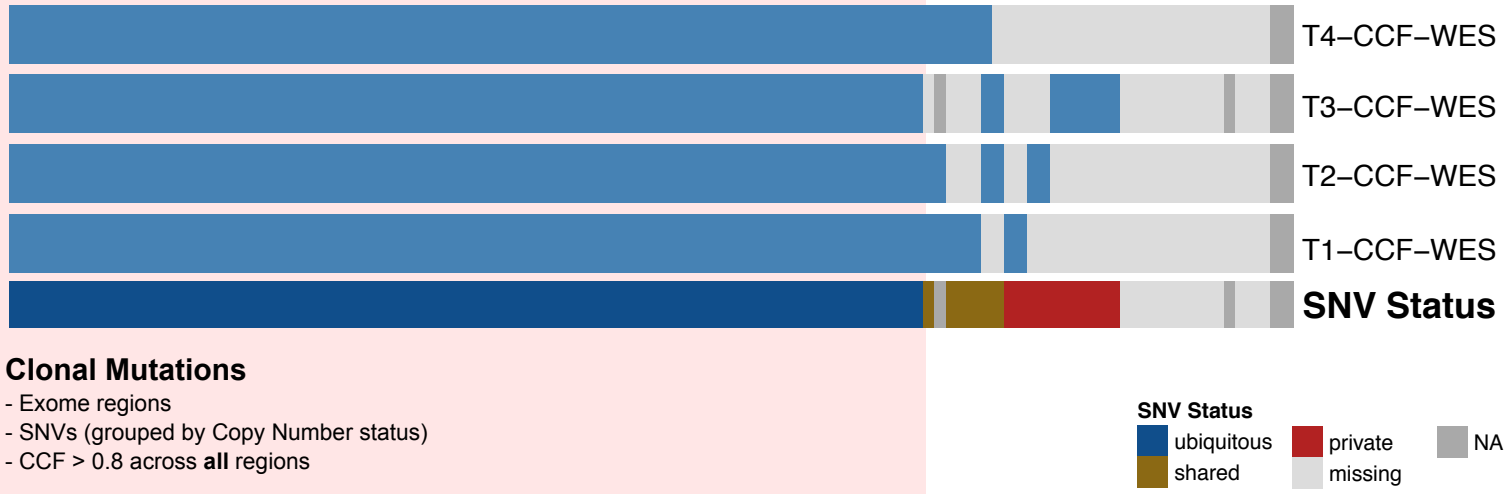
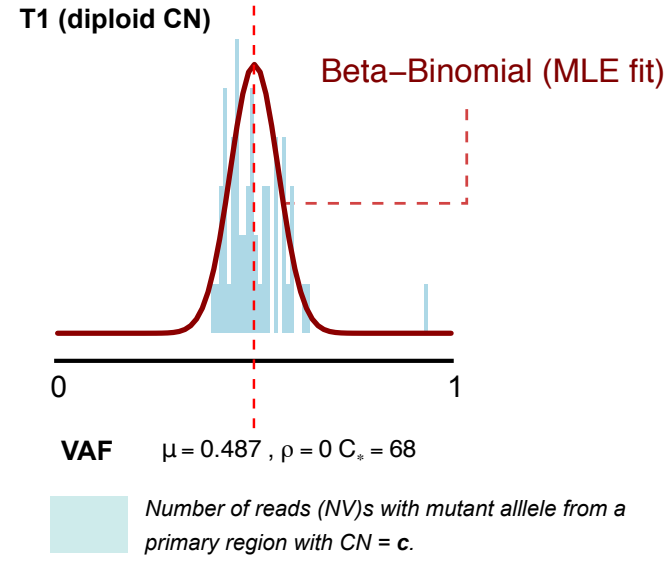
A PATIENT 52

Cancer Cell Fractions (CCF) from Whole Exome Sequencing of 4 primary tumour regions

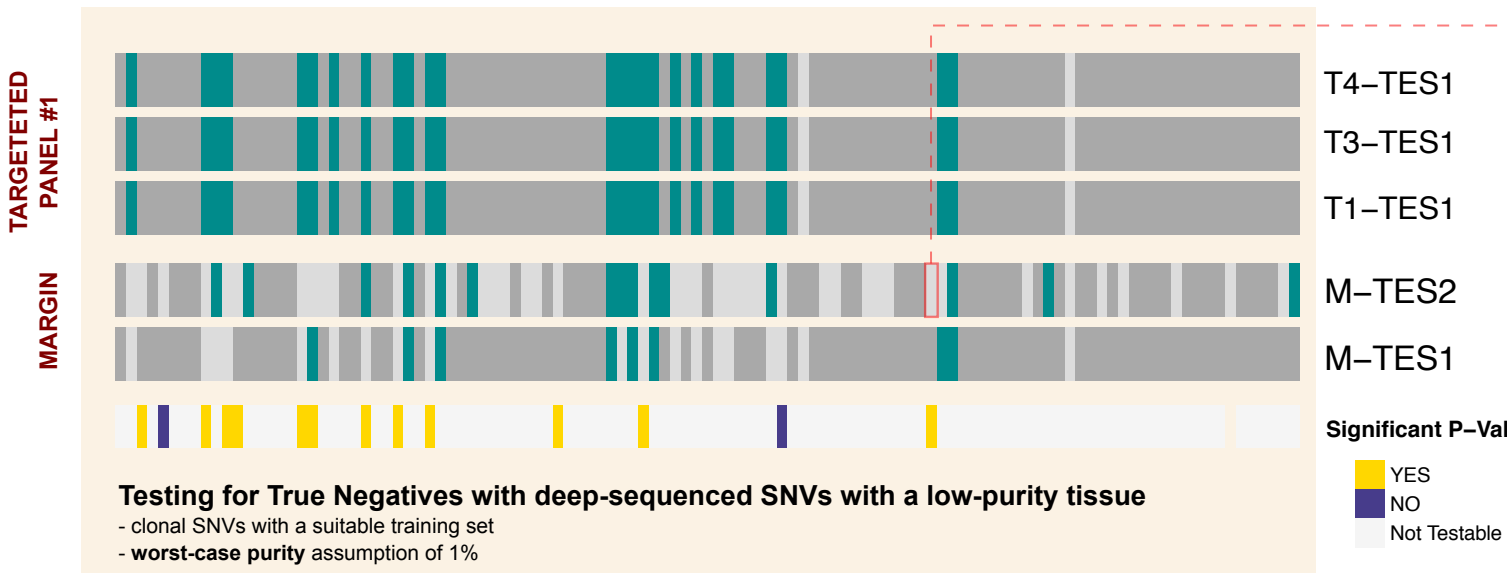


B Training model.

Expected read counts harbouring a variant allele, for a clonal SNV (adjusted for Copy Number)



C Test data. *Deep Sequencing reveals clonal SNVs in the primary tumour that are missing in the margin samples.*



Idea *Assume they are clonal, the frequency of theit mutant allele should follow the same distribution for the frequency of all the other clonal SNVs* (**B**)

Test *Use the fit distribution fit to write a null hypothesis* (H_0) *for the model in which these SNVs are clonal, but undetected in the targeted panels.*

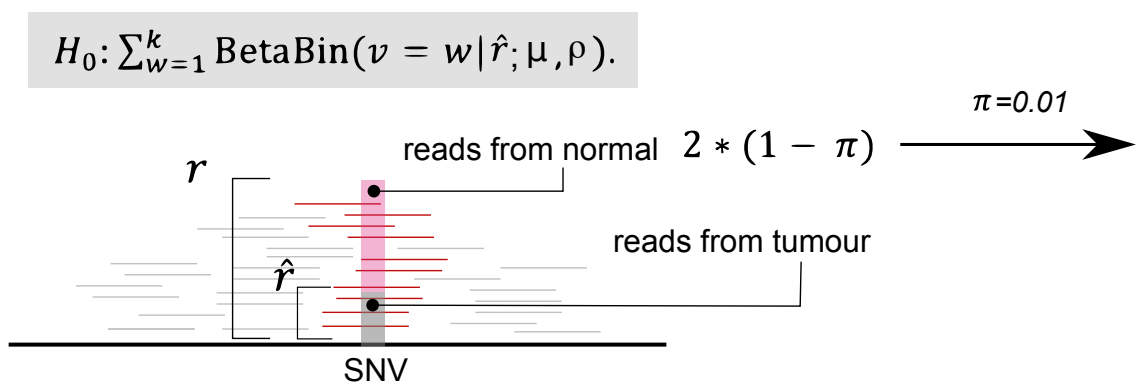
Rejecting the null means having evidence that those SNVs are unlikely clonal. This, combined with a phylogenetc analysis allows to establish that they are ancestral.

D

Deep-resolution clonal SNVs (~*3000x*)

NV < k in M; tested with read coverage from tumour (NR), adjusted for multiple comparisons.

$$H_0: \sum_{w=1}^{k} \text{BetaBin}(v = w | \hat{r}; \mu, \rho).$$



Test power

μ = 0.5 and ρ =5 x 10^{-2} *at significance level* α