

INTRODUCTION

- *ALK*-gene fusions occur in 4% of non-small cell lung cancers (NSCLC)
- Tyrosine kinase inhibitors (TKIs) are highly effective, but treatment resistance is inevitable
- Resistance is associated with genetically diverse cancer clones
- The extent of clonal diversity at diagnosis and during treatment remains unknown
- **Measuring clonal diversity in the clinic could inform treatment decisions**

METHODS

- **Patients:** Advanced *ALK*-positive lung cancer patients; blood samples collected at diagnosis or at development of treatment resistance
- **CTC isolation:** Individual circulating tumour cells (CTCs) identified, isolated and retrieved using the AccuCyte–CyteFinder platform
- **Nucleic acid extraction:** Concurrent RNA and DNA extraction from the same CTC using ResolveOME
- **DNA analysis:** Targeted enrichment with the SureSelect lung cancer panel; sequenced on Illumina MiSeq i100 Plus
- **RNA analysis:** Ion Torrent Genexus System with the Oncomine Precision Assay

DISCUSSION AND CONCLUSION

Key Finding

- Comprehensive genomic profiling of single circulating tumour cells is achievable from a routine blood draw, enabling per-cell detection of driver mutations and fusions relevant to therapy selection.

Future Directions

- Scaling this workflow to patient cohorts could support non-invasive monitoring of clonal evolution and treatment resistance, guiding real-time therapy decisions in advanced cancer.

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- **Patients and their families**



AI Disclosure: Claude, developed by Anthropic, was used to assist with minor editing and formatting of text on this poster.

RESULTS

- Patient 1 was diagnosed 2 years before blood collection and had oligoprogression on second-line lorlatinib after alectinib.
- H3122 cell line; EML4(13) – ALK(20) fusion, BRAF G469E, MET Y1253
- Controls: 10 pg gDNA and CD4+ T cell

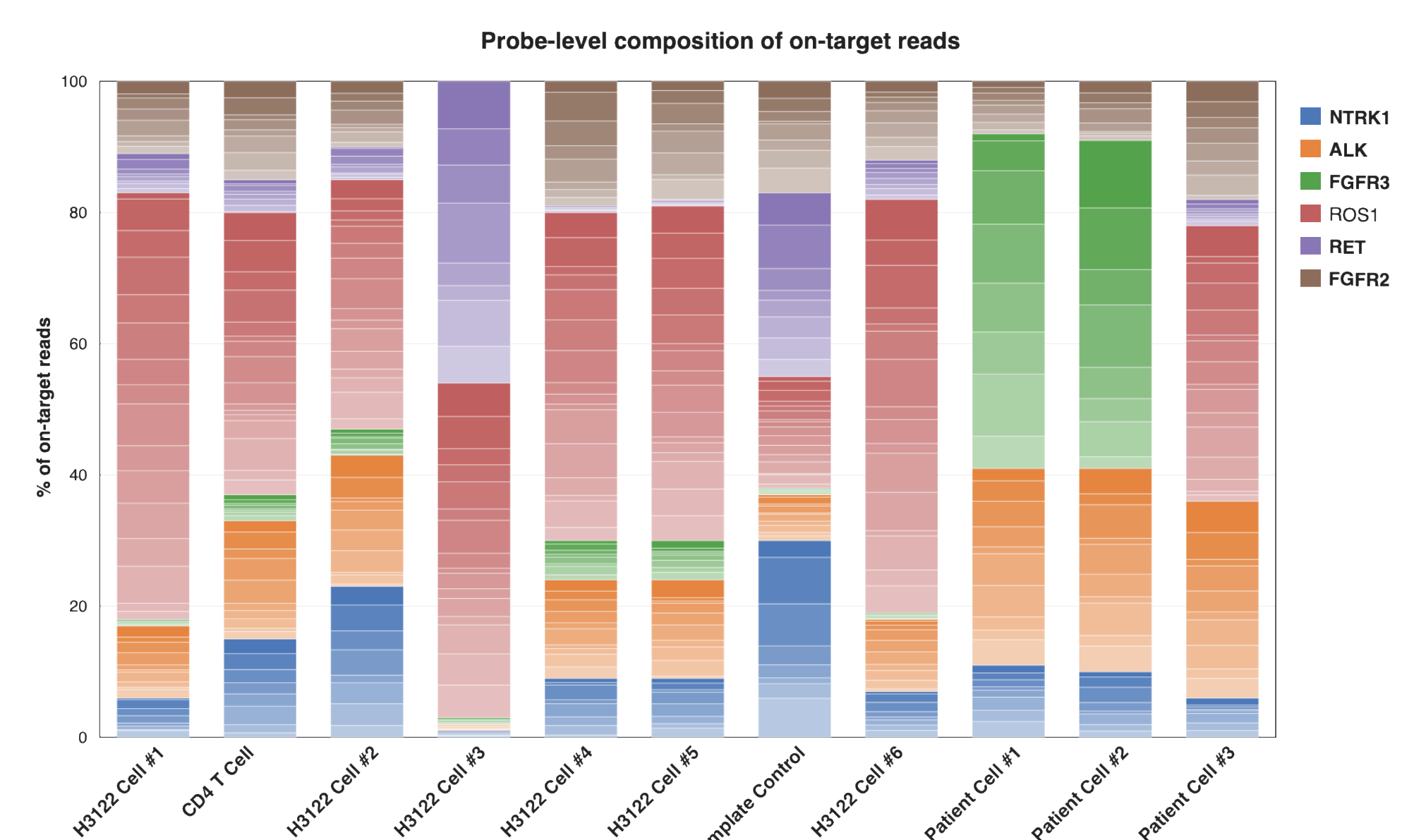


Figure 2: Complete panel coverage across all samples. Bars show share of on-target reads per probe, coloured by gene, shaded 5'→3'.

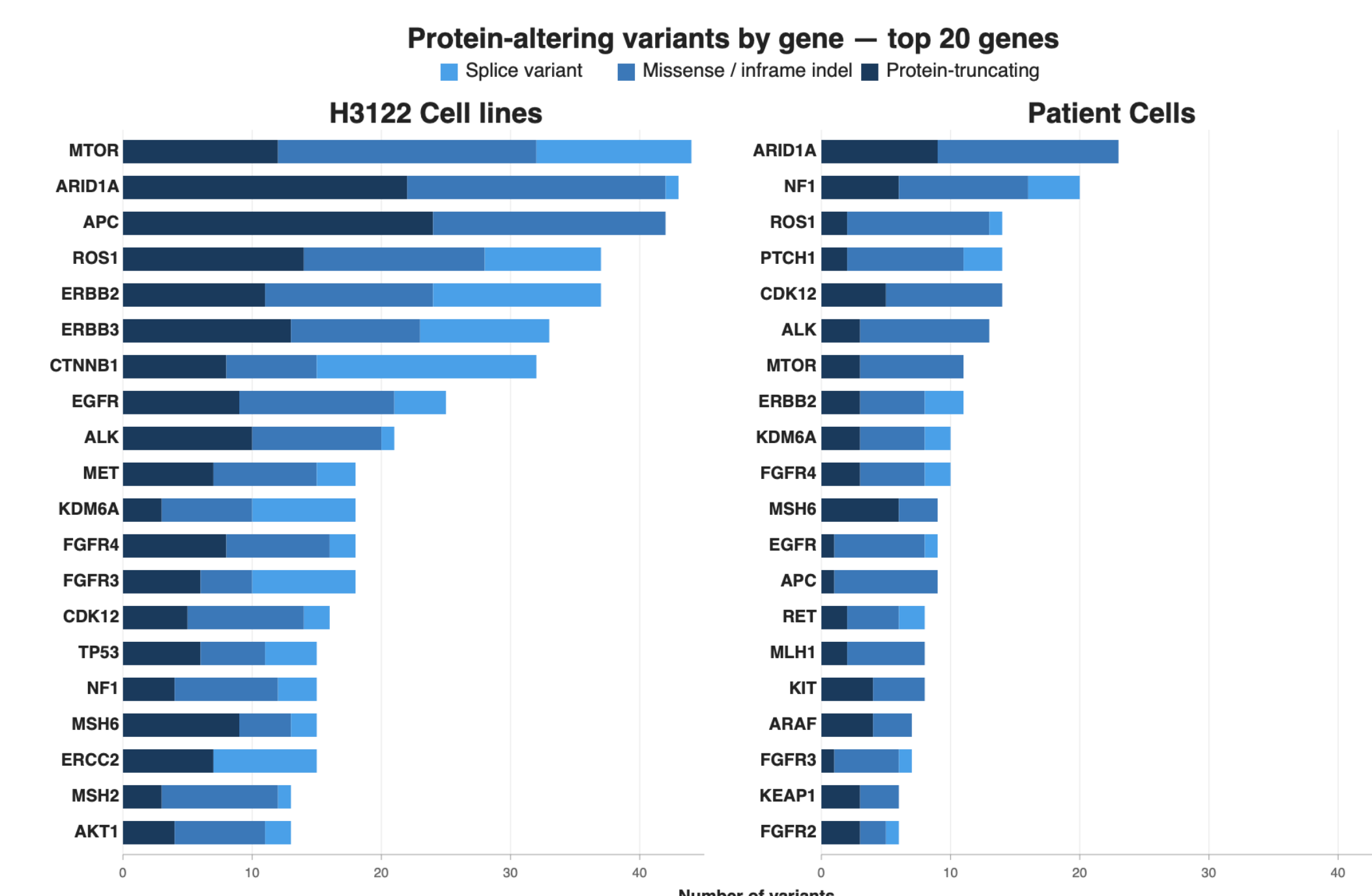


Figure 3: Protein-altering variants per gene. H3122 cells carry higher variant counts overall; patient cells show a distinct top-gene ranking led by *ARID1A* and *NF1*.

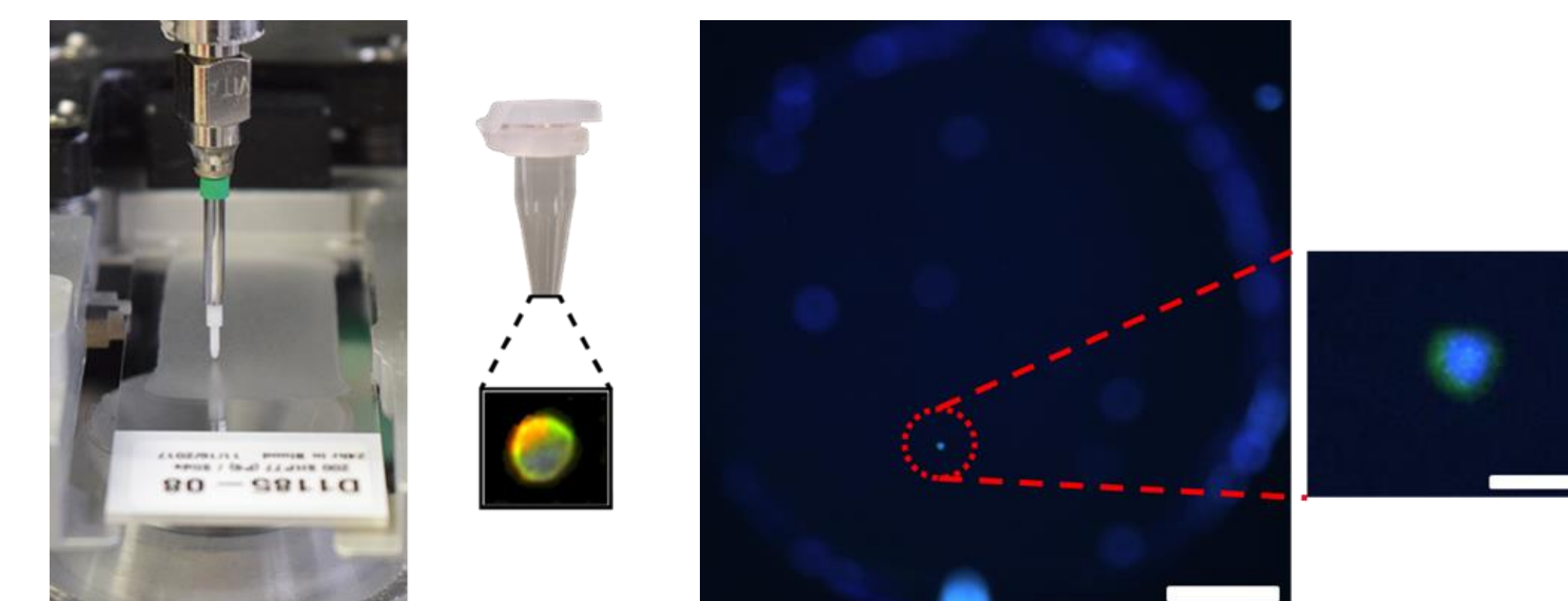


Figure 1: Single-CTC isolation with the AccuCyte–CyteFinder system. Candidate CTCs are identified and then picked from the slide and deposited into a PCR tube for downstream sequencing.

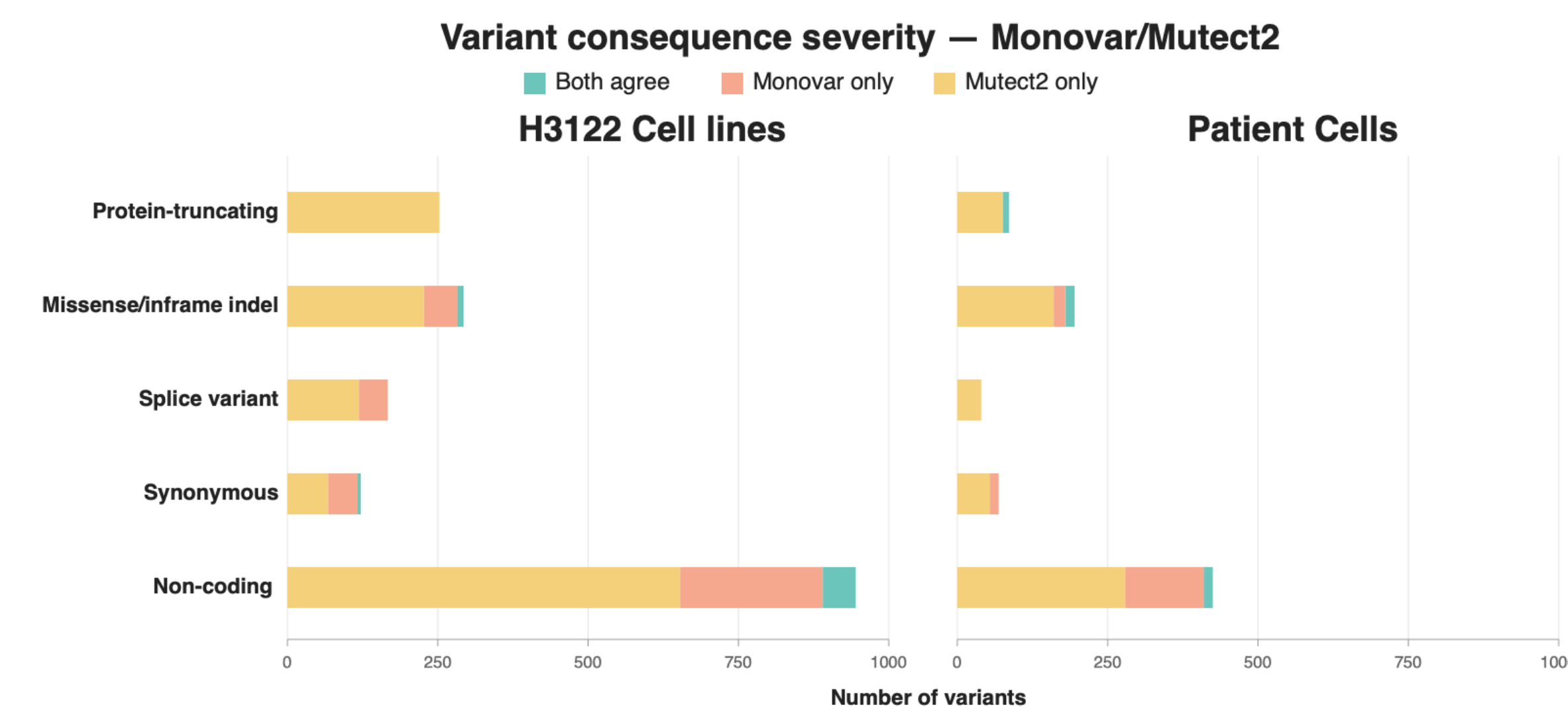


Figure 4: Variant calls by predicted consequence in H3122 cell lines and patient cells. Most calls are Mutect2-only; few are shared between callers, particularly in coding regions.

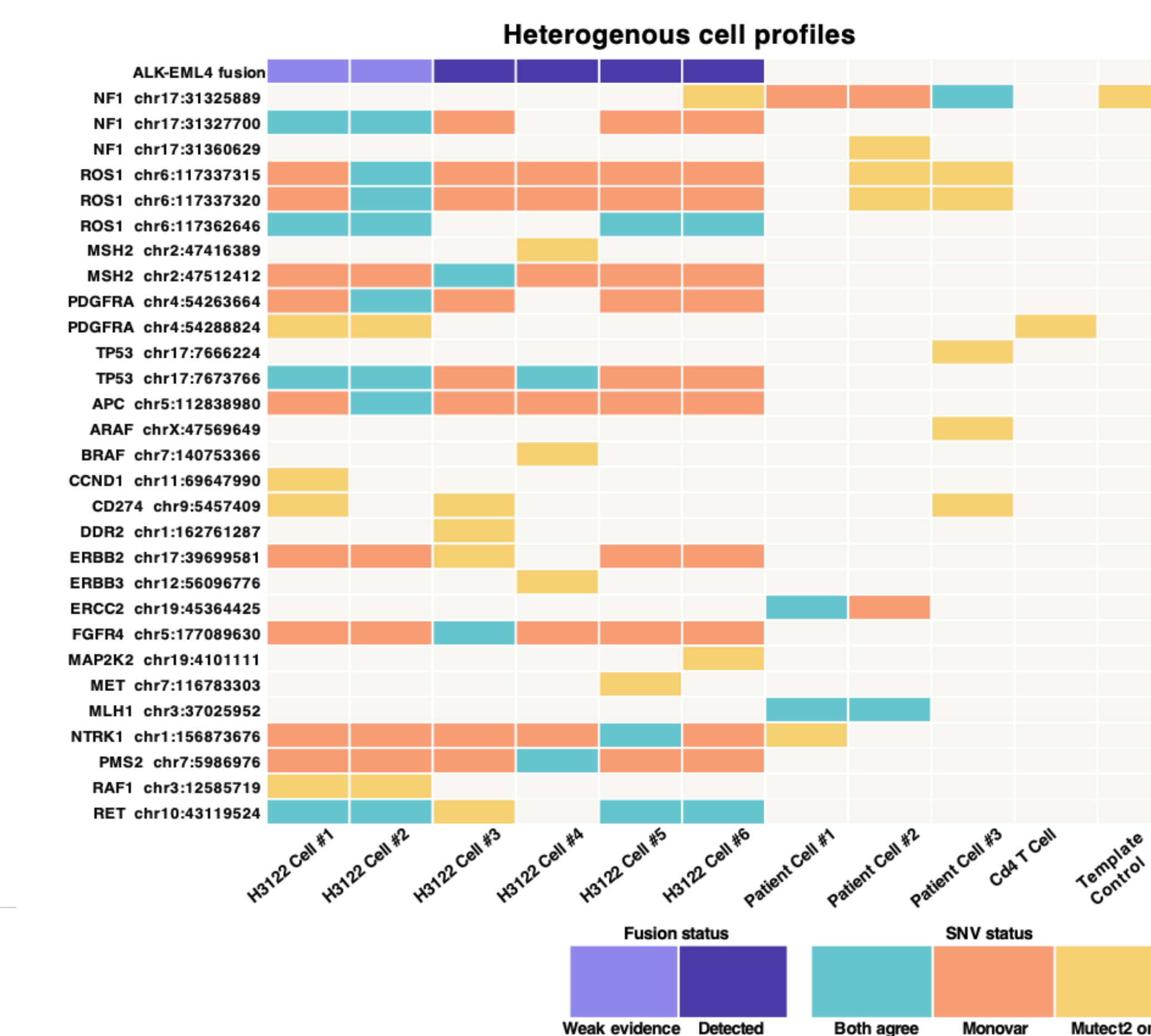


Figure 5: Per-cell variant and fusion calls across H3122 cells, patient CTCs, and controls. EML4–ALK fusion is detected in all H3122 cells; SNV calls (Both agree / Monovar-only / Mutect2-only) vary cell-to-cell, revealing heterogeneity within and between sample types.