Abstract 5587

Ultra-deep targeted sequencing of cell-free DNA and patient-matched white blood cells for treatment response evaluation in patients with metastatic colorectal cancer

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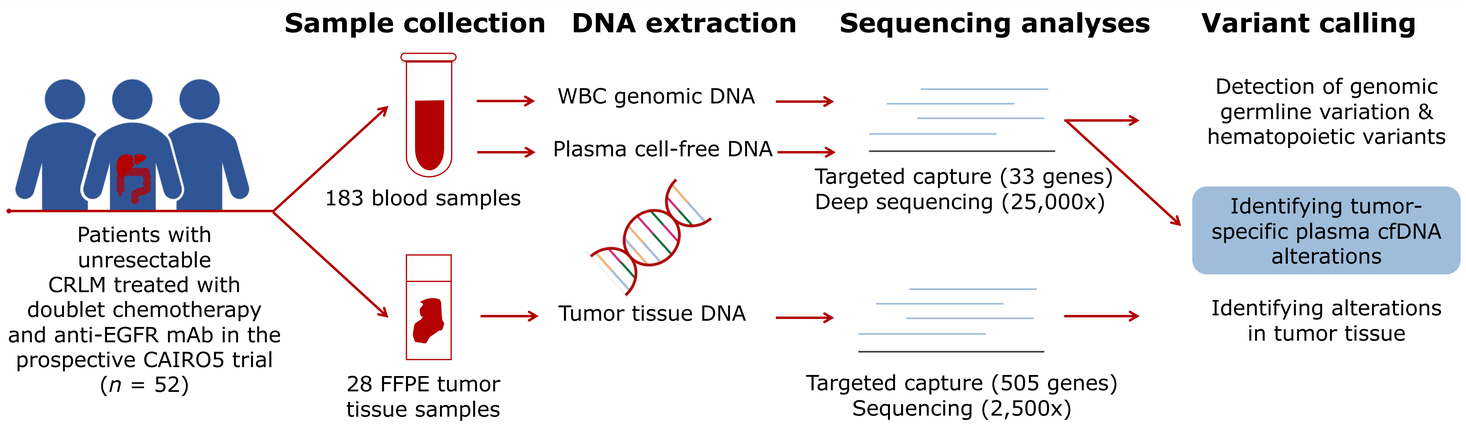
Aim

Germline and clonal hematopoiesis related mutations can complicate identification of tumor-specific mutations in cell-free DNA, necessitating additional tumor tissue sequencing. This study evaluated if monitoring treatment response using **circulating tumor DNA** (ctDNA) in colorectal cancer patients with liver-only metastases (CRLM) could be done without relying on tumor tissue. Our approach combined deep sequencing of cfDNA with **patient-matched white blood cell DNA and tumor tissue.**

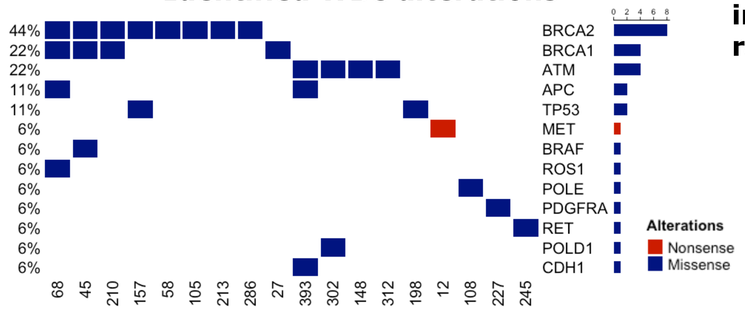
Methods



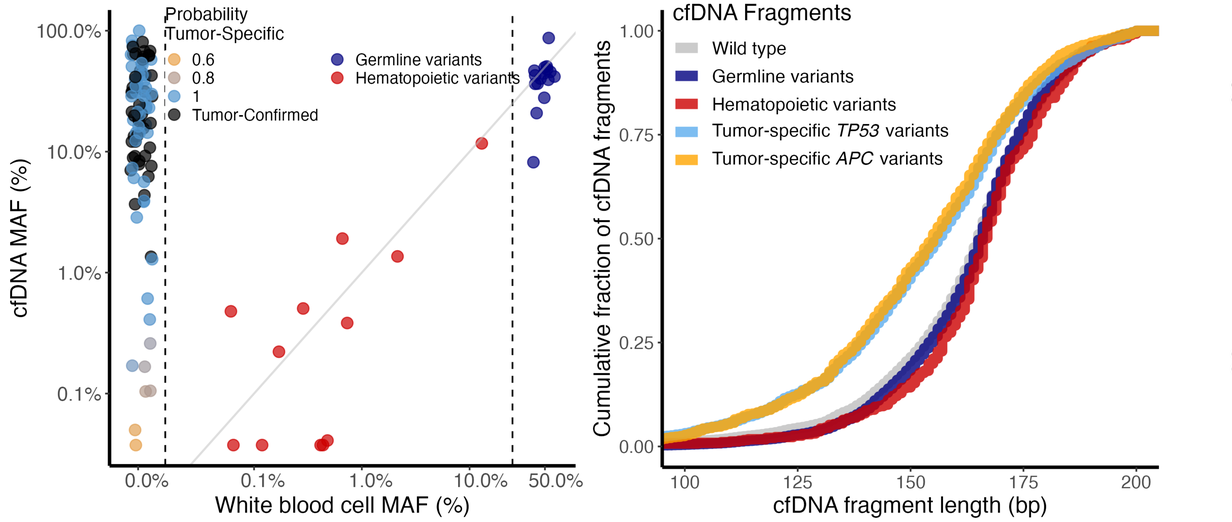
Results

Combined cfDNA and WBC analysis prevented reporting of false positives due to germline or hematopoietic variants in **40%** of patients.

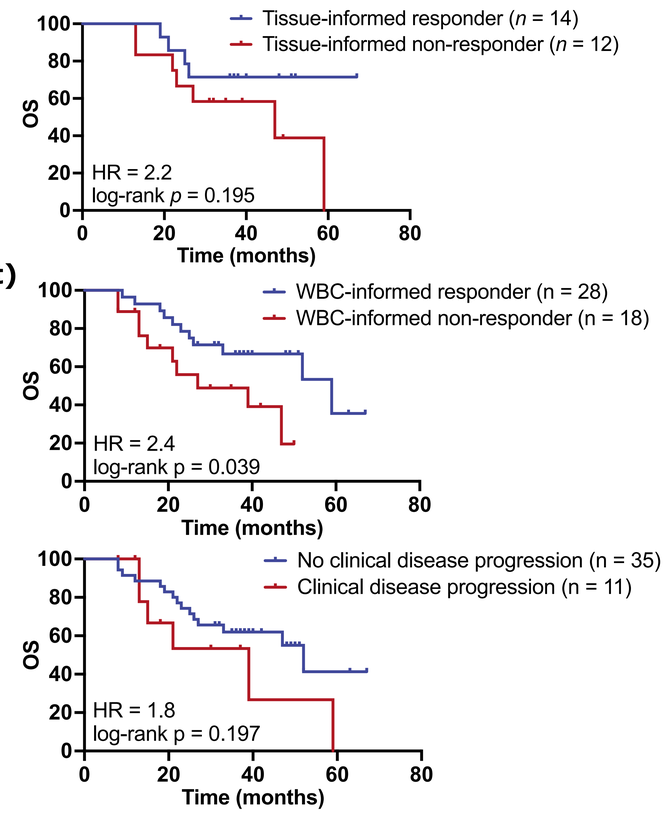
Identified WBC alterations



cfDNA and WBC variant frequencies (left) and fragment length distributions (right)



Overall survival based on tissue-informed (top) and WBC-informed (middle) molecular response assessment and radiological response evaluation (bottom) after treatment



Conclusions

Accurate calling of ctDNA mutations for treatment response monitoring in patients with mCRC is feasible in a **tumor tissue-independent manner** by combined cfDNA and patient-matched WBC genomic DNA analysis. This tissue biopsy-independent approach simplifies sample logistics and facilitates the application of liquid biopsy ctDNA-testing for evaluation of emerging therapy resistance, opening new avenues for early adaptation of treatment regimens.

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