Case reports

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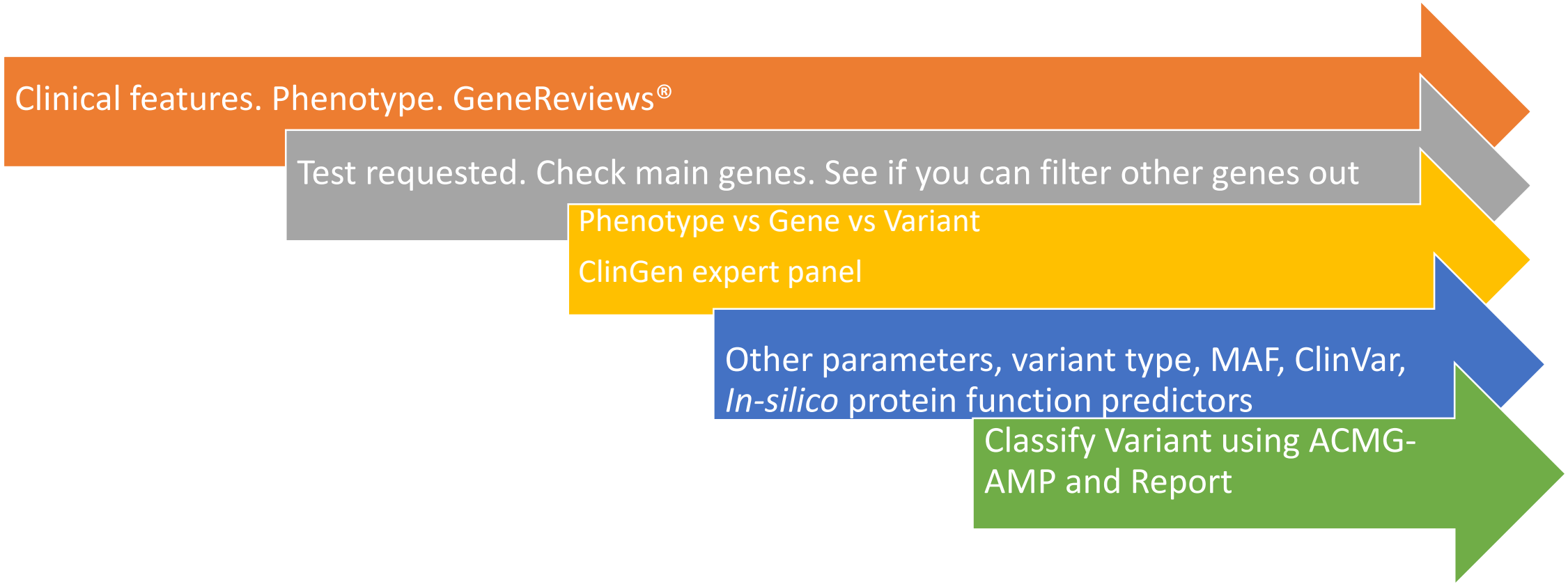
Clinical features. Phenotype. GeneReviews®
Test requested. Check main genes. See if you can filter other genes out
Phenotype vs Gene vs Variant
ClinGen expert panel
Other parameters, variant type, MAF, ClinVar,
In-silico protein function predictors
Classify Variant using ACMG-AMP and Report

NGS test

- NGS method =Targeted panel / WES
- Phenotype
- Only proband
- Sanger only when necessary
  - Parental DNA
  - Poor coverage
- Clin Gen expert panel
- ACMG-AMP
- Analysis = Phenotype

Example: Case 1

- Six month old female patient presenting with failure to thrive, Webbed neck, widely spaced nipples, low set ears and dysmorphic features.
- Cardiac assessment showed pulmonary value stenosis and atrial septal defect
- DNA testing for Noonan syndrome was requested.

https://www.ncbi.nlm.nih.gov/books/NBK1124/

On GeneReviews®, check genes on the Molecular genetic test table

Go back to the excel file and find genes associated with the disorder and filter accordingly.

Excel file: Example case 1

- Annotated data
- NCBI/GeneReviews® link for the disorder
  - Phenotype details
  - Gene details
- Find gene associated with the phenotype
- Go back to the Excel file
- Prioritise potential variant
- Apply ACMG-AMP rules where you can

Example: Case 2

- Suspected to have neurodevelopmental genetic disorder of unknown cause and presented with the following clinical
- features: atrial septal defect and ventricular septal defect, macrocephaly,
- developmental delay, cryptorchidism, hypoplastic nails and dysmorphic features
- including a broad chest, short palpebral fissures, hooded eyelids and cup shaped ears.

https://www.ncbi.nlm.nih.gov/medgen/934663

Excel file: Example case 2

- Annotated data
- NCBI/GeneReviews® link for the disorder
  - Phenotype details
  - Gene details
- Find gene associated with the phenotype
- Go back to the Excel file
- Prioritise potential variant
- Apply ACMG-AMP rules where you can