



# moon

analyse rare disease  
NGS data in minutes



## ***DIAGNOSING RARE DISEASES CAN BE LIKE SEARCHING FOR A NEEDLE IN A HAYSTACK.***

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When interpreting whole genome data for rare disease diagnostics, geneticists must identify the one or two mutations responsible for the patient's condition hidden amongst 4.5 million variants.

This process takes between 20 and 40 hours when performed by highly skilled staff using specialised software<sup>1</sup>. This is prohibitively slow for many clinical applications.

*Moon changes all this.*

<sup>1</sup> Wenger A.M., et al. (2016). Systematic reanalysis of clinical exome data yields additional diagnoses: implications for providers. *Genetics in Medicine*, 19, 209-214



## What is Moon?

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Moon is an innovative decision-support software package that, through automation and using artificial intelligence (A.I.), helps genetic labs identify causal variants for rare diseases. Moon reduces analysis time from days or weeks to mere minutes, making it the fastest variant interpretation software on the planet.

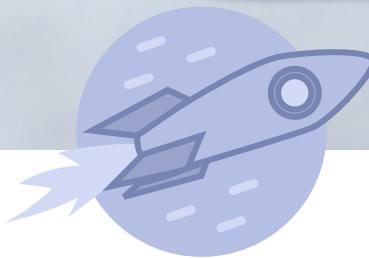


## How does Moon work?

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Geneticists upload NGS data (SNV/CNV) as a standard VCF file (e.g. directly from GATK) and they enter the patient's symptoms, gender and age of onset.

Moon takes this input and, using proprietary A.I. algorithms and a proprietary disorder model, suggests the causal variant in 2 minutes for WES and in 5 minutes for WGS. For each suggested candidate variant, a wide range of annotations are shown, thereby providing scientific evidence for Moon's choices. The results can then easily be verified in the Filter view, and reported.



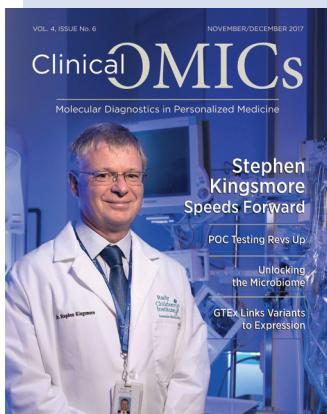
## Fast

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Rapid genome sequencing and interpretation can be crucial in the acute care of infants with genetic diseases in neonatal and paediatric intensive care units. Moon can go from standard VCF to clinical report in a ground-breaking 2 minutes for WES data, and in 5 minutes for WGS data. As such, Moon can be instrumental for this new wave of time-sensitive NGS-based diagnostics. Moon's fast analysis times contributed to a new world record for fastest genome diagnosis, set by researchers at Rady Children's Hospital in San Diego.

In February 2018, scientists at the Rady Children's Institute for Genomic Medicine were able to achieve a remarkable new world record for whole genome sequencing and interpretation. They went from blood sample to diagnosis of a life-threatening genetic disorder in just 19.5 hours.

Among the leading technology used for this landmark achievement was Moon from Diploid, now Invitae. For this world record, Moon was able to provide variant annotation and interpretation in just 5 minutes.



"Our hope is that paediatric genomic medicine will one day become routine so that ultimately all children who need it can have access to this life-saving technology," said Dr. Kingsmore, CEO at Rady Children's Institute for Genomic Medicine.



Moon was honoured with a Best of Show Award at Bio-IT World Expo 2018 in Boston. The Best of Show program relies on a panel of expert judges from academia and industry who screen eligible new products and hear presentations from the finalists on site. Judges considered 46 new products and viewed presentations on site from 18 finalists.

A screenshot of the Moon software interface on a MacBook. The interface shows a genetic analysis for a "0 year old male patient with the following phenotype: • Neurodegeneration". The patient's phenotype might be caused by mutations in the PLA2G6 gene. Two variants are highlighted: one at position 22:38,512,190 (GA to AA) and another at position 22:38,511,835 (GA to AA). Both variants are associated with "Parkinson disease 14, autosomal recessive" and "AR - compound heterozygous". A yellow arrow points to the second variant. Below the variants, a schematic diagram of the PLA2G6 gene shows its structure with exons and a poly-A tail. The gene is labeled "ENST332509". The bottom of the screen displays the text "Analysed by Cyrielle Kint on 09 May 2019 at 13:13 | Annotation sources".

Moon's clean and intuitive interface makes it fast and easy to perform WES or WGS interpretation.

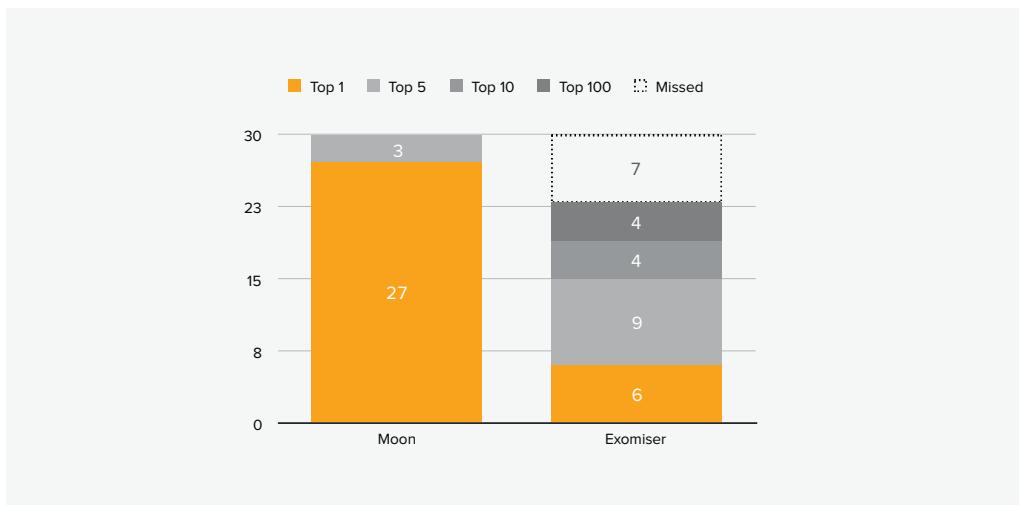


## Accurate

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We tested Moon using 30 real-life single exome cases that had previously been solved by our expert geneticists. The cases were previously unknown to Moon, and the software had not been trained on the cases in any way. In 100% of the cases, the causal variant was listed in Moon's top 3. For cases with family data available, Moon performs even better. In a study on about 100 whole genomes conducted by Rady Children's Hospital, Moon reached 99% precision, confirming the results of the internal study.<sup>1</sup>

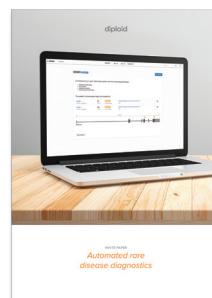
1. Clark MM et al. (2019). Diagnosis of genetic diseases in seriously ill children by rapid whole-genome sequencing and automated phenotyping and interpretation. *Science Translational Medicine*; 11(489).



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The fraction of cases from the test set, in which the causal variant was ranked in the top 1, top 5, top 10, top 100 or outside of the 100 first ranked variants ('Missed') by either Moon or Exomiser.

Download the white paper from  
[invitae.com/moon](https://www.invitae.com/moon) and see how  
Moon compares to Exomiser





## Up to date

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Traditional software packages allow their users to define pipelines which are then applied to every exome analysed. However, despite the fact that new gene-phenotype correlations are published every day, the gene panels used by these pipelines often remain untouched for months or even years. Moon is different in that it automatically scans the literature on a daily basis, integrating new scientific insights as they are published. As a result, Moon always gives you the best chance of reaching a diagnosis.

*Moon has accelerated our diagnostic process.  
It is not only fast but also very up to date:  
we diagnosed cases with pathogenic mutations in  
genes that were just published as disease genes.  
With Moon, yesterday's publication is today's diagnosis.*



Prof. dr. Frank Baas, MD  
Head, Laboratory Diagnostic Genome Analysis  
Leiden University Medical Center, The Netherlands



## Infinite

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Since Moon can operate fully unsupervised, it's the perfect tool to re-run older analyses. Patients for whom no diagnosis is available today, might be diagnosable next month. Or next year. With Moon's Autopilot, infinite interpretation becomes a reality as automatically re-running analyses is easy, fast and free.

*Moon is a real added value to our diagnostic pipeline for NGS: very user-friendly, performant and up-to-date with the newest data from the recent literature.*

Prof. dr. Geert Mortier, MD  
Chairman, Department of Medical Genetics  
Antwerp University Hospital, Belgium





## Secure

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Moon is deployed in ISO27001 or HIPAA compliant data centres that are always located in the customer's country. That way, genetic data remains in the country where it has been generated. Moon runs on dedicated physical servers that adhere to the highest security standards and are operated in compliance with HIPAA and GDPR.

At the application level, Moon offers two factor authentication, making sure that only your lab members can access Moon.



General  
Data  
Protection  
Regulation

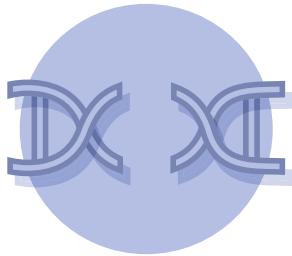


Moon is registered as an In Vitro Diagnostic Medical Device on the European market, in accordance with European Union directive 98/79/EC.

*In whole exome and genome sequencing, variant interpretation is a big challenge. Moon can provide the disease-underlying variant(s) with a few clicks in a couple of minutes, even among a large number of whole-genome variants. As a medical geneticist, I really appreciate Moon's speed and easy HPO-based workflow. Moon helps us to diagnose rare diseases, presenting clinically important variants we should not miss.*



Dr. Gabor Matyas, PhD, FAMH Medical Genetics  
Head, Swiss Foundation for People with Rare Diseases  
Zentrum für Kardiovaskuläre Genetik und Gendiagnostik, Switzerland



## CNV

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While array-based methods have long been the standard to detect pathogenic CNVs, the relatively low resolution only allows to detect CNVs of approximately 20,000 base pairs in size or larger. Since the majority of CNVs in the human genome are smaller, this means that about 80% of all human CNVs are missed with the traditional approach. NGS-based CNV detection provides a solution to this problem, as CNVs as small as 100 base pairs can be detected with this method. Fast interpretation of these called CNVs can now be performed with Moon.

Moon's automated filtering and ranking algorithms quickly guide you to the relevant CNVs for your patient's phenotype. Moon can even detect relevant combinations of SNVs and CNVs, as SNV and CNV analyses are performed simultaneously. Finally, the rich CNV annotations and automated reporting allow for easy manual review of the Moon results.



## API

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Moon offers an easy-to-use REST API to import NGS and patient data, run analyses and retrieve results. As such, Moon can be easily integrated into any existing pipeline.



## Cost-efficient

By reducing manual analysis time from between 20 and 40 hours per exome interpretation<sup>1</sup> to less than an hour, Moon can potentially save between 19 and 39 hours of labor. The additional expert time that becomes available by using Moon, can be highly valuable for in-depth analysis of difficult, unsolved cases.



## Automated Report

Not content to reduce the time to answer to just a few minutes, Moon squeezes even more time out of the process via natural language generation (NLG) technology to automatically write a first draft of the diagnostic report. This draft can then be edited.

Phenotype						
<p>Gender: male Age of onset: 0</p> <ul style="list-style-type: none"><li>Intellectual disability</li><li>Seizures</li><li>Unilateral deafness</li><li>Visual impairment</li><li>Brachydactyly</li><li>Febrile seizures</li><li>Congenital visual impairment</li><li>Status epilepticus</li></ul>						

99411 SNPs were analysed.

7 SNPs are discussed in this report

Classification	Gene	Disease	Inheritance	p-notation	c-notatio	Zygosity
Likely pathogenic	WDR81	Microcephaly, WDR81-related	AR	p.Thr1684I	c.5048_5049in	heterozygous
Likely pathogenic	MYO7A	Usher syndrome, type 1B	AR	p.Arg806Cys	c.2506C-T	heterozygous
VUS	KCNQ2	Epileptic encephalopathy, early infantile, 7	AD	p.Pro78Arg	c.2633C-G	heterozygous
VUS	WDR81	Microcephaly, WDR81-related	AR	p.Glu1686Val	c.5057A-T	heterozygous
VUS	DEAF1	Mental retardation, autosomal dominant 24	AD	p.Gln909C	c.1470G-C	heterozygous
VUS	MYO7A	Usher syndrome, type 1B	AR	p.Gly74Ser	c.2140G-A	heterozygous
Likely pathogenic	TRIOBP	Deafness, autosomal recessive 28	AR	p.Arg612*	c.1834A-T	heterozygous

**Missense variant in PLA2G6** G/A - ref: G

Location 22:38512190

Disorder Parkinson disease 14, autosomal recessive - AR

Segregation GA — GG

Transcripts

Transcript	Effect	p.notatio	c.notatio	Exon rank
ENST000002509	missense	p.Arg591Tp	c.1771C-T	13/17
ENST0000035539	missense	p.Arg577Tp	c.1609C-T	12/16
ENST0000042064	missense	p.Arg577Tp	c.1609C-T	12/16

Frequency 0.0032% 0 1 HETEROZYGOTES  
0.228% INTERNAL FREQUENCY

Quality 77 DEPTH 37,40 ALLELE DEPTH 99 GENOTYPE QUALITY

Notes

Two variants, a previously described missense variant and a previously described stop gained variant, were detected in compound heterozygous state in the PLA2G6 gene (ENST000002509; c.1771C-T; p.Arg591Tp; rs1043378899 and ENST0000035539; c.1933C-T; p.Arg645\*). The performed family analysis, including the healthy mother and healthy father of this patient, indicates co-segregation of these variants with the clinical phenotype following an autosomal recessive inheritance pattern.

Mutations in PLA2G6 have been shown to cause Parkinson disease 14, autosomal recessive (MIM: 612953), an autosomal recessive condition. The reported clinical phenotype of this patient overlaps with the manifestations of this condition regarding neurodegeneration.

Finally, it should be noted that the typical age of onset of Parkinson disease 14, autosomal recessive, which ranges from 20 to 40,

## Free Moon trial

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Give Moon a try with your own samples.

Visit [invitae.com/moon](https://invitae.com/moon) for a Moon trial account  
that will allow you to analyse your own WES or WGS data.



Scan the QR code  
or visit [invitae.com/moon](https://invitae.com/moon)  
to try Moon for free

