**Testing association between sequence similarity and complementation relationships for human-yeast paralogs.** In addition to the percent sequence identity (PID) score used in the main text, which was defined as the percentage of aligned positions with identical residues, we examined three other sequence-identity calculation methods. The PIDai score was defined as the ratio of number of identical aligned positions relative to the sum of aligned and internal-gap positions. The PIDsl score was defined by the ratio of number of identical positions to the total number of position in the shorter sequence, while PIDal was defined by the ratio of number of identical positions to the average length of the human and yeast gene pairs. Regardless of which sequence-identity calculation method was used, where yeast genes having more than one human paralog were tested, the paralogous pairs that complemented showed higher sequence identity (*P*-value = 0.0072 for PID; *P*-value = 0.0089 for PIDai; *P*-value = 0.0037 for PIDsl ; *P*-value = 0.0046 for PIDal; Wilcoxon Test). For human genes having multiple yeast paralogs, those paralogous pairs that complemented showed higher sequence identity in all cases except PIDai which considered both the aligned positions and internal gaps (*P*-value = 0.0034 for PID; *P*-value =0.1995 for PIDai; *P*-value = 0.0090 for PIDsl; *P*-value = 0.02 for PIDal; Wilcoxon Test). Differences between results based on PIDai and PID scores are consistent with the observation that human genes tend to be longer than their yeast counterparts.