UNIVERSITY OF CAMBRIDGE

GRID

Genomics of Rare Immune Disorders

A CLINICAL GENE PANEL TEST TO DIAGNOSE PATIENTS WITH PRIMARY IMMUNE DISORDERS

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BACKGROUND AND AIM

Primary Immune disorders (PID) affect 15,000 new patients every year in Europe. Genetic tests are usually performed on a single or very limited number of genes leaving the majority of patients without a genetic diagnosis.
We aimed to develop a new comprehensive gene panel and a robust bioinformatics pipeline to diagnose patients with PID.

RESULTS

GENE PANEL CONTENT

279 GENES, including 2015 IUIS* genes

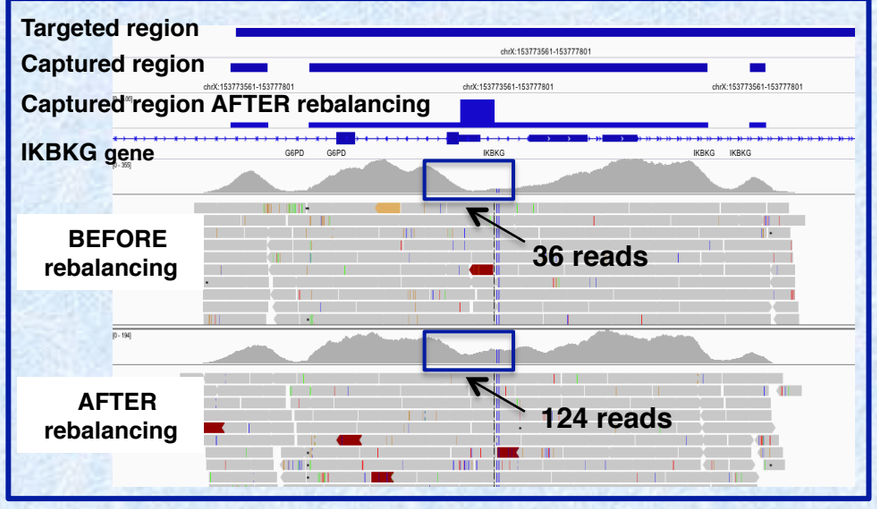
Panel design - targeted regions:

- **All exons ± 100bp of each gene**
- **2000 bp at the 5' of all very first exons**
- **100bp at the 3' of all last exons**
- **All HGMD variants (± 25bp)**

Regular updates with new genes

*IUIS = The International Union of Immunological Societies
J. Clin. Immunol. (2015) 35:727-738

OPTIMIZATION

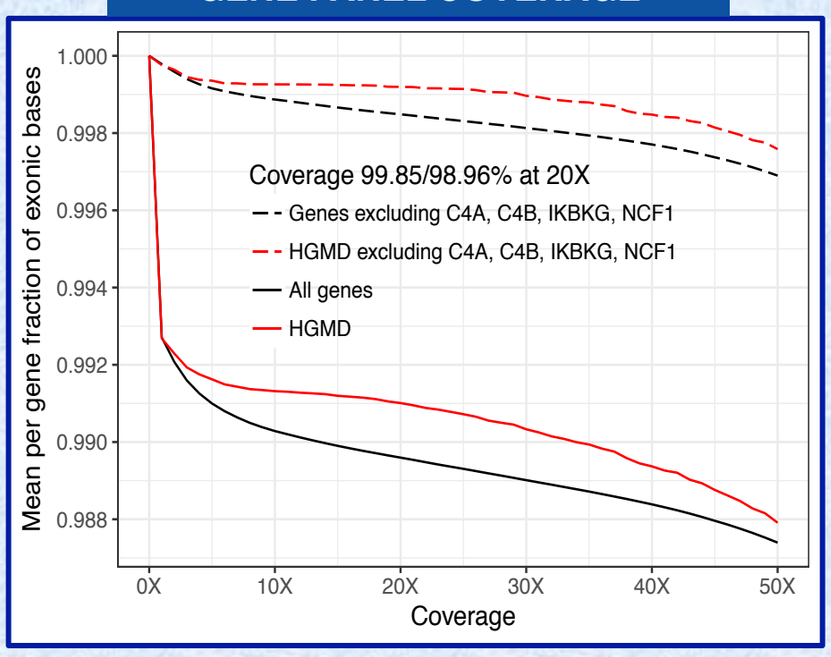


VALIDATION

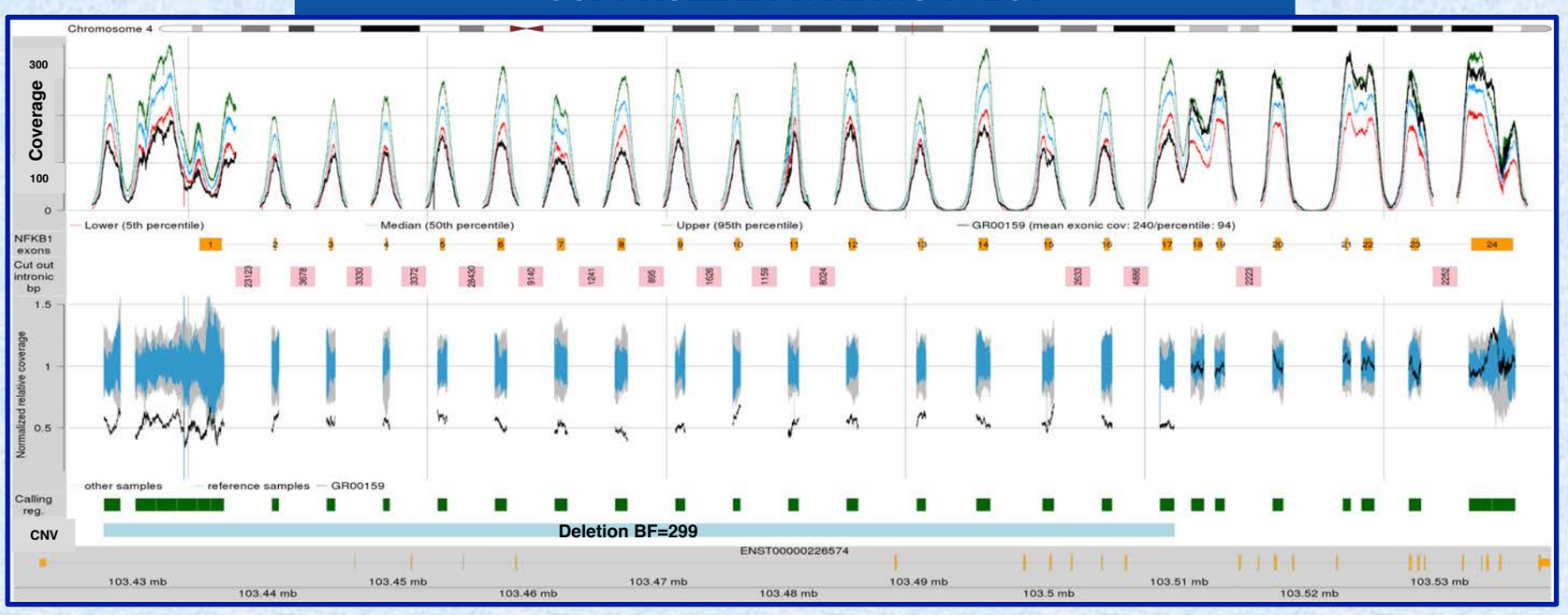
Validation performed comparing GRID results with clinical-grade WGS data from 176 samples

- **3,220 SNVs - sensitivity = 100%**
- **267 INDELs (145 INS and 122 DELs) sensitivity = 100 %**
- **7 CNVs (large deletions) sensitivity = 100 %**

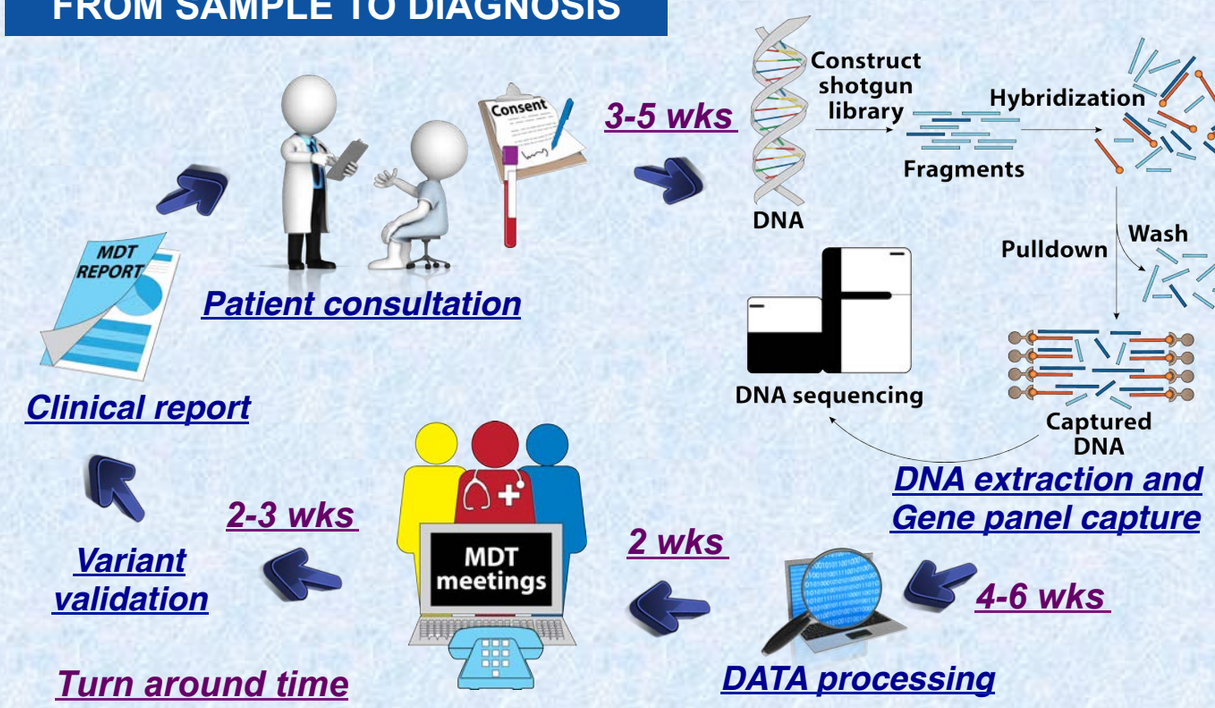
GENE PANEL COVERAGE



COPY NUMBER VARIATION PLOT



FROM SAMPLE TO DIAGNOSIS



GRID METRICS

Minimum depth for reporting	**20x**
Coverage per gene at 20X	Provided in the patient's report
Variant type reported	SNV, INDELs and CNVs
Variant classification reported	Clearly pathogenic (CP) Likely pathogenic (LP) Variant of Uncertain Significance (VUS)
Genes with problematic regions	C4A; C4B; IKBKG; NCF1
Aligner and variant caller	BWA, GATK HaplotypeCaller
Turn around time	16 weeks
Sequencing	HiSeq4000, 150bp PE, 96 patients/lane

CONCLUSIONS

1. **We designed, optimized and validated a new clinical gene panel for patients with PID.**
2. **We developed a robust bioinformatics pipeline for clinical reporting including the detection of copy number variations.**
3. **Variant(s) are evaluated by an MDT and labelled with pathogenicity and contribution to phenotype.**

To submit samples visit www.gridgenomics.org.uk

Take a GRID leaflet with you to your Clinic

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