IV SIMPOSIO
Biopsia líquida
EL CAMINO A LA ONCOLOGÍA DE PRECISIÓN

From technical validation to Clinical utility of Oncomine for Liquid Biopsy

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PRESENTATION

CIMA LAB DIAGNOSTICS

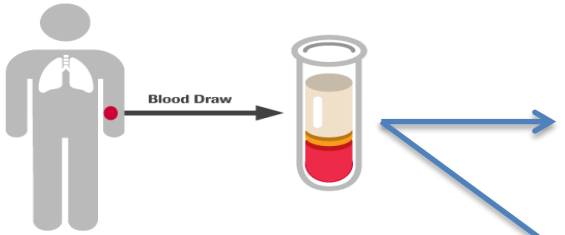
- Universidad de Navarra
- Genetics in hematological, oncological and constitutional diseases
- Biomarkers for diagnosis, prognosis or therapeutic decision making

IdiSNA Genomics Core Facility

- Health Research Institute of Navarra
- Support research projects and/or clinical trials
- ddPCR, pyrosequencing, Sanger and NGS sequencing

ASSESSING LIQUID BIOPSY BY NGS

- Obtaining a solid biopsy is not always possible
- *BRAF* and *EGFR* point mutations by ddPCR
- Two commercial products:



GUARDANT HEALTH

ThermoFisher SCIENTIFIC

GUARANTEEING RESULT REPRODUCIBILITY

- Standardize the optimal sample collection, conservation and subsequent manipulation within CIMA LAB Diagnostics.

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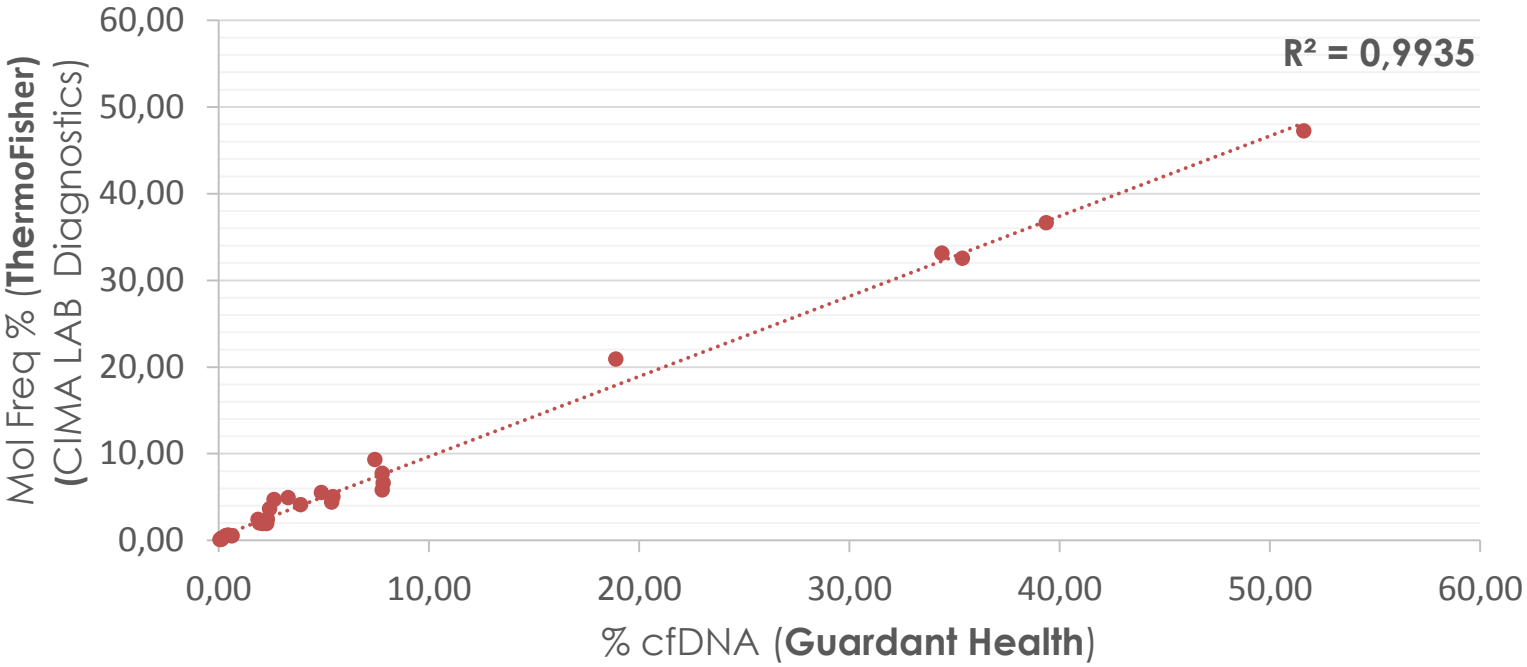
- 17 plasma samples studied by Guardant Health and ThermoFisher's Oncomine PanCancer assay by CIMA LAB Diagnostics.
    - 29 variants that both tests identified.

- **Are the frequencies of the variants obtained by CIMA LAB Diagnostics with ThermoFisher's Oncomine PanCancer reagents comparable to those of Guardant Health?**

VARIANT ALLELE FREQUENCY (VAF)

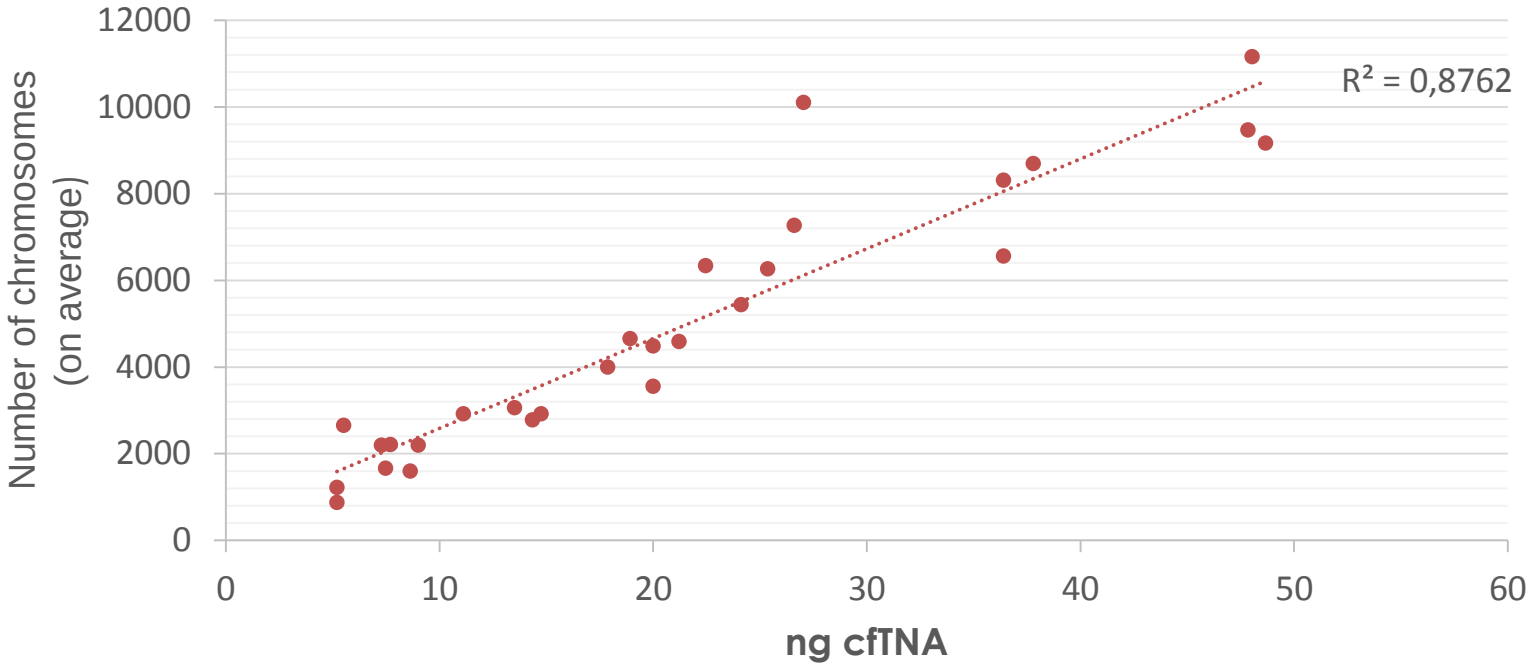


LIMIT OF DETECTION (LOD)

- “The assay provides the reagents and a single pool of multiplex PCR primers for preparation of an amplicon library from cell-free total nucleic acid (cfTNA) obtained from the plasma fraction of a single **10-mL tube of whole blood**.”
- “From a single tube of blood, generates an amplicon library from both DNA and RNA with a detection limit of **0.1% for SNVs.”**
    - 2 out of 2000 studied chromosomes

- **What is the quantity of cfTNA that CIMA LAB Diagnostics needs to sequence on average > 2000 chromosomes with ThermoFisher’s Oncomine PanCancer reagents?**

LIMIT OF DETECTION (LOD)



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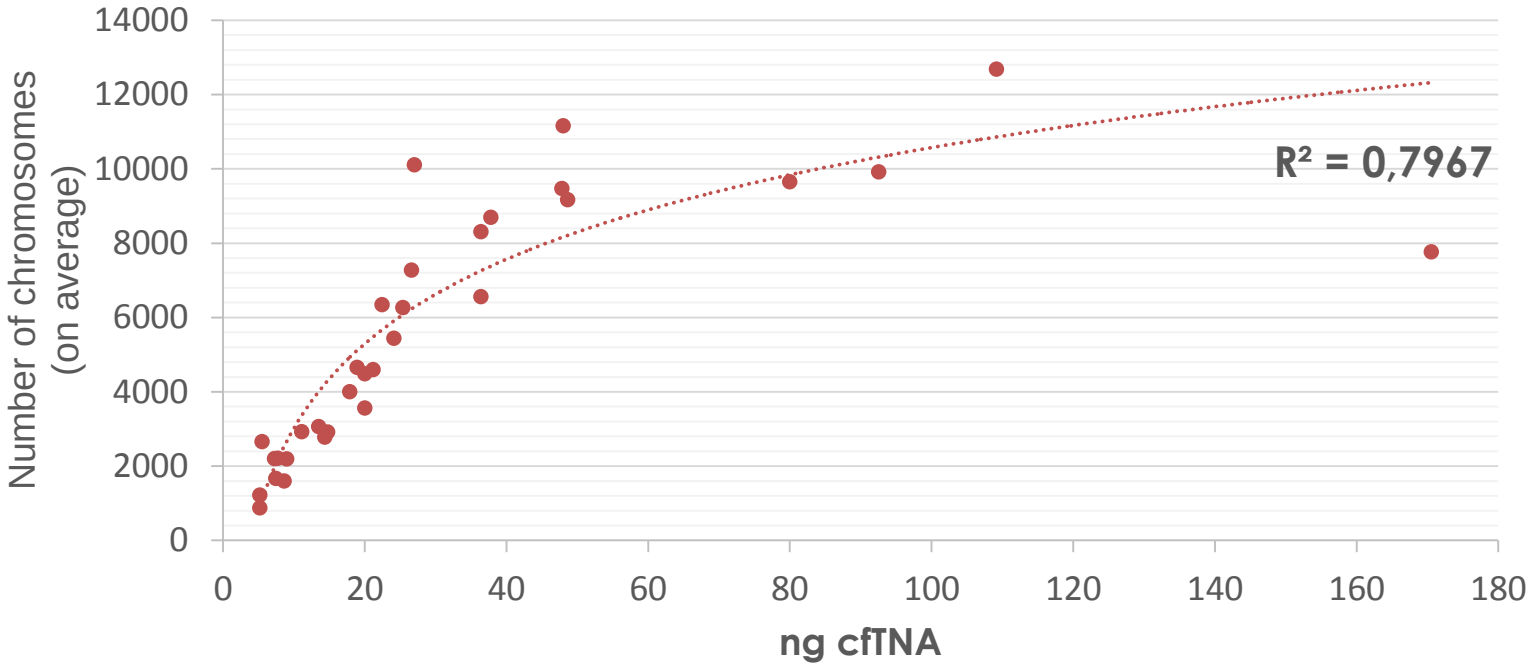


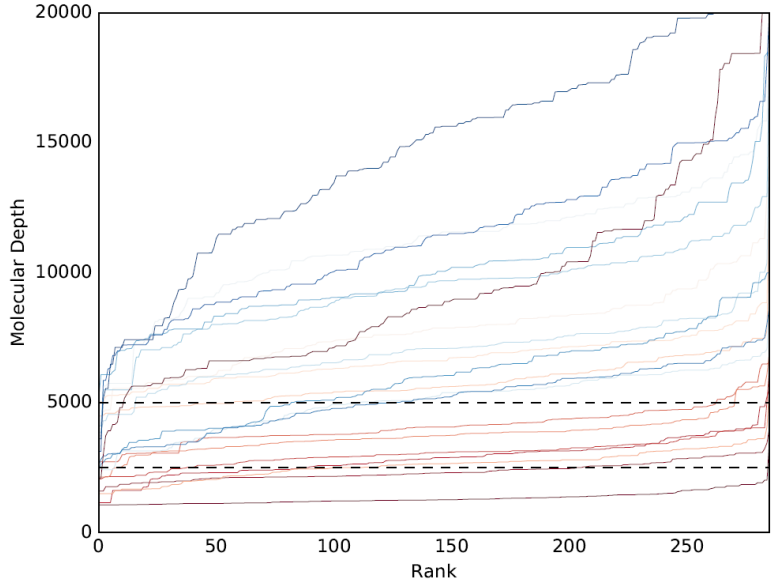
PRELIMINARY CLINICAL VALIDATION

- Do identified variants modify patient's treatment or segregate individuals based on their prognoses and/or response to treatment?

- High-risk GI cancer clinic blood samples from control individuals or individuals with more than 10 polyps or metastatic colon cancer.
    - Somatic *APC* mutations in 2 out of 4 CCR patients.
    - Somatic TP53 mutations in 5 out of 6 control samples.
        - 3 out of 5 with <5 mm polyps
        - *TP53* mutations are crucial for the disease to become invasive - 5% of adenomas, 59% of malignant polyps and 75% of invasive CRC show TP53 mutations.

LOD *vs*. (INPUT CFTNA & TARGETED REGION)

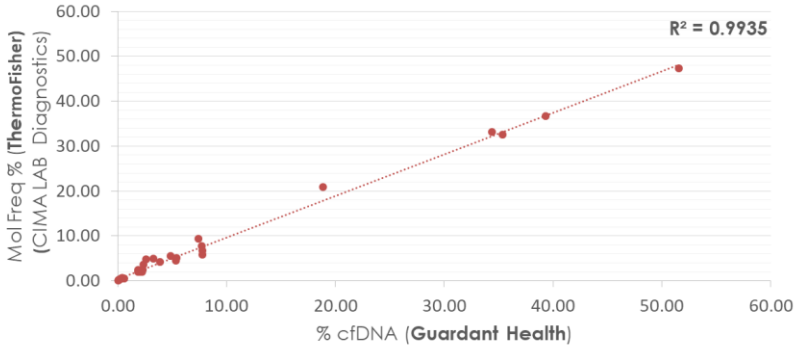
- *APC* mutations at **265x** and 1191x positions
- LOD varies by input cfTNA but also regionally



cfTNA (ng)	% (>2500x)	% (>5000x)
5.2	0.3	0.0
7.71	28.6	0.0
14.35	69.5	0.7
14.76	86.7	0.7
17.88	100.0	8.0
20	96.5	5.2
21.21	62.6	0.3
24.12	100.0	79.7
25.37	100.0	100.0
26.6	100.0	97.9
27.04	100.0	99.3
36.4	97.6	61.2
36.4	100.0	94.4
37.8	100.0	99.3
47.84	100.0	100.0
48.04	99.6	71.3
48.67	100.0	55.6
92.56	100.0	99.3
109.2	100.0	99.3
170.56	99.3	96.2

CONCLUSION

- A great potential in precision medicine
- Proficiency testing/interlaboratory comparison
- Comparable VAF values across laboratories



- Proper LOD values should be reported

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THANKS & QUESTIONS

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