# Article information:

Revisiting the morbid genome of Mendelian disorders | Genome Biology | Full Text
<https://genomebiology.biomedcentral.com/articles/10.1186/s13059-016-1102-1>

# Article summary:

1. Many rare and benign "disease mutations" listed in public databases can be reclassified as likely benign using population-specific resources.

2. The Saudi Human Genome Program database, which represents the largest database of genetic variants from individuals of Arab ethnicity, can uncover Arab-specific and Arab-enriched common variants that cannot be identified using publicly available variant databases.

3. The study highlights the importance of revisiting disease-related databases using public resources and population-specific resources to improve the specificity of the morbid genome of Mendelian diseases in humans.

# Article rating:

Appears moderately imbalanced: The article provides some useful information, but is missing several important points or pieces of evidence that would be required to present the discussed topics in a balanced and reliable way. You are encouraged to seek a more balanced perspective on the presented issues by exploring the provided research topics and looking at different information sources.

# Article analysis:

The article "Revisiting the morbid genome of Mendelian disorders" discusses the limitations of current databases in accurately classifying disease-related mutations and proposes the use of population-specific resources to improve specificity. The authors collated all disease-related mutations listed in HGMD and ClinVar, including variants of uncertain significance (VOUS), and found that many can be reclassified as likely benign based on population frequency and their presence in disease-free individuals. They also suggest that the high degree of inbreeding among Saudi Arabians can render homozygous some disease mutations in individuals who lack the phenotype, allowing for further reclassification.

The article provides a thorough analysis of the limitations of current databases and highlights the importance of population-specific resources. However, there are potential biases and limitations to consider. Firstly, the study focuses solely on Saudi Arabians, which may not be representative of other populations. Secondly, while the authors acknowledge that large-scale sequencing efforts have challenged the view that truncating variants are always pathogenic, they do not discuss other factors such as epigenetic modifications or gene-gene interactions that may influence variant pathogenicity.

Additionally, while the authors suggest that many previously reported variants can be reclassified as benign based on their rarity in public databases, they do not provide evidence to support this claim beyond their own database. It is possible that these variants are rare for a reason and may still have unknown effects on health outcomes.

Furthermore, while the authors highlight the importance of using public resources to improve specificity, they do not address potential biases within these databases such as underrepresentation of certain populations or ascertainment bias towards certain diseases.

Overall, while this article provides valuable insights into improving specificity in disease-related mutation classification, it is important to consider potential biases and limitations when interpreting its findings. Further research is needed to fully understand variant pathogenicity and improve accuracy in classification.

# Topics for further research:

* Epigenetic modifications and variant pathogenicity
* Gene-gene interactions and variant pathogenicity
* Bias in public databases for disease-related mutations
* Underrepresentation of certain populations in disease-related mutation databases
* Ascertainment bias in disease-related mutation databases
* Large-scale sequencing efforts and variant pathogenicity

# Report location:

<https://www.fullpicture.app/item/a09d6587c6821d38c6e3035cb6e436f9>