PATIENT 52 Cancer Cell Fractions (CCF) from Whole Exome Sequencing of 4 primary tumour regions T4-CCF-WES T3-CCF-WES **Read counts** T2-CCF-WES T1-CCF-WES **SNV Status** SNV **Clonal Mutations** - Exome regions SNV Status - SNVs (grouped by Copy Number status) ubiquitous NA private - CCF > 0.8 across all regions shared missina Training model. Expected read counts harbouring a variant allele, for a clonal SNV (adjusted for Copy Number) T1 (diploid CN) T2 (diploid CN) T3 (diploid CN) T4 (diploid CN) Beta-Binomial (MLE fit) μ = 0.487 , ρ = 0 C_{\ast} = 68 $\pmb{V\!AF} ~~\mu = 0.49$, $\rho = 0.001~C_* = 85$ VAF μ = 0.501 , ρ = 0.004 C_* = 97 VAF μ = 0.501 , ρ = 0.004 C_* = 97 Number of reads (NV)s with mutant alllele from a primary region with CN = c. Test data. Deep Sequencing reveals clonal SNVs in the primary tumour that are missing in the margin samples. Phylogenetic analysis. The tree supports margin samples being ancestral to primary tumour regions. **B WES** T4-TES1 TARGETETED
PANEL #1 T3-TES1 M WES sequencing error T2-TES1 SVZ WES T1-TES1 T3 CCF MARGIN M-TES2 M-TES1 T2 CCF Significant P-Value T4 CCF YES Branch length Testing for True Negatives with deep-sequenced SNVs with a low-purity tissue NO - clonal SNVs with a suitable training set T1 CCF Not Testable - worst-case purity assumption of 1% **Test power for** $\mu = 0.5$ and $\rho = 5 \times 10^{-2}$ at significance level $\alpha = 0.05$ **Deep-resolution clonal SNVs** ($\sim 3000x$) NV < k in M; tested with read coverage from tumour (NR). Accept H₀ $\alpha = 0.05$ 0.01 $H_0: \sum_{w=1}^k \operatorname{BetaBin}(v = w | \hat{r}; \mu, \rho).$ Reject H₀ $\pi = 0.01$ 1e-04 P-value reads from normal $2 * (1 - \pi)$ 1e-06 reads from tumour 1e-08 H_0 SNV 1e-10 30 40 50 60 100 10 20 410 Coverage (adjusted for purity)