Circulating cell free DNA (cfDNA) in the plasma of cancer patients may provide oncogenic mutation status in late stage NSCLC. Recently, specific phagocytic stromal cells found in blood, i.e. associated macrophage-like cells (CAMLs), have been shown to contain large quantities of tumor DNA. We hypothesized that a single blood sample may provide cfDNA and parallel CAML DNA, providing more sensitive tumor mutation screening on a broader array of patients. We screened untreated NSCLC patients with a range of stages (stage I-3, stage II-5, stage IIIa=10, stage IIIb=7, & stage IV=5), that had available primary tissue for NGS. Blood was drawn after induction to radiotherapy treatment and plasma was sequenced using a 50 gene oncpanel. Separately, CAMLs were isolated from the plasma cell pellet, lysed and sequenced. Our data suggests that CAMLs contain clinically relevant oncogenic variants that correspond to both the primary tumor and the matched plasma.

### RESULTS

- **Primary tumor had 43 mutations (average=1.4 variants in 87% of patients).** (Table 1)
- **cfDNA had 28 mutations (average=0.9 variants in 47% of patients)**
- **One patient (#302) had TP53 mutations in both cfDNA and tumor, though different variants**
- **CAML lysate had 78 mutations (average=2.6 variants in 80% of patients)**
- **Two patients had variants in TP53 & Kras that exactly matched in CAMLs and primary tumor**
- **Patients with higher cfDNA or CAML mutation numbers had lower PFS, with at least 1 variant in cfDNA (HR=4.0, 95%CI=1.4-11.3, p=0.021) and 4 variants in CAMLs (HR=4.3, 95%CI=1.4-12.9, p=0.002)**

### CONCLUSIONS

- **CAMLs represent a population of tumor stroma cells that may promote tumor progression**
- **Monitoring the mutations of giant CAMLs may predict cancer progression or death**
- **A single blood sample can screen for oncogenic tumor mutations in plasma and phagocytic stromal cells, increasing sensitivity and identifying a comparison to cfDNA alone**
- **High numbers of mutations in variable cfDNA or CAMLs may be indicative of highly aggressive NSCLC.**

### References


### Funding Sources

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