



Additional Figure M3. Sensitivity analysis for pre-treatment substitution rate, using a variety of clonality cutoffs. Each panel shows per-patient comparisons of the estimated pre-treatment substitution rate, in substitutions per Mb-yr, for two different clonality cutoffs. (A) Mutant cellular frequency ≥ 0.92 (x-axis) versus ≥ 0.98 (y-axis). (B) Mutant allele frequency ≥ 0.1 (x-axis) versus ≥ 0.2 (y-axis). (C) Mutant cellular frequency as computed by Verhaak, et al.⁴¹ ≥ 0.92 (x-axis) versus ≥ 0.98 (y-axis). (D) Mutant allele frequency ≥ 0.15 (x-axis) versus mutant cellular frequency ≥ 0.95 (cutoff used in Main Text, y-axis). (E) Mutant cellular frequency as computed by Verhaak, et al.⁴¹ ≥ 0.95 (x-axis) versus mutant cellular frequency ≥ 0.95 (cutoff used in Main Text, y-axis). (A, B, C, D, E) Each symbol shows median estimate for a patient; error bars show interquartile range. Dashed diagonal shows case of perfect agreement between the two cutoffs. Formula and R^2 shown for orthogonal linear regression of \log_{10} values.