



CAGI6 - RGP challenge Moon

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CAGI slide pack guidelines

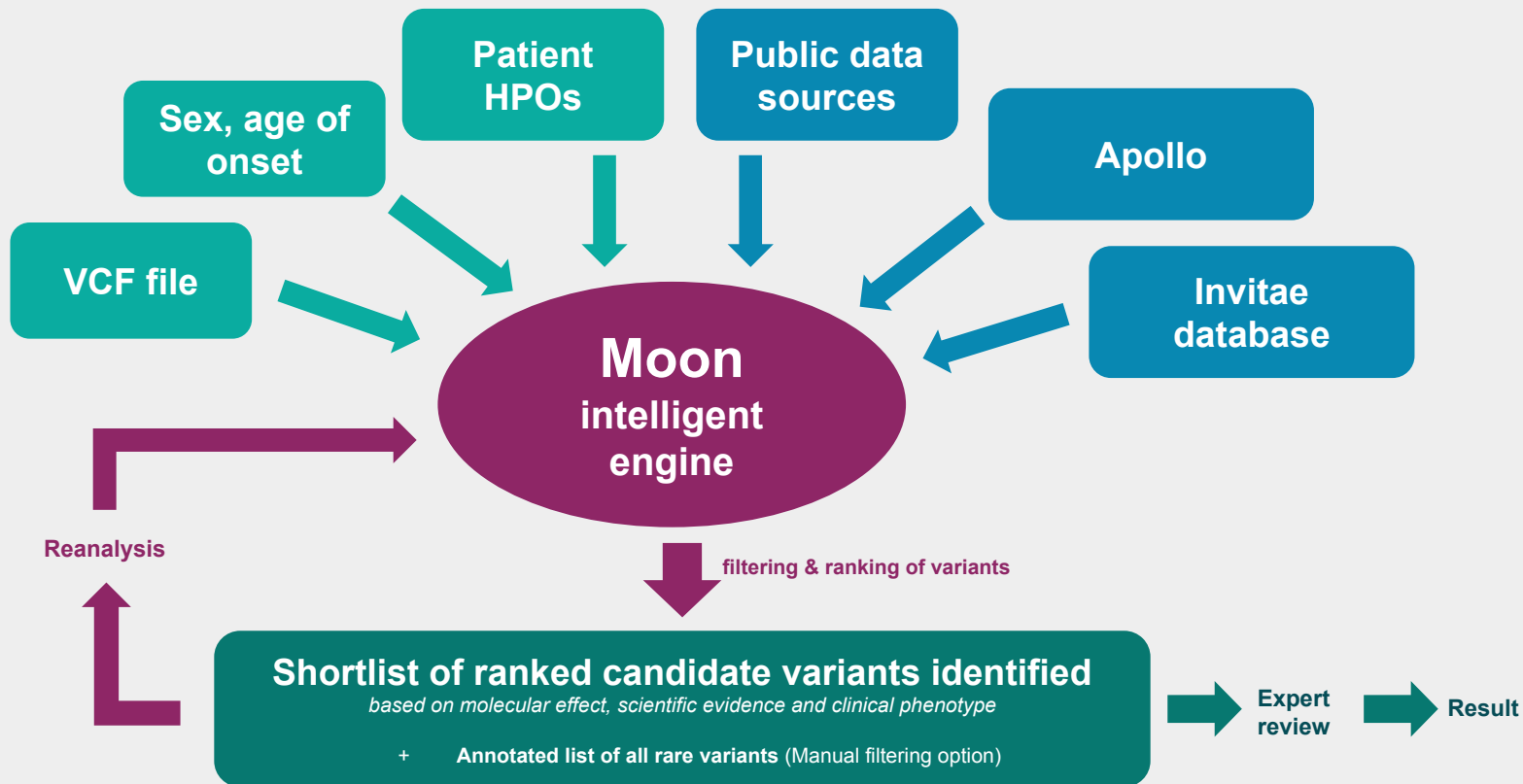
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Moon: How does it work?



Apollo: How does it work?

Apollo stores knowledge of gene-disease and disease-phenotype correlations

- Disease name
- Gene name
- Inheritance pattern
- Disease-associated phenotype (HPO terms)
- Other metadata: e.g. disease molecular mechanism

Apollo drives the phenotype matching in Moon

- Variants in disease-associated genes are filtered and ranked based on phenotype overlap and genotype/inheritance concordance using the information stored in Apollo

Apollo stays up-to-date

- Text-mining algorithm scans the genetic literature on a daily basis and identifies new relevant publications with gene-disease/phenotype associations
- New available knowledge is included in Apollo after manual review by expert genetic scientists



Apollo: How does it work?



De novo variants of NR4A2 are associated with neurodevelopmental disorder and epilepsy.

Abstract

This study characterizes the clinical and genetic features of nine unrelated patients with de novo variants in the NR4A2 gene. Variants were identified and de novo origins were confirmed through trio exome sequencing in all but one patient. Targeted RNA sequencing was performed for one variant to confirm its splicing effect. Independent discoveries were shared through GeneMatcher. Missense and loss-of-function variants in NR4A2 were identified in patients from eight unrelated families. One patient carried a larger deletion including adjacent genes. The cases presented with **neurodevelopmental delay**, **hypotonia** (six cases), and **epilepsy** (six cases). De novo status was confirmed for eight patients. One variant was demonstrated to affect splicing and result in expression of abnormal transcripts likely subject to nonsense-mediated decay. Our study underscores the importance of NR4A2 as a disease gene for neurodevelopmental disorders and **epilepsy**. The identified variants are likely causative of the **seizures** and additional developmental phenotypes in these patients.

Genes

NR4A2

Disorder	Inheritance	Overlap	Export
Intellectual disability and autism, NR4A2-related	AD	2/3	Add source
New disorder	-	-	



Moon Shortlist

moon Samples Lab

Proband_demo ▾

Patient Filter Shortlist Report

Search...

Male patient presenting at 1 year with the following phenotype:

- Nystagmus HP:0000639
- Neurodegeneration HP:0002180
- Cerebellar atrophy HP:0001272
- Spastic tetraplegia HP:0002510
- Developmental regression HP:0002376

Family members

- healthy father [Father_demo](#) ✓
- healthy mother [Mother_demo](#) ✓

SNVs

Carrier SNVs

SV/CNVs

Manually Filtered

The patient's phenotype might be caused by:

PLA2G6 ▾ 22:38,512,190 ▾ rs1043378899	GA ref: G	missense p.Arg591Trp 10 publications	Infantile neuroaxonal dystrophy 1 AR - compound heterozygous 2 comments
KB P Invitae P ClinVar P			
PLA2G6 ▾ 22:38,511,635 ▾ rs1484455290	GA ref: G	stop gained p.Arg645* 11 publications	Infantile neuroaxonal dystrophy 1 AR - compound heterozygous
KB P ClinVar P			





Thank you!



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