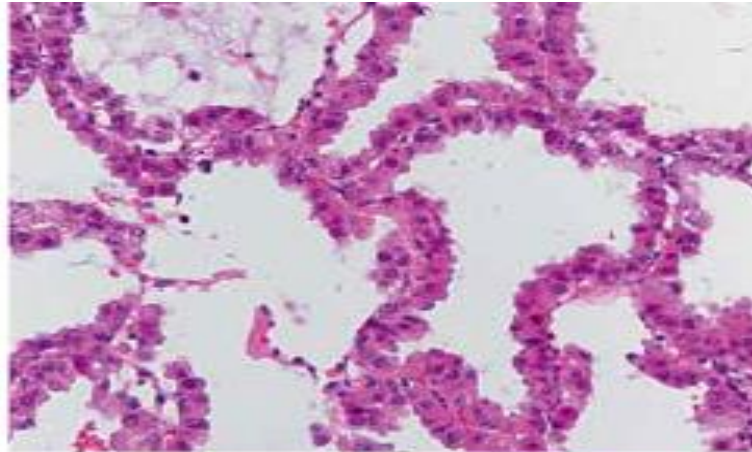
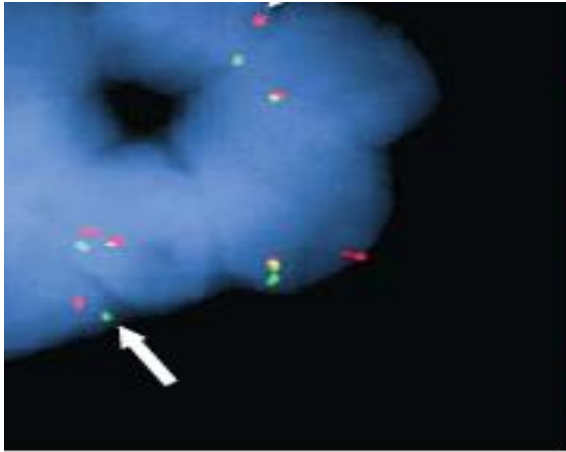
Barlesi et al. Routine molecular profiling of patients with advanced non-small-cell lung cancer: results of a 1-year nationwide programme of the French Cooperative Thoracic Intergroup (IFCT). *Lancet*. 2016 Jan 14. pii: S0140-6736(16)00004-0.

# Background

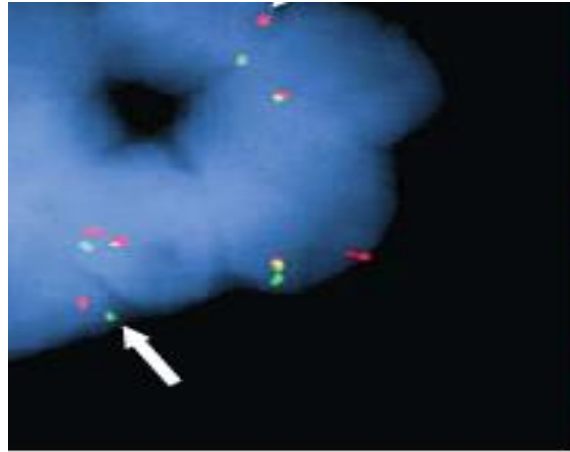


Barlesi et al. Routine molecular profiling of patients with advanced non-small-cell lung cancer: results of a 1-year nationwide programme of the French Cooperative Thoracic Intergroup (IFCT). *Lancet*. 2016 Jan 14. pii: S0140-6736(16)00004-0.

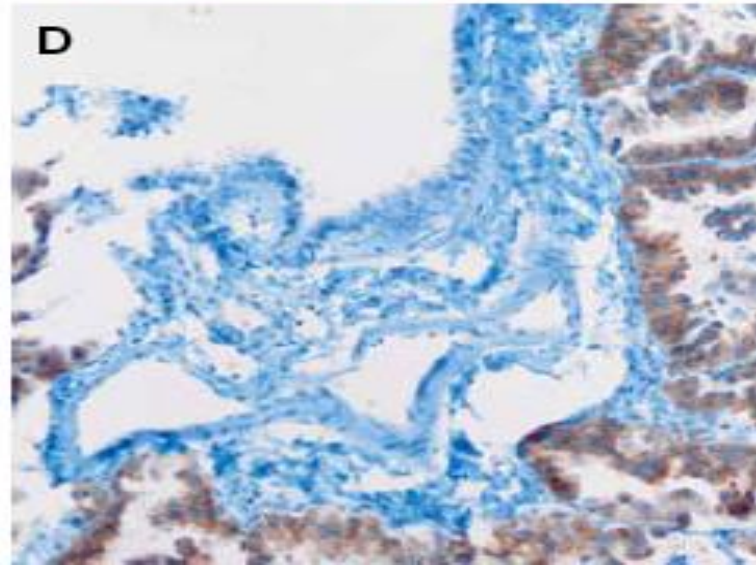
# Background



# Background



- Cost
- Interpretation
- No identification of the partner gene



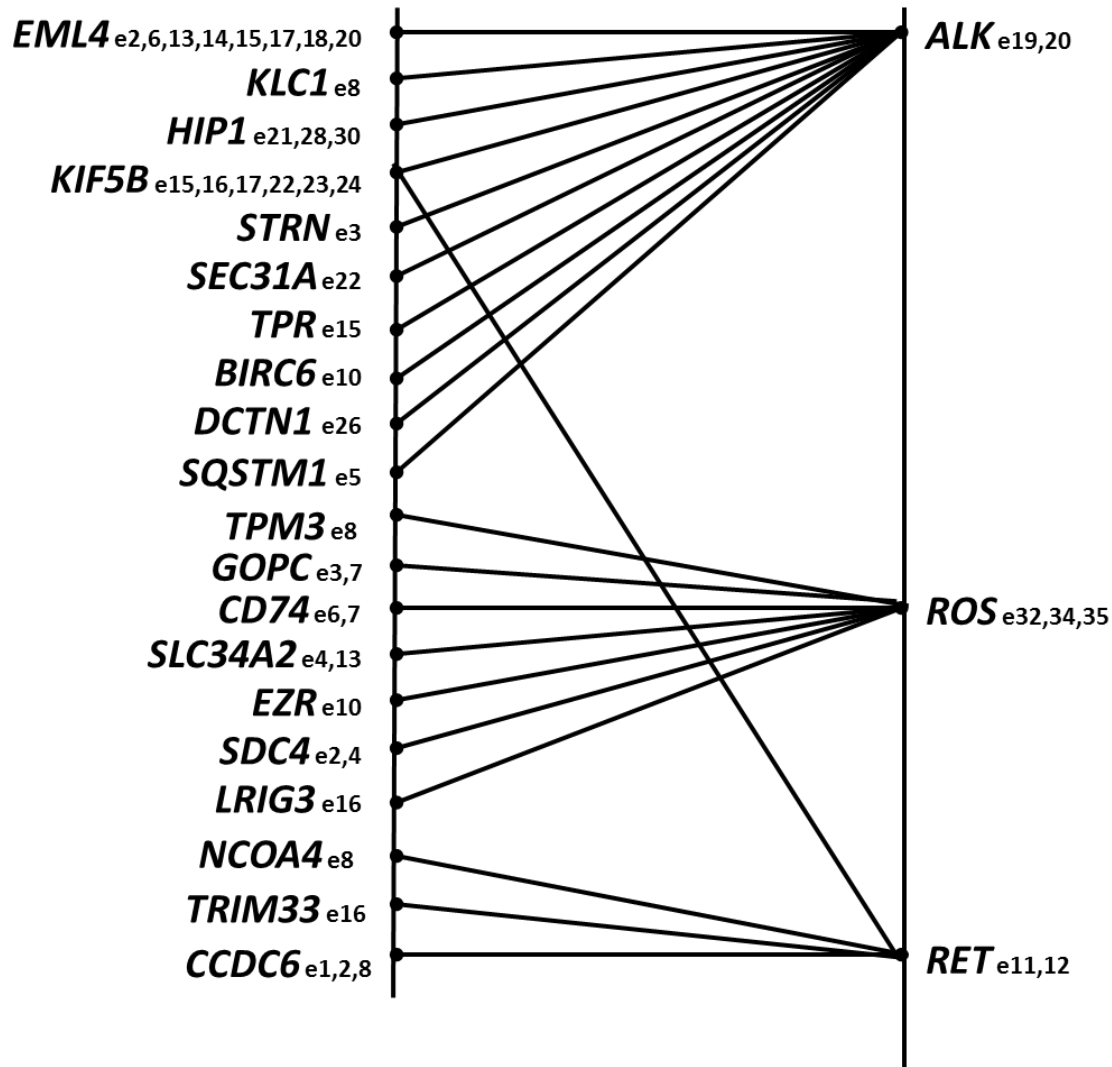


Laboratory Investigation (2018) 98, 371–379  
© 2018 USCAP, Inc All rights reserved 0023-6837/18

## Ligation-dependent RT-PCR: a new specific and low-cost technique to detect *ALK*, *ROS*, and *RET* rearrangements in lung adenocarcinoma

Nicolas Piton<sup>1,2</sup>, Philippe Ruminy<sup>2</sup>, Claire Gravet<sup>1</sup>, Vinciane Marchand<sup>2</sup>, Élodie Colasse<sup>1</sup>, Aude Lamy<sup>1</sup>, Cécile Le Naoures Mear<sup>3</sup>, Frédéric Bibeau<sup>3</sup>, Florent Marguet<sup>1</sup>, Florian Guisier<sup>4</sup>, Mathieu Salaün<sup>4</sup>, Luc Thiberville<sup>4</sup>, Fabrice Jardin<sup>3</sup> and Jean-Christophe Sabourin<sup>1,2</sup>

# Background

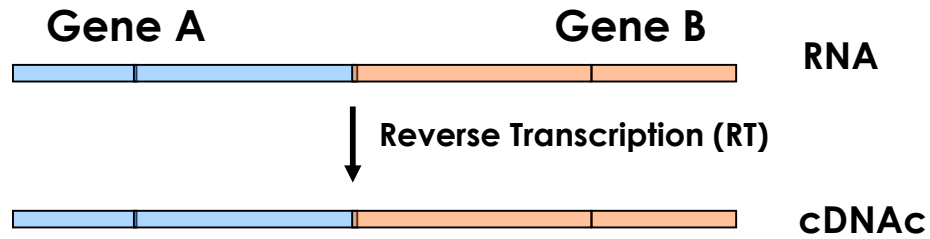




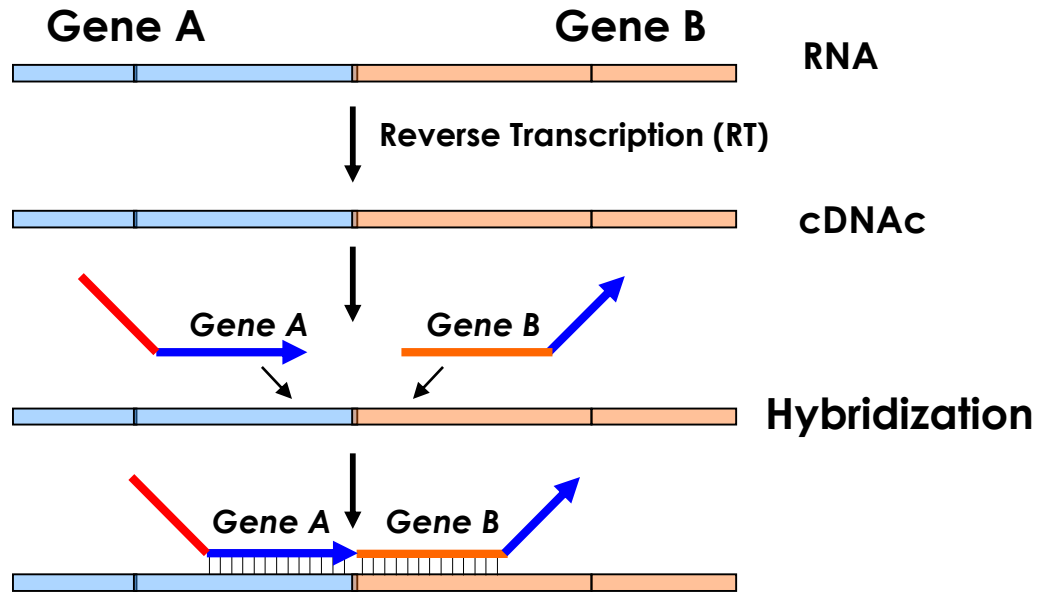
# Background



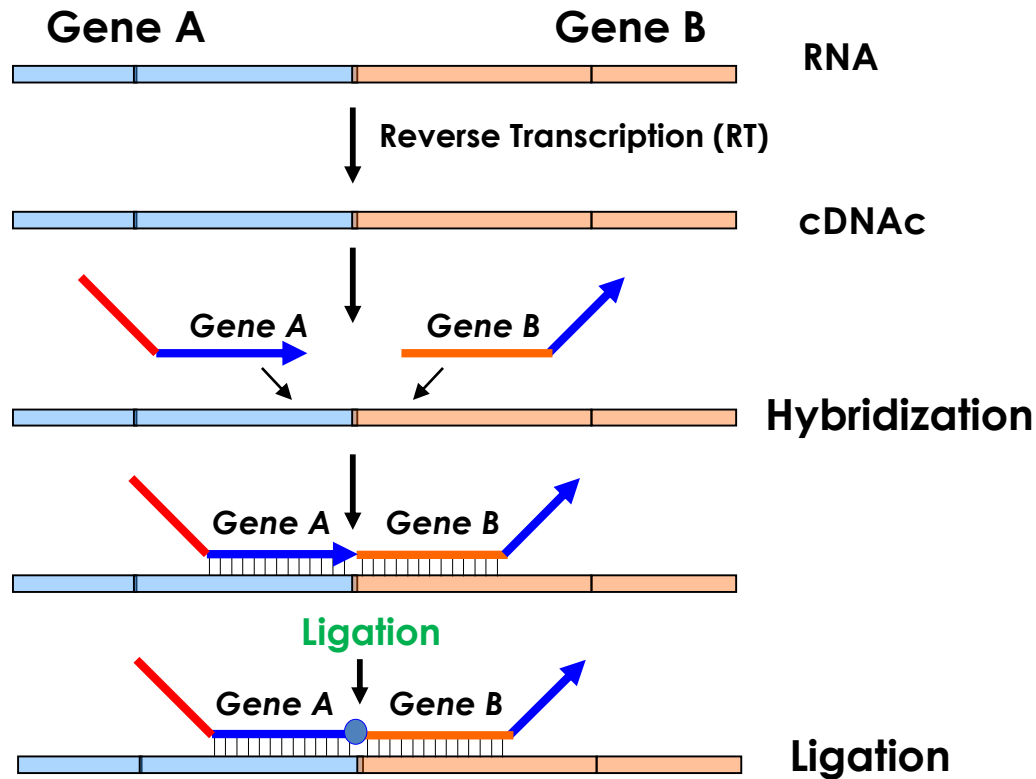
# Background



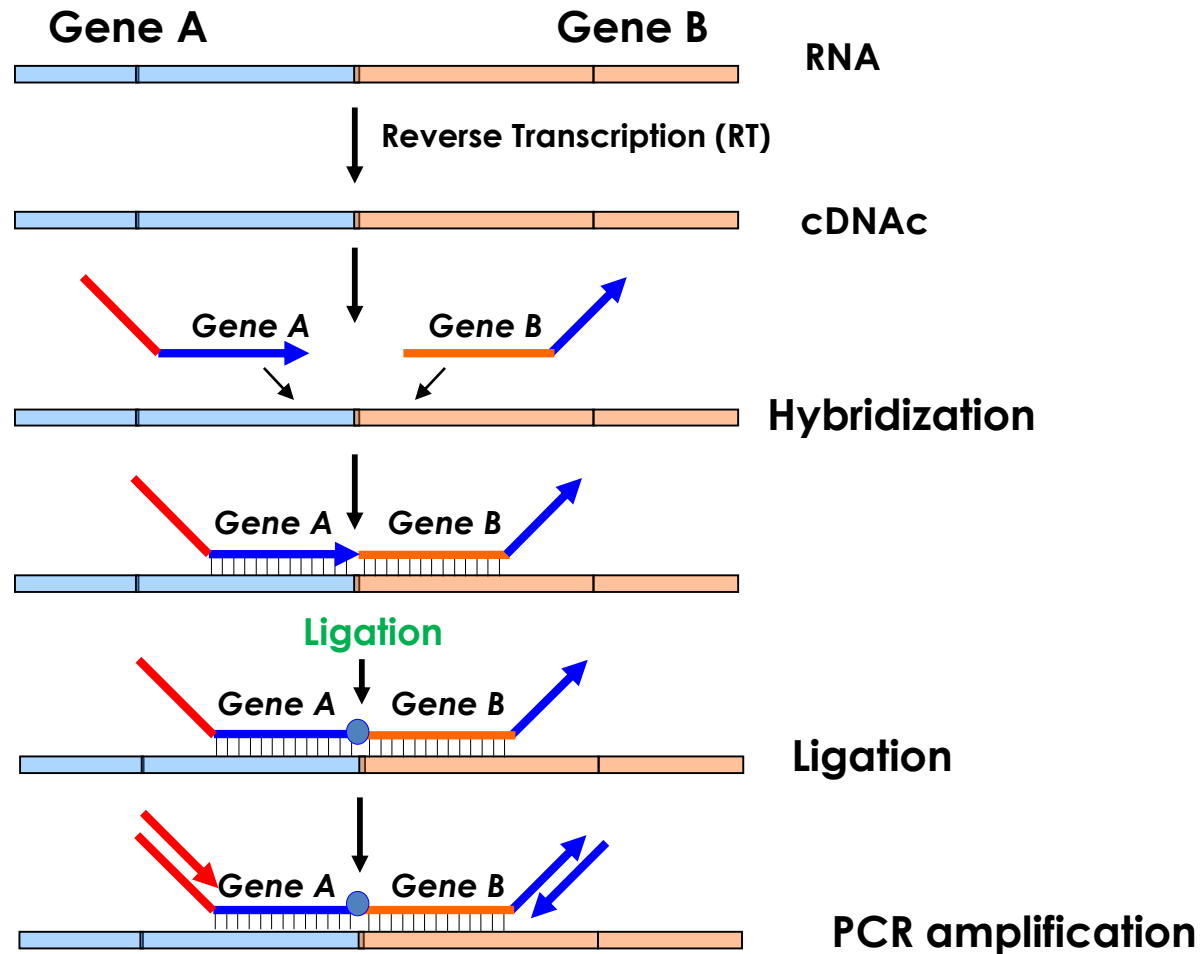
# Background



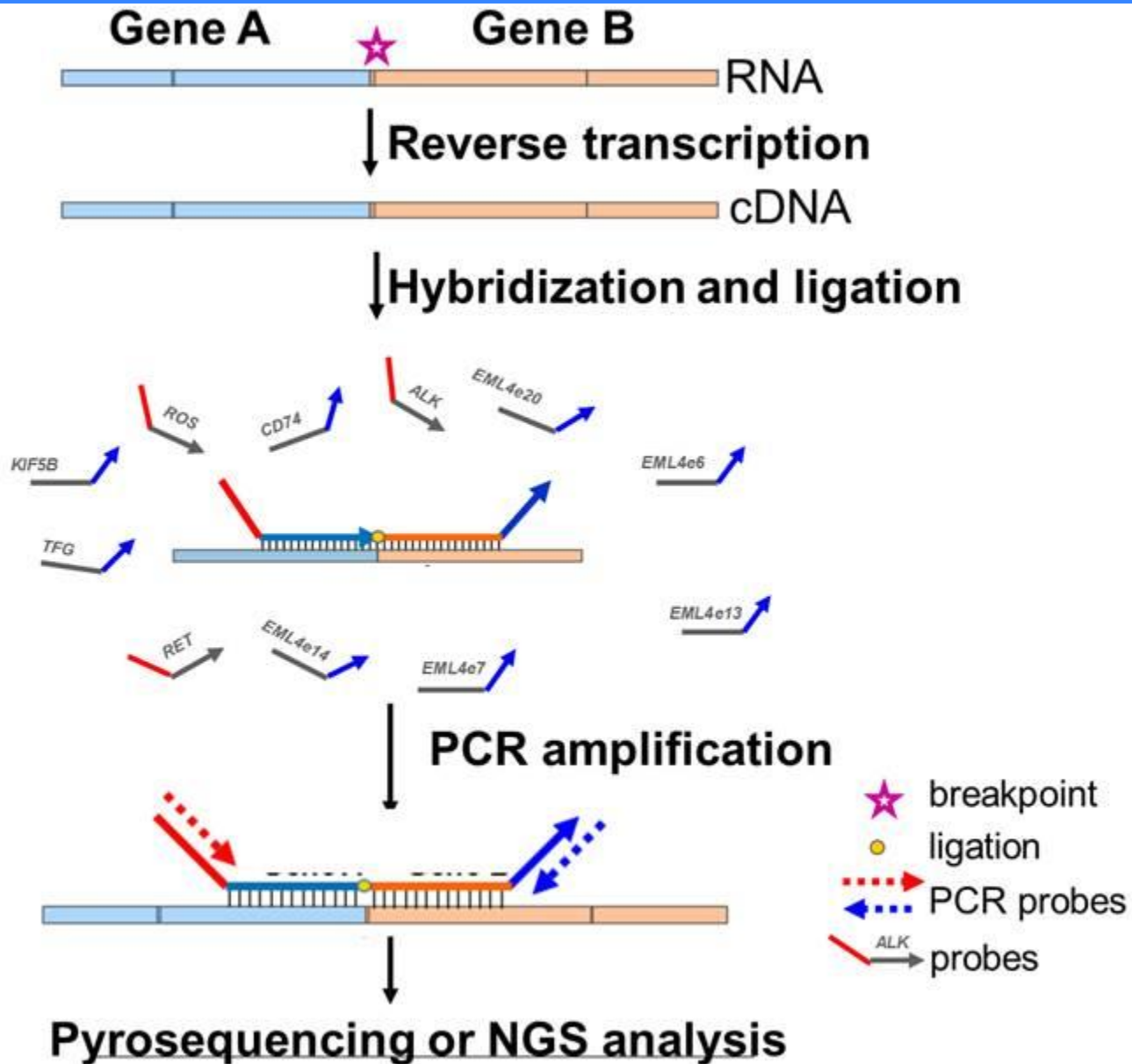
# Background



# Background



# Background



Retrospective study on:

- 24 *ALK* translocated
- 14 *ROS* translocated and
- 1 *RET* translocated tumors

# Background

**Tumors *ALK* + (n = 24)**

**Sensitivity: 63%    Specificity: 100 %**

**Tumors *ROS* + (n = 14)**

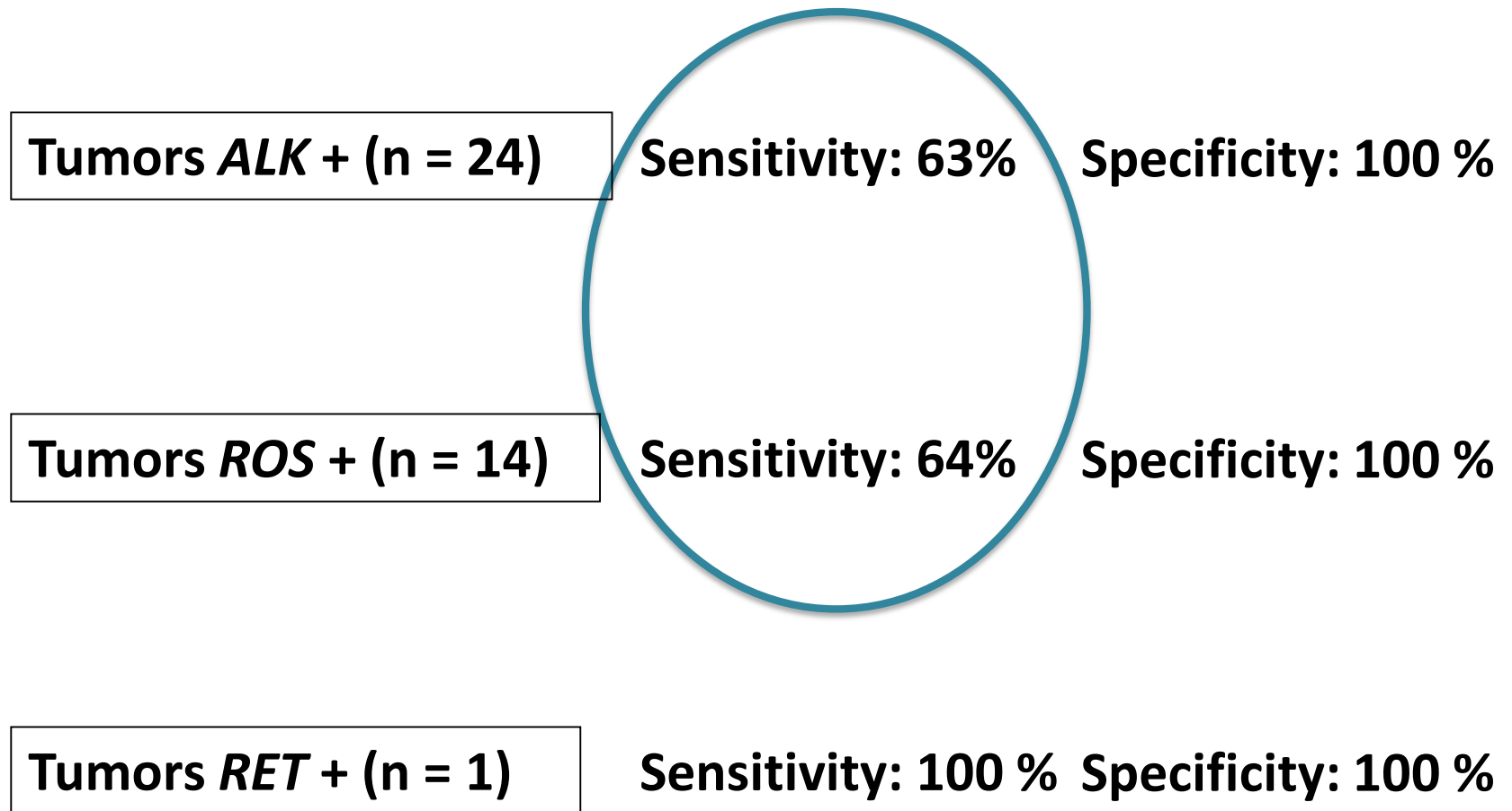
**Sensitivity: 64%    Specificity: 100 %**

**Tumors *RET* + (n = 1)**

**Sensitivity: 100 %    Specificity: 100 %**



# Background

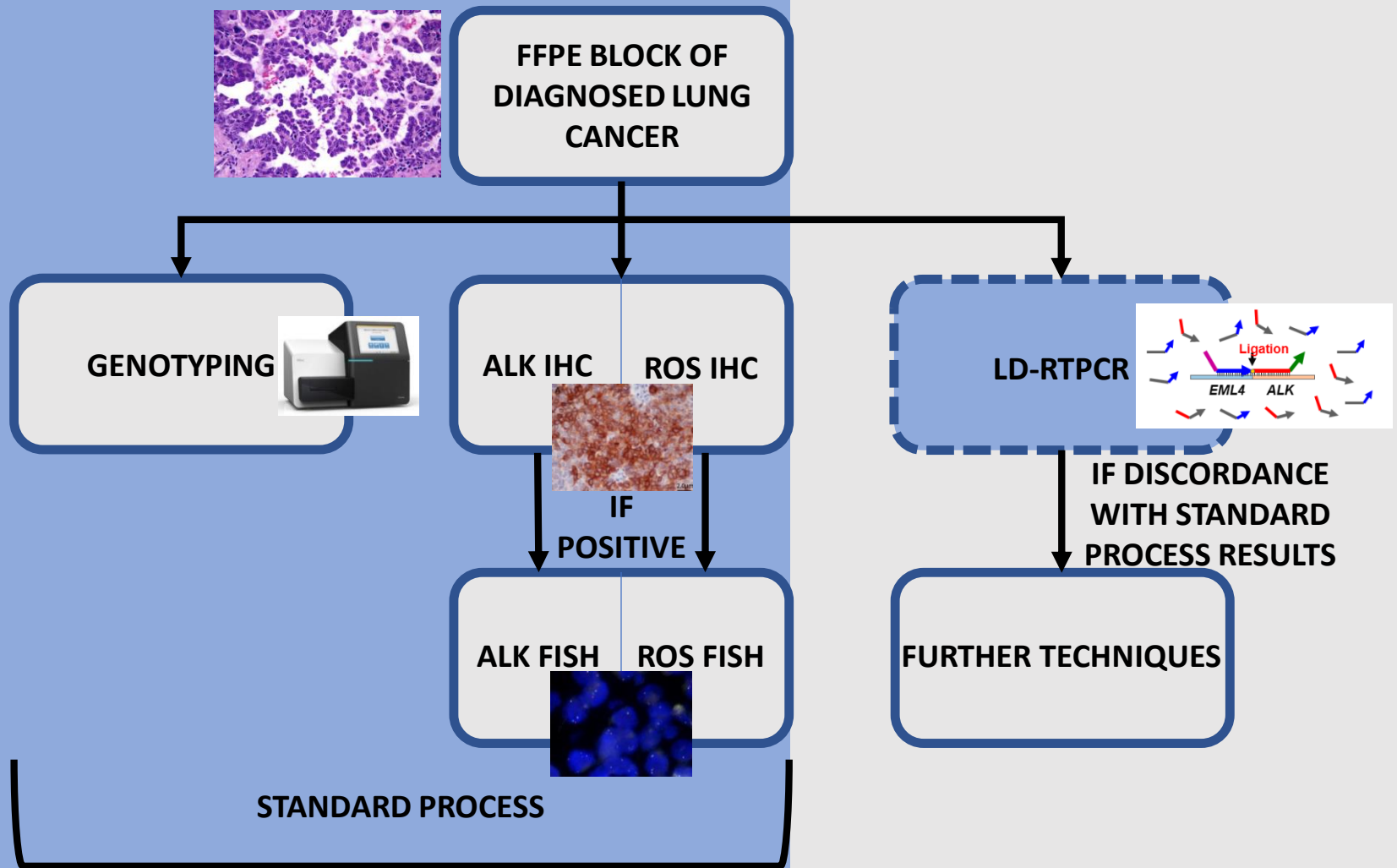


To assess an upgraded version of this assay in a routine prospective cohort of lung carcinomas for one year

### Improvements:

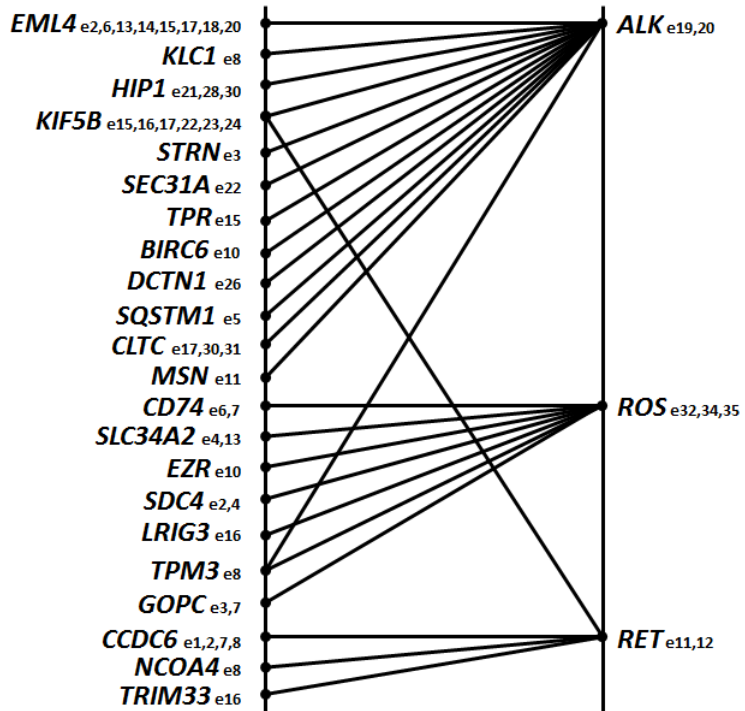
- More probes
- High throughput sequencing
- Detection of *MET* exon 14 skipping

# Material and methods



# Material and methods

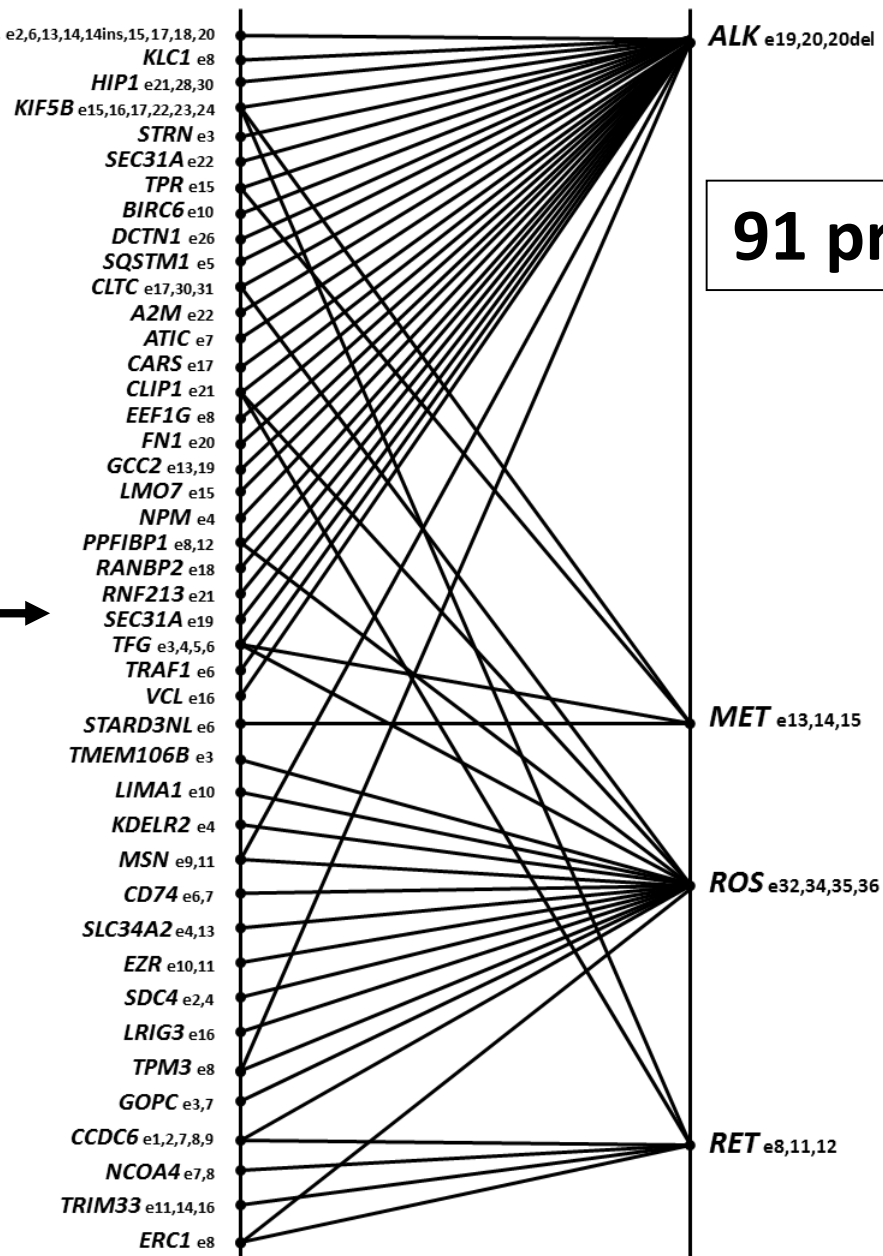
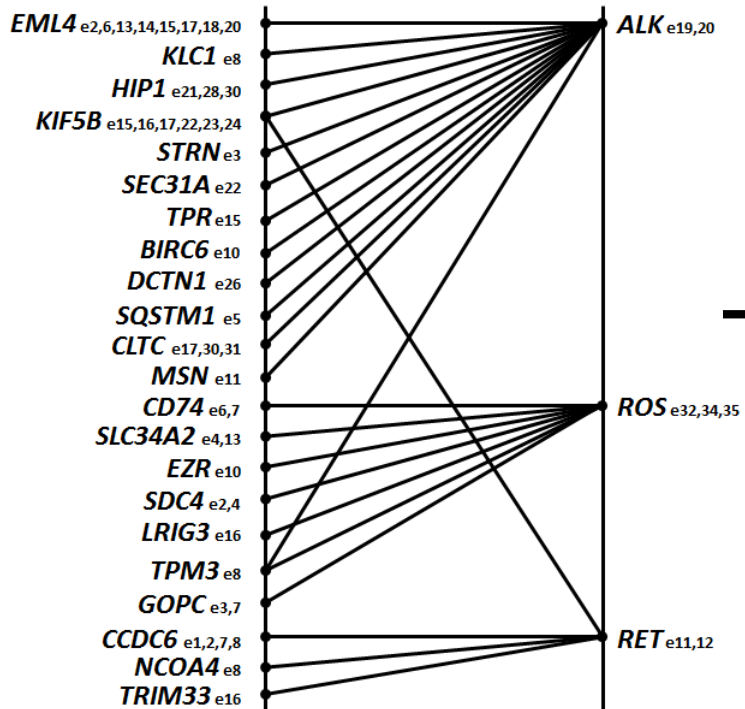
47 probes



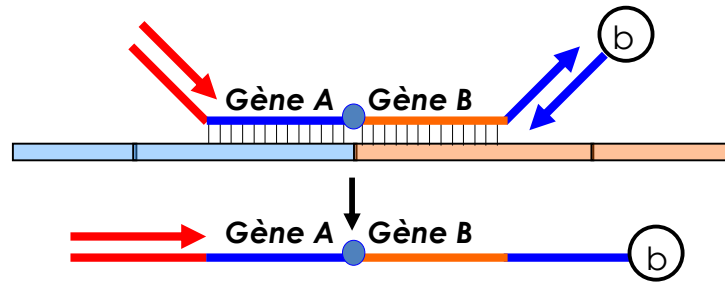
# Material and methods

47 probes

91 probes

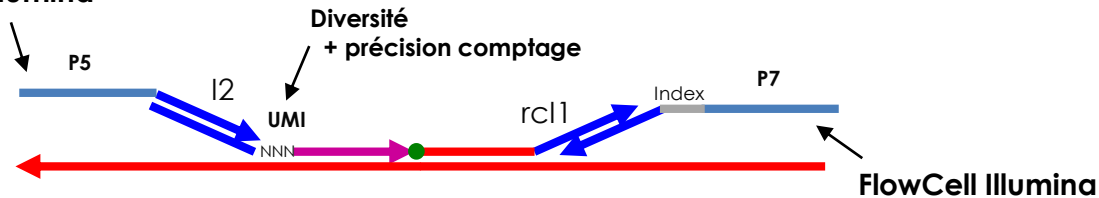


# Material and methods

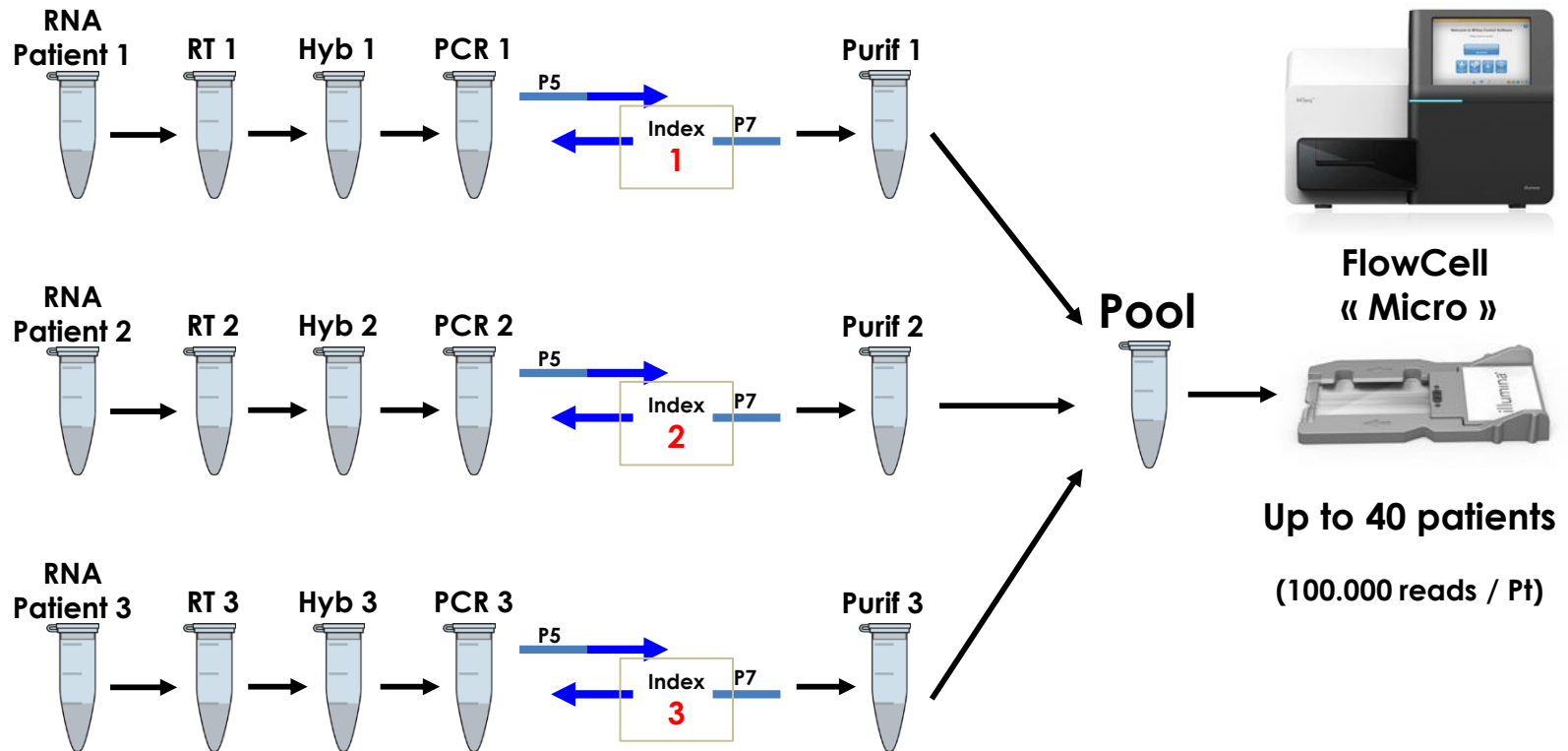
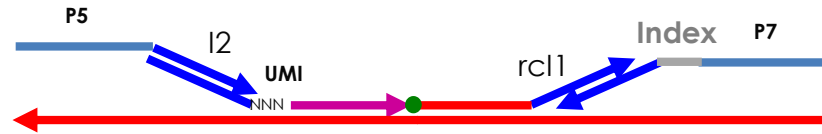


## Sequencing

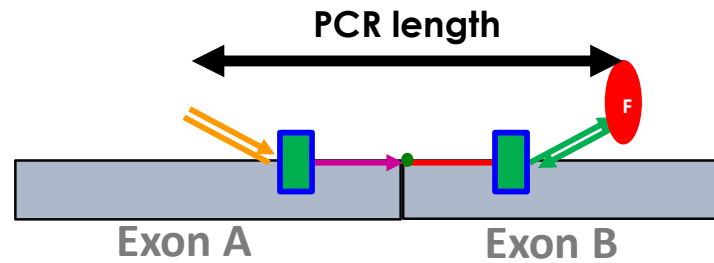
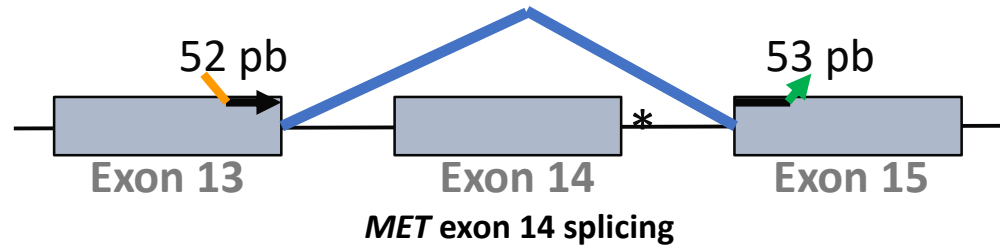
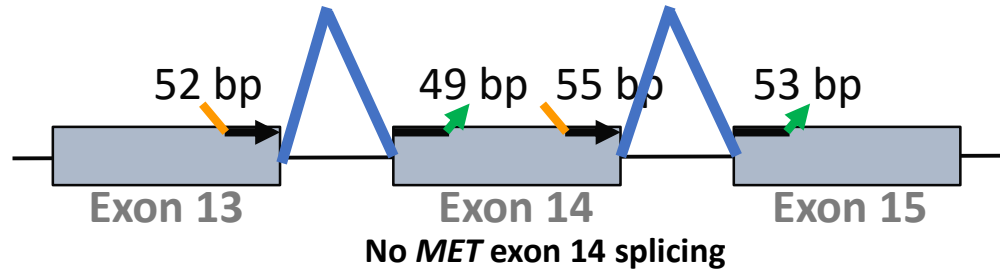
FlowCell Illumina



# Material and methods



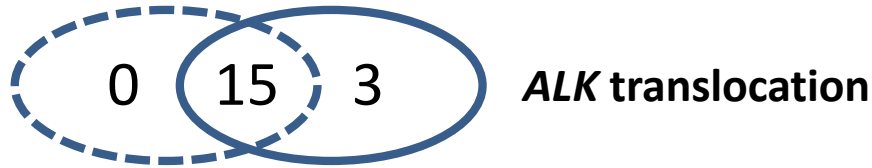
# Material and methods





# Results and discussion

LD-RTPCR   Routine analysis



- **1 year prospective study**
- **413 newly diagnosed lung tumors**

# Results and discussion

## Routine analysis

		<b><i>ALK, ROS or RET translocation / MET exon 14 splicing</i></b>		
		<b>Positive</b>	<b>Negative</b>	<b>Total</b>
<b><u>Routine techniques</u></b>	<b>Positive</b>	28	0	28
	<b>Negative</b>	7	378	385
	<b>Total</b>	35	378	413

		<b>95% CI</b>
<b>Se =</b>	80.00%	63.06% to 91.56%
<b>Sp =</b>	100.00 %	99.03% to 100.00%
<b>PPV =</b>	100.00%	
<b>NPV =</b>	98.18 %	96.53% to 99.05%
<b>Accuracy =</b>	98.31%	96.54% to 99.32%

# Results and discussion

## LD-RTPCR

		<b><i>ALK, ROS or RET translocation / MET exon 14 splicing</i></b>		
		<b>Positive</b>	<b>Negative</b>	<b>Total</b>
<b><u>LD-RTPCR</u></b>	<b>Positive</b>	32	0	32
	<b>Negative</b>	3	378	381
	<b>Total</b>	35	378	413

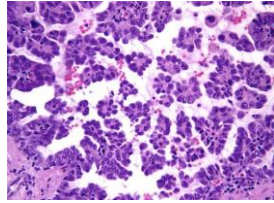
<b>Se =</b>	<b>91.43%</b>	<b>95% CI</b>	76.94% to 98.20%
<b>Sp =</b>	100.00 %		99.03% to 100.00%
<b>PPV =</b>	100.00%		97.59% to 99.72%
<b>NPV =</b>	99.21 %		97.71% to 99.73%
<b>Accuracy =</b>	99.27%		97.89% to 99.85%

- **Cheap (< 10 € / test)**
- **Very fast (results < 1 week)**
- **Multiplex analyses**
- **100% specific**
- **> 90% sensitivity**
- **Easily upgradable (e.g. *NTRK* and *NRG1* genes)**

- Cheap (< 10 € / test)
- Very fast (results < 1 week)
- Multiplex analyses
- 100% specific
- > 90% sensitivity
- Easily upgradable (e.g. *NTRK* and *NRG1* genes)

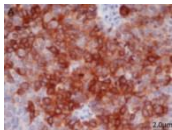
**A new technique of reference**

# Results and discussion



**Non small  
cell lung  
carcinoma**

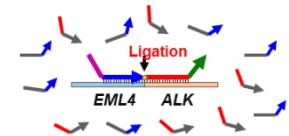
**IHC ALK ROS**



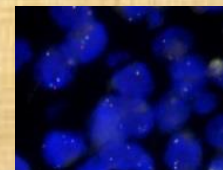
**Genotyping**



**LD-RTPCR**



**FISH**



*only if discordance*



The authors would like to thank **Dr Clotilde Descarpentries** (Lille University Hospital) for genotyping some discordant cases and **Pr Frédéric Bibeau** (Caen University Hospital) for performing *RET* FISH.

**Thanks for your attention!**