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**Abra Brisbin\*** (brisbin.abra@mayo.edu), Mayo Clinic, 200 First St SW, Rochester, MN 55905, and **Brooke L. Fridley**. *Association testing in sequencing studies: Accommodating risk and protective variants.*

Many existing methods address the question of identifying associations between a phenotype and a set of rare variants. However, the majority of these methods implicitly assume that the direction of effect is the same for all rare variants, and are subject to loss of power in the presence of both risk and protective rare alleles. We developed a new method for analysis of rare variants, the Difference in Minor Allele Frequency (D-MAF), which allows combined analysis of common and rare variants, and makes no assumptions about the direction of effects. We tested our method and 9 other methods on simulated genomic regions with varying mutation and recombination rates, and a variety of phenotypic models. We found that several methods, including D-MAF, performed well when all rare variants were either risk alleles or neutral; however, D-MAF and two other methods, C-alpha and CMC, outperformed the others when protective variants were present. D-MAF can also be extended to the analysis of pooled sequencing data, for which many collapsing methods are not applicable. (Received August 16, 2011)