#152P; Nanopore Sequencing of cfDNA Captures Key Copy Number Alterations in Lung Adenocarcinoma: A Non-invasive Approach For Prognosis, Therapy and Subtyping

K. Roohollahi , A. Foster, E. Post ,D. Vessies, J. van den Berg, D. Makarawung, F. van Asch
RenovaroCube, Amsterdam, The Netherlands

Introduction

- RenovaroCube developed a machine learning-powered multi-omics cell-free DNA (cfDNA) cancer prediction workflow using Oxford Nanopore Technology (ONT).
- Copy Number Variations (CNVs) provide crucial insights for cancer diagnosis and prognosis.
- Study explores non-invasive detection of CNVs in lung adenocarcinoma (LUAD) and healthy controls' circulating cfDNA.

Methods

- Processing of raw ONT-POD files (Figure 1).
- Counting bin-level reads.
- Counts processing and normalization by ichorCNA, generating two key CNV parameters:
  - Tumor fraction.
  - Genome-wide copy number variations log2(cancer/normal).

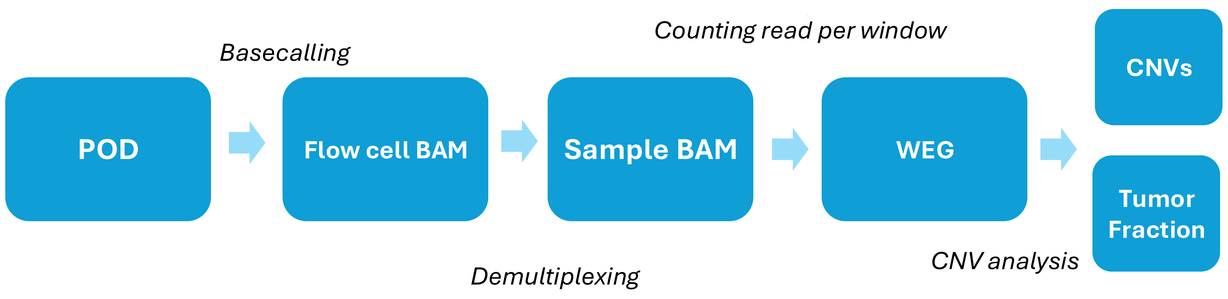

Figure 1. *RenovaroCube cfDNA-derived CNV processing pipeline*

Results

- Most cancer samples showed detectable tumor fractions (TF > 0.01) in plasma, distinguishing cancerous from healthy samples (Figure 2).
- Higher tumor fractions in patients with advanced cancer stages.
- CNV analysis revealed clinically significant lung cancer hallmark alterations (Figure 3) such as:
  - ***1q amp*** (prognosis, therapy response)
  - ***3q amp*** (cancer progression)
  - ***7p-EGFR* amp** (actionable target)
  - ***8q amp*** (prognosis)

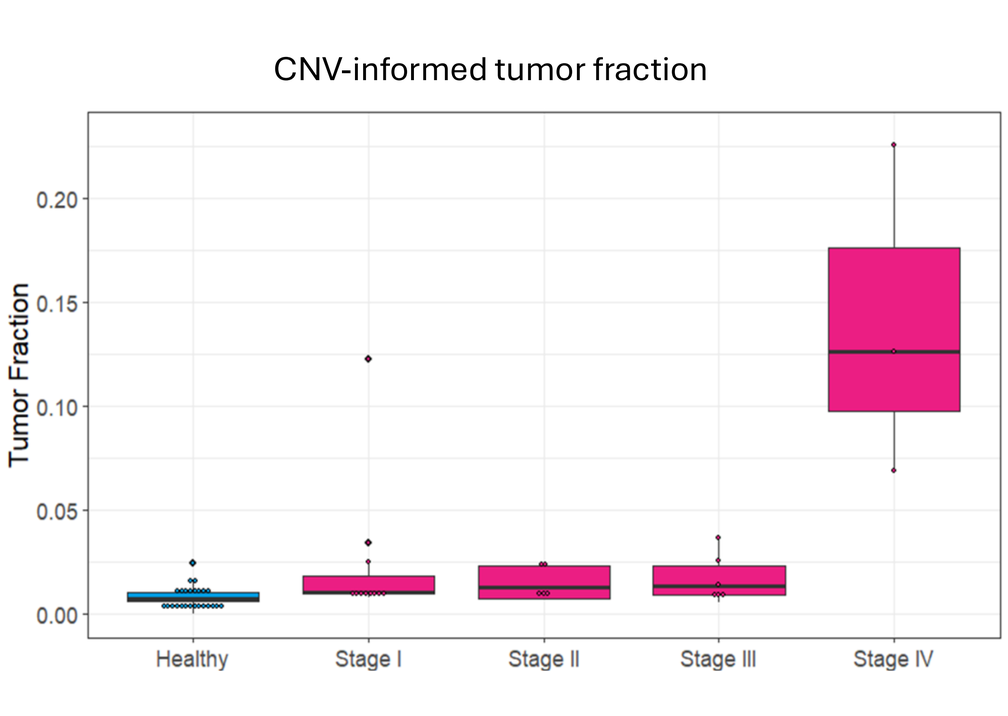

Figure 2. *Tumor fraction values by cancer stage. Higher tumor fractions are observed in advanced cancer stages, with occasional false positives in healthy samples.*

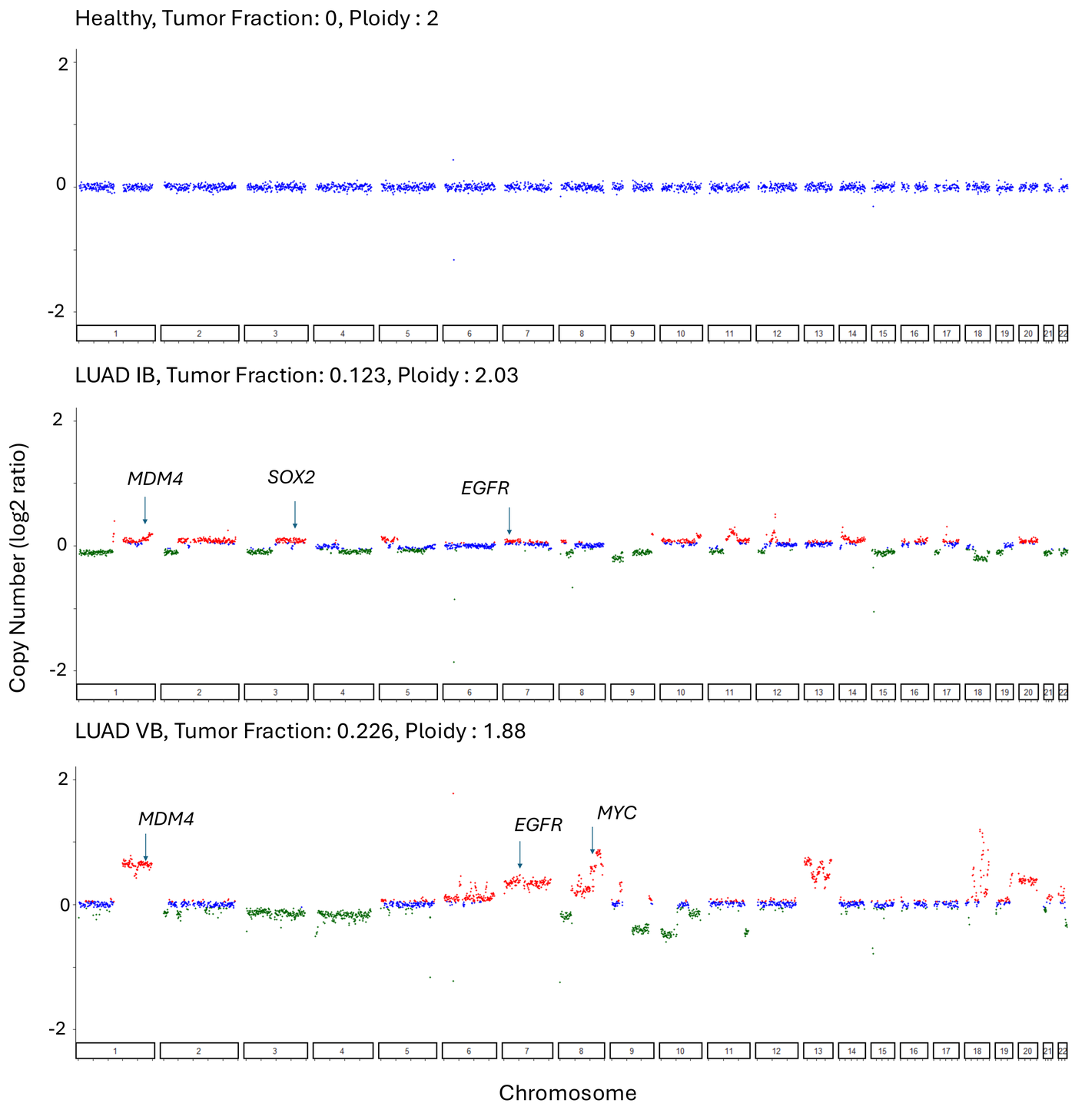

Figure 3. *Genomic alterations detected in cell-free DNA from lung adenocarcinoma (LUAD) samples, including amplifications of 1q (MDM4) and chromosome 7 (EGFR). Neutral (Blue), Amplification (Red), Deletion (Green).*

Conclusions

- **Nanopore sequencing of cfDNA** efficiently captures major and clinically significant genomic changes in lung cancer samples.
- These genomic alterations may be utilized to predict disease progression and guide more effective therapeutic strategies.
- **cfDNA profiling** offers a safe, non-invasive alternative to traditional tissue biopsy methods.

Disclaimer

The first and presenting author disclose holding stock options in RenovaroCube.

Corresponding author : Khashayar@renovarocube.com