Supplementary Material online

An accompanying interactive Mathematica file can be downloaded from the following link:
https://dl.dropboxusercontent.com/u/11866163/Sup_interactive.nb

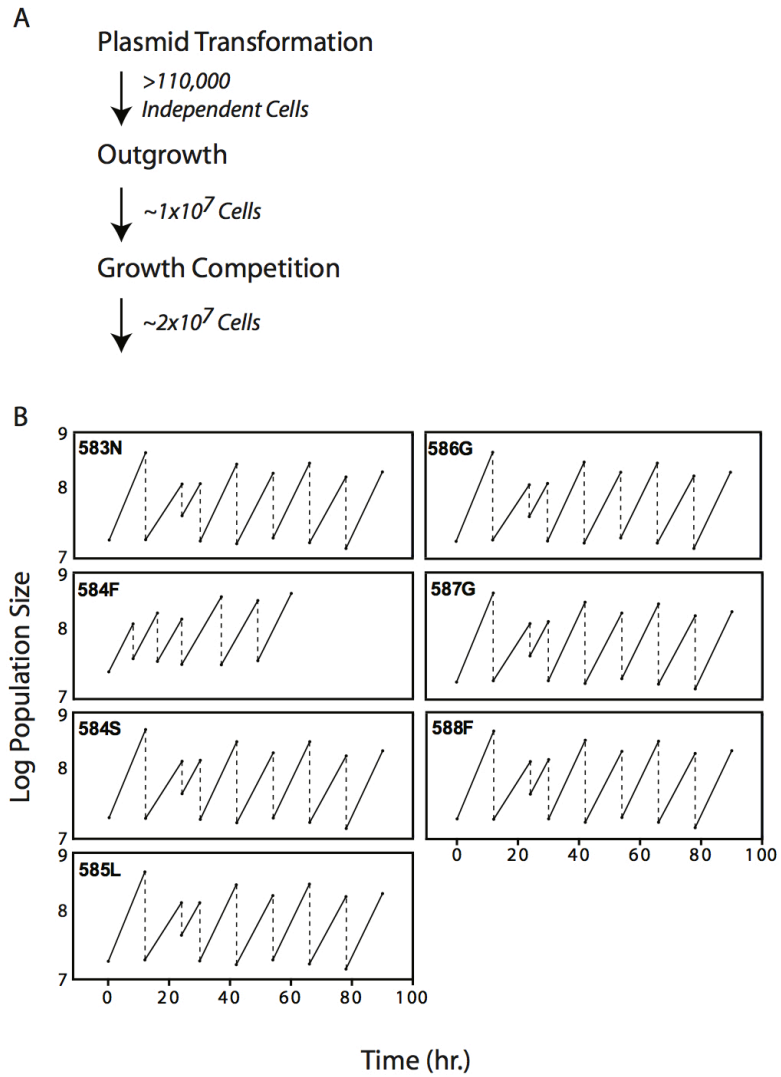

Figure S1: Population management. (A) Preparation of cells for library selection. Population size was maintained at $>10^7$ cells to ensure complete library sampling. (B) Growth and dilution scheme for experimental populations. Solid lines indicate growth and dashed lines indicate dilutions. 584F competition was performed separately from other competitions therefore dilution and time in selection differs.

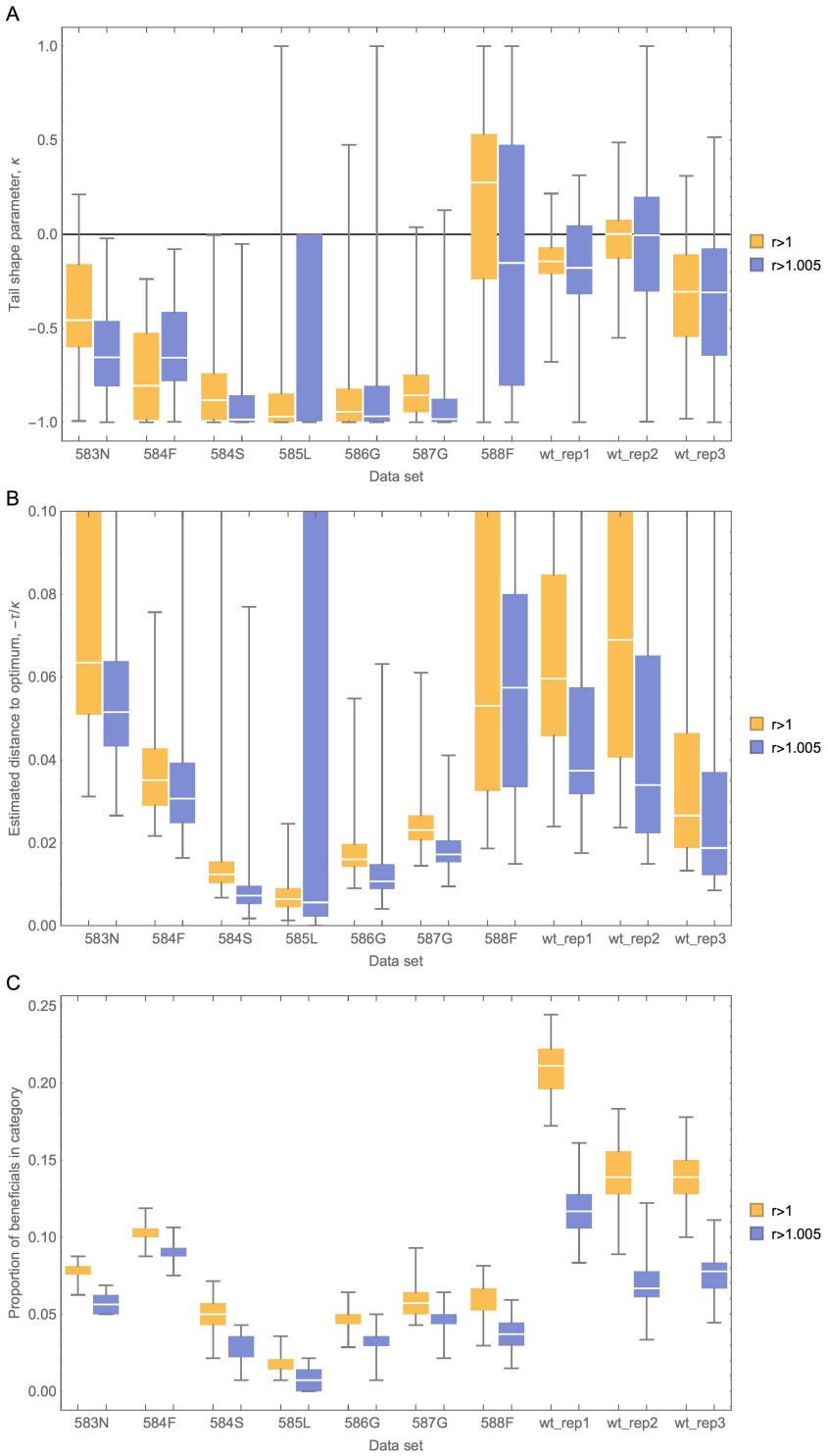

Figure S2: Estimation of the tail shape parameter of a Generalized Pareto Distribution (cf. Joyce et al. 2008; Bank et al. 2014), using two different cutoffs for categorization of beneficial mutations as indicated in the figure legend. (A) Estimation of the tail shape parameter κ, which describes whether the tail of the DFE is bounded ($\kappa<0$), exponential ($\kappa=0$), or heavy-tailed ($\kappa>0$; estimation procedure was restricted to $-1<\kappa<1$). For all but one of the anchor data set, there is evidence for a bounded DFE. (B) Resulting distances to the optimum (considering the subset of negative estimates of the shape parameter). Estimated distances are highly variable, with the 583N and 588F anchors showing the largest potential for adaptation. (C) Proportion of mutations in the respective category used for tail estimation ($r>1$ vs. $r>1.005$), again demonstrating the higher density of wild-type-like mutations in the replicate single-step data sets.

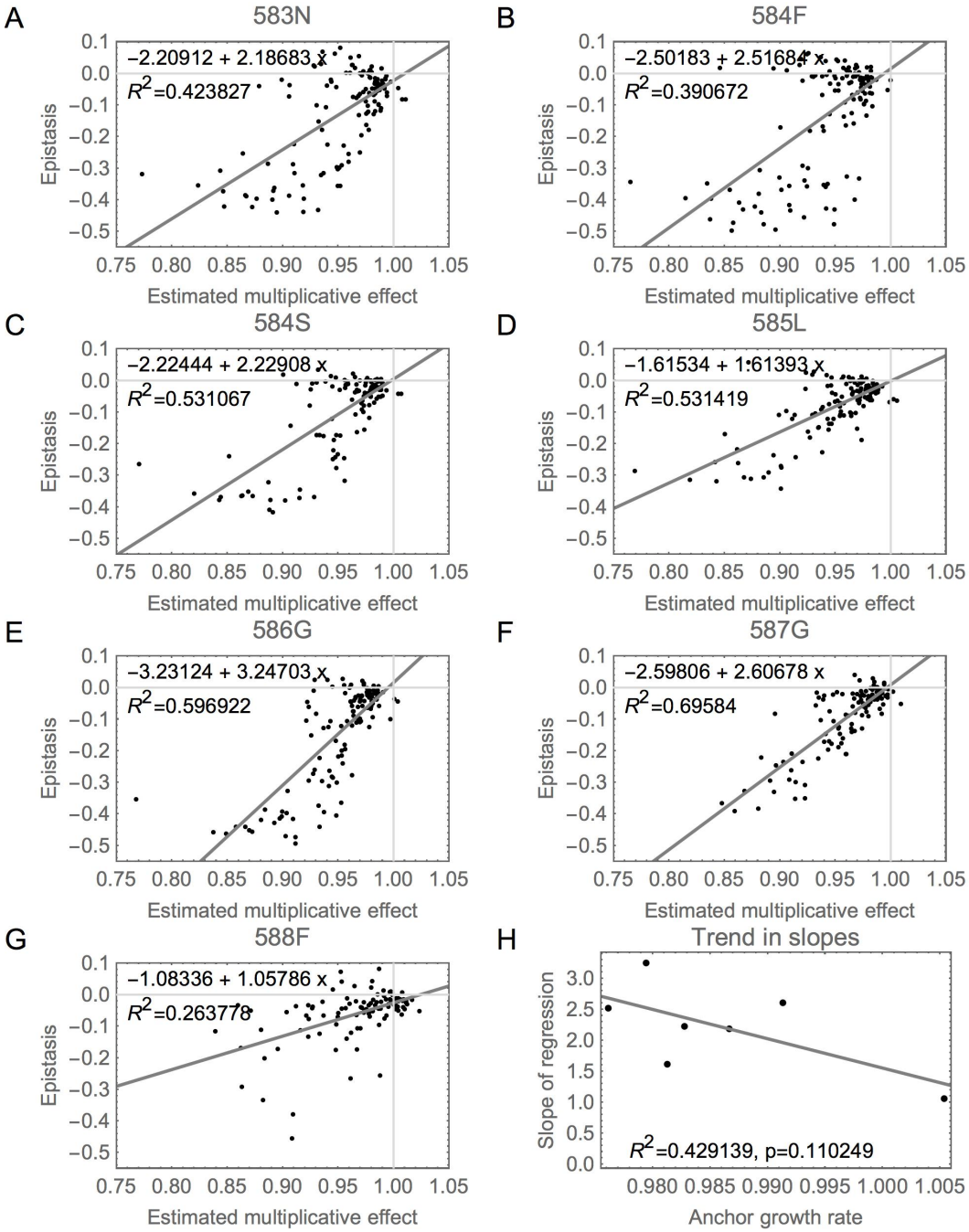

Figure S3: (A)-(G) Correlation between single mutational effects and strength of epistasis. For each anchor data set, we find a strongly significant positive correlation (ANOVA, $p<10^{-6}$). In addition, we see a trend towards a negative correlation between anchor growth rates and the slopes of the estimated linear regression (H), which would be consistent with a concave shape of the fitness landscape, in which epistatic effects become stronger with increasing fitness deficit of the anchor mutation.

References:

Bank C, Hietpas RT, Wong A, Bolon DN, Jensen JD. 2014. A Bayesian MCMC approach to assess the complete distribution of fitness effects of new mutations: uncovering the potential for adaptive walks in challenging environments. Genetics 196:841–852.

Joyce P, Rokyta DR, Beisel CJ, Orr HA. 2008. A general extreme value theory model for the adaptation of DNA sequences under strong selection and weak mutation. Genetics 180:1627–1643.