Contents

09/21/2020

1   Masks

- VEST3_rankscore, CADD_raw_rankscore, DANN_rankscore, Eigen-PC-raw_rankscore, and M-CAP_score inequalities should return FALSE if the value is missing

- ∋ denotes containment of the right value in the left (equality will not work since many variants will have values with multiple predictions recorded similar to "D,D,D,D,A,A,A")

- ! denotes negation

1.1   LoF_HC

Include variants that pass the following filter ...

1. LoF == HC

1.2   15of15

Include variants that pass any of the following filters ...

1. LoF == HC

2. VEST3_rankscore > 0.9 & CADD_raw_rankscore > 0.9 & DANN_rankscore > 0.9 & Eigen-PC-raw_rankscore > 0.9 & FATHMM_pred ∋ D & fathmm-MKL_coding_pred ∋ D & PROVEAN_pred ∋ D & MetaSVM_pred ∋ D & MetaLR_pred ∋ D & M-CAP_score > 0.025 & Polyphen2_HDIV_pred ∋ D & Polyphen2_HVAR_pred ∋ D & SIFT_PRED ∋ deleterious & LRT_pred ∋ D & MutationTaster_pred ∈ [D,A]

1.3   11of11

Include variants that pass any of the following filters ...

1. LoF == HC

2. FATHMM_pred ∋ D & fathmm-MKL_coding_pred ∋ D & PROVEAN_pred ∋ D & MetaSVM_pred ∋ D & MetaLR_pred ∋ D & M-CAP_score > 0.025 & Polyphen2_HDIV_pred ∋ D & Polyphen2_HVAR_pred ∋ D & SIFT_PRED ∋ D & LRT_pred ∋ D & MutationTaster_pred ∈ [D,A]

1.4   5of5

Include variants that pass any of the following filters ...

1. LoF == HC

2. Polyphen2_HDIV_pred ∋ D & Polyphen2_HVAR_pred ∋ D & SIFT_PRED ∋ D & LRT_pred ∋ D & MutationTaster_pred ∈ [D,A]

09/21/2020

1.5   5of5_LoF_LC_1pct

Include variants that pass any of the following filters ...

1. LoF == HC

2. Polyphen2_HDIV_pred $\ni$ D & Polyphen2_HVAR_pred $\ni$ D & SIFT_PRED $\ni$ D & LRT_pred $\ni$ D & MutationTaster_pred $\in$ [D,A]

3. IMPACT == HIGH & LoF == LC & MAF < 0.01

1.6   1of5_1pct

Include variants that pass any of the following filters ...

1. LoF == HC

2. Polyphen2_HDIV_pred $\ni$ D & Polyphen2_HVAR_pred $\ni$ D & SIFT_PRED $\ni$ D & LRT_pred $\ni$ D & MutationTaster_pred $\in$ [D,A]

3. IMPACT == MODERATE & (Polyphen2_HDIV_pred $\ni$ D | Polyphen2_HVAR_pred $\ni$ D | SIFT_PRED $\ni$ D | LRT_pred $\ni$ D | MutationTaster_pred $\in$ [D,A]) & MAF < 0.01
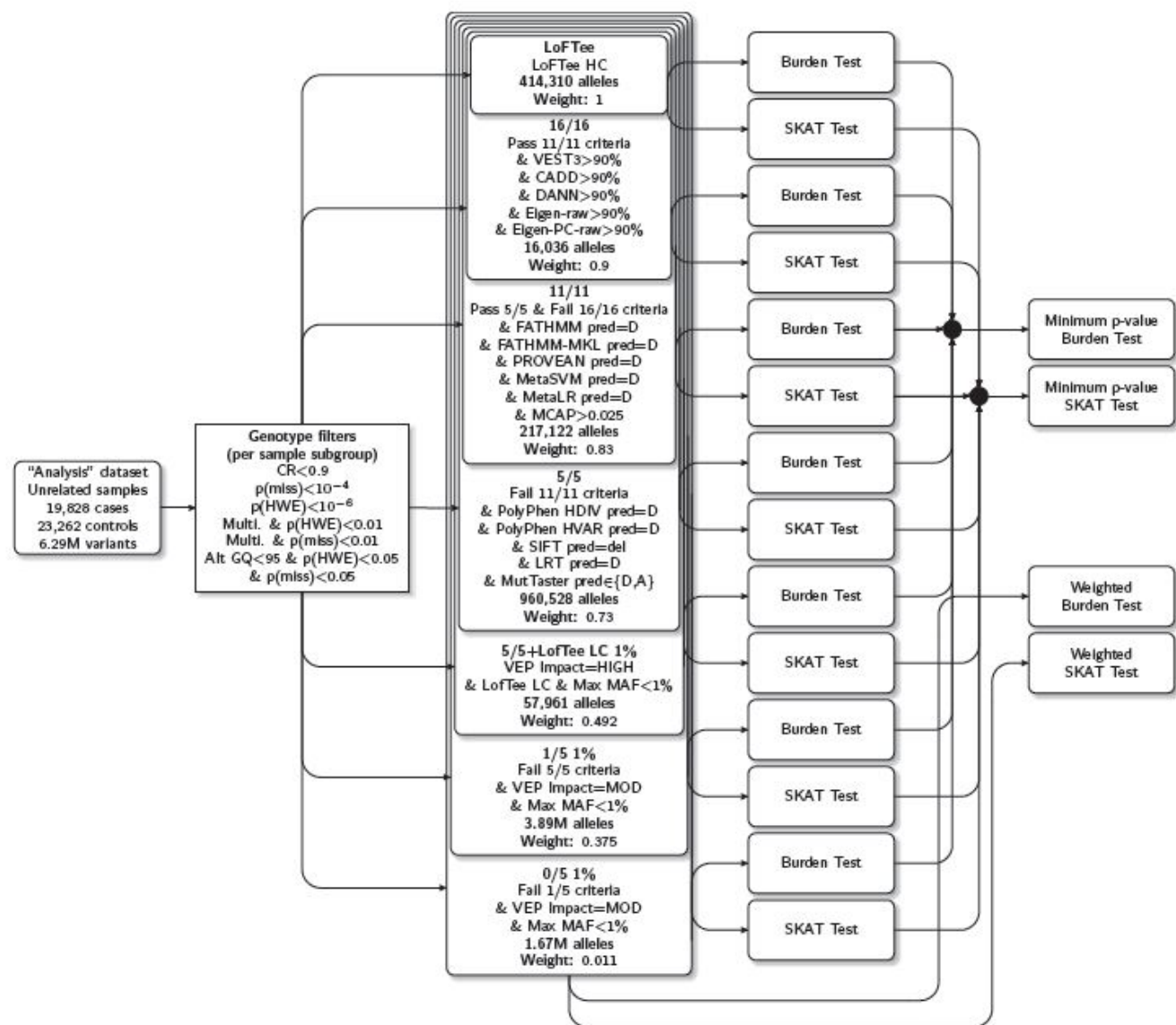
1.7   0of5_1pct

Include variants that pass any of the following filters ...

1. LoF == HC

2. Polyphen2_HDIV_pred $\ni$ D & Polyphen2_HVAR_pred $\ni$ D & SIFT_PRED $\ni$ D & LRT_pred $\ni$ D & MutationTaster_pred $\ni$ [D,A]

3. IMPACT == MODERATE & MAF < 0.01

2   schematic

The following is the schematic describing the masks used in the Nature paper.

(a) Nature Paper Masking Schema