Supporting Information

Lo et al. 10.1073/pnas.0805242105



Fig. S1. $P(V \ge t)$ under the null estimated by permutations and the P values of the observed marginal effects.



Fig. S2. Correlation between P values from the Curve and Rank methods, for Mean-ratio statistics.



Fig. S3. Correlation between P values from the Curve and Rank methods, for Quantile-ratio statistics.

(M,R)plane, 3way Interaction Below the curve Above the curve (based on the permutation 99.5th percentile) Median R value of 100 permutations (smoothed) 99.5th percentile of R based on 100 permutations (smoothed) number of gene triplets selected: 10

Fig. S4. (*M*, *R*) plane: observed data and permutation quantiles, three-way interactions. 1, *RAD51 TP53 BRCA1*; 2, *SLC22A18 RAD51 BRCA1*; 3, *RB1CC1 BRCA1* PHB; 4, *KRAS2 BRCA1 PPM1D*; 5, *RB1CC1 PALB2 BRCA1*; 6, *ESR1 KRAS2 BRCA1*; 7, *KRAS2 BRCA1 BRIP1*; 8, *PALB2 BRCA1 PHB*; 9, *BARD1 BRCA1 PHB*; 10, *KRAS2 BRCA1 CHEK2*.

Μ

0.0020

0.0025

0.0015

0.0010

Ц

Ö

0.0005

0.0030

(M,Q)plane, 3way Interaction Below the curve Above the curve (based on the permutation 99.5 th percentile) S Median Q value of 100 permutations (smoothed) 99.5th percentile of Q based on 100 permutations (smoothed) number of gene triplets selected: 8 0. 2 Ø Б Ö 0.0 0.0005 0.0010 0.0015 0.0020 0.0025 0.0030 Μ

Fig. S5. (M, Q) plane: observed data and permutation quantiles, three-way interactions. 1, CASP8 TP53 BRCA1; 2, RAD51 TP53 BRCA1; 3, CASP8 PALB2 BRCA1; 4, RAD51 PALB2 BRCA1; 5, RB1CC1 PALB2 BRCA1; 6, ESR1 KRAS2 BRCA1; 7, KRAS2 BRCA1 CHEK2; 8, BARD1 TSG101 BRCA1.



Fig. S6. Three-way interaction network based on 10 genes identified by Mean-ratio method.

PNAS



Fig. S7. Three-way interaction network based on eight genes identified by quantile-ratio method.

PNAS PNAS