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Many Clinical Laboratories Performing Next-Generation Sequencing Have No Future Plans to Migrate to the Most Recent Human Reference Genome Build (GRCh38)

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Many Clinical Laboratories Performing Next-Generation Sequencing Have No Future Plans to Migrate to GRCh38

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Introduction

Analysis of clinical next-generation sequencing (NGS) data requires the Human Reference Genome (HRG) for alignment. Build GRCh38 was released in December 2013 and resolved ~1,000 issues from GRCh37, including erroneous calls within clinically-relevant genes such as *F5, ADAMTSL2, RECQL4, NCF1*, and *RPS17*, among others. As most clinical laboratories are using build GRCh37, we were interested to learn their plans for migration to GRCh38, including their proposed timelines and related concerns; therefore, we conducted a survey to define the current landscape of genome alignment in clinical NGS.

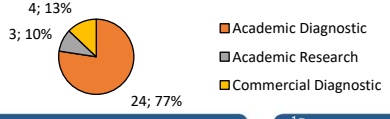
Methods

71 clinical laboratories performing constitutional NGS testing were invited to participate in an unvalidated online survey to understand general laboratory characteristics as well as motivation for migrating or not migrating to GRCh38.

Results

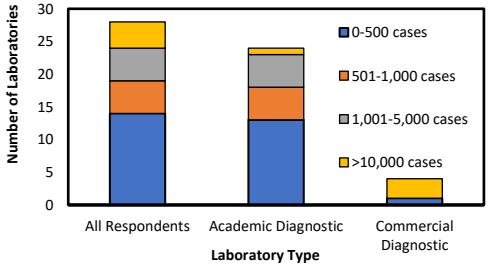
33 of 71 laboratories responded (46%), 31 of which confirmed NGS was conducted in their laboratory.

Predominant Laboratory Focus

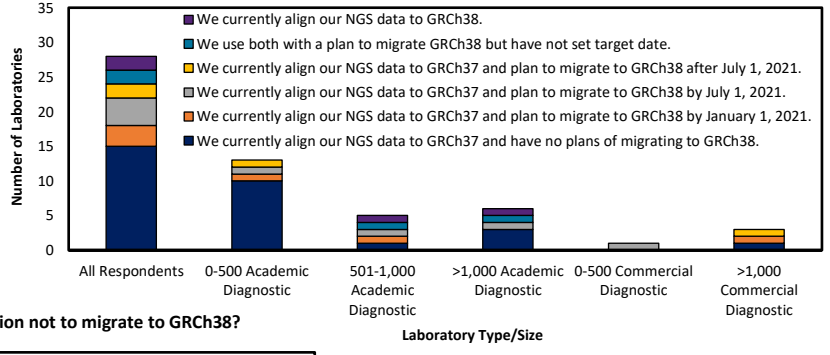


Results

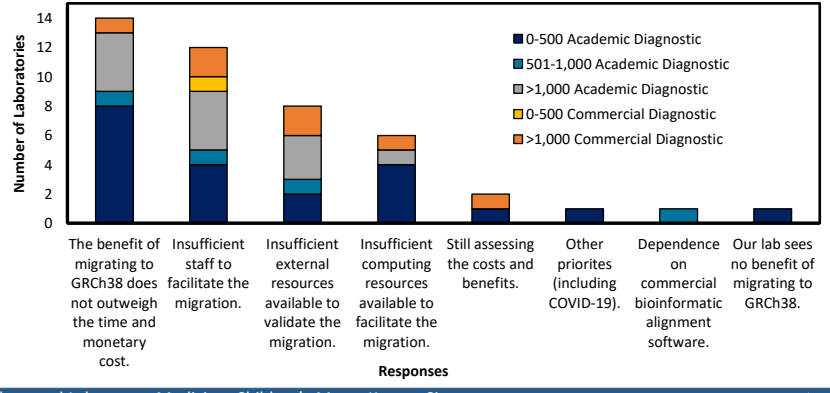
2019 Clinical Constitutional NGS Testing Volume



Which of the following best applies to the clinical NGS testing in your laboratory?



What factors influence your laboratory's decision not to migrate to GRCh38?



Conclusions

Clinical laboratories are divided about migrating to build GRCh38 due to limited resources. This is expected to change within the next 1 to 2 years as a variety of large-scale databases (i.e. gnomAD, Genomics England, ClinVar, HGMD, etc.) have already transitioned. We conclude that increased awareness of clinically-relevant variation that may be missed by NGS pipelines using build GRCh37 is needed, and orthogonal bioinformatics approaches to reduce the likelihood of missing such variants should be considered.

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