# Comprehensive multi-omics analysis categorises distinct pathogenic processes in CLL

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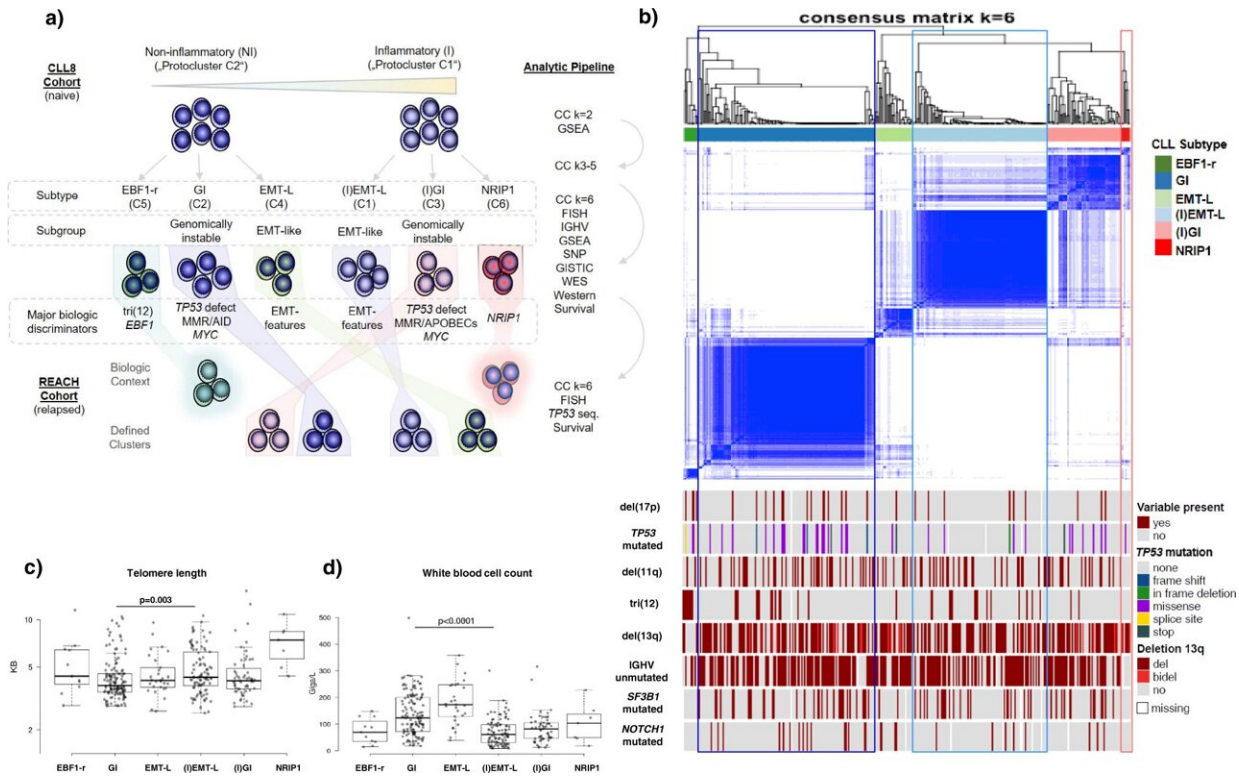


Fig. 1: Composition and relationship of CLL subtypes in clustered data. a Schematic representation for analysis, identification of CLL subtypes in the CLL8, and confirmation in the REACH cohort. The four largest clusters (GI, (I)GI, EMT-L, (I)EMT-L), and associations of NRIP1 with the inflammatory or tri(12) with the EBF1-r signature were also identified in the independent validation cohort of the REACH trial. Co-clustering of GI/(I)GI and EMT-L/(I)EMT-L cases in the REACH cohort supports the selection of subgroup-specific characteristics during treatment. b Heatmap showing the consensus

clustering for k = 6 used for defining CLL subtypes (n = 337). The distribution of genetic characteristics is shown below the heatmap. Significant enrichment of variables in clusters is observed for del(17p) (p = 0.05), TP53 mutation (p = 0.01), tri(12) (p = 7e−06), del(13q) (p = 0.03), and IGHV mutation status (p = 0.008) (all Fisher's exact test (two-sided)). TP53 frameshift mutations occur exclusively in GI and splice site mutations in EBF1-r cases. Tri(12) is strongly overrepresented in EBF1-r (72.7%). c Telomere length is significantly different across CLL subtypes (p