

NGS in diagnostics - where things can go wrong

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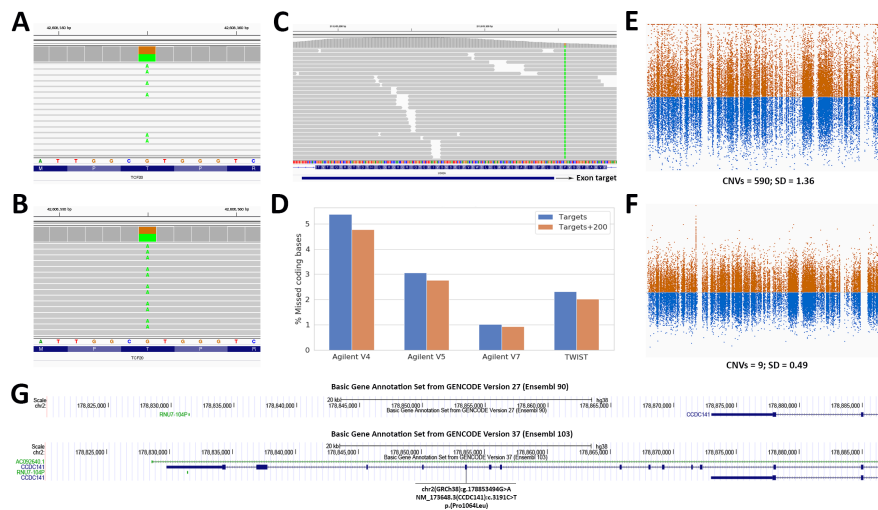
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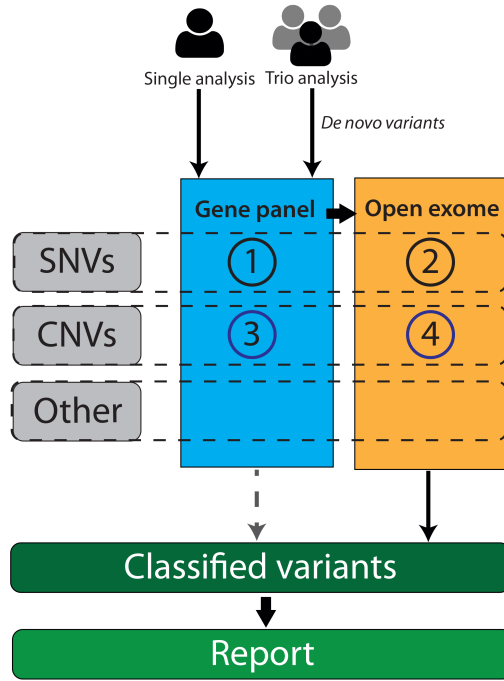
Abstract

Massive parallel sequencing technology has become the predominant technique for genetic diagnostics and research. Many genetic laboratories have wrestled with the challenges of setting up genetic testing workflows based on a completely new technology. The learning curve we went through as a laboratory was accompanied by growing pains while we gained new knowledge and expertise. Here we discuss some important mistakes that have been made in our laboratory through ten years of clinical exome sequencing but that have given us important new insights on how to adapt our working methods. By providing these examples and the lessons that we learned from them, we hope that other laboratories do not need to make the same mistakes.

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Clinical exome sequencing - where things can go wrong.docx available at <https://authorea.com/users/428677/articles/532484-ngs-in-diagnostics-where-things-can-go-wrong>





- 1 SNV Panel filtering**
Variants that are:
 - Rare de novo
 - Known pathogenic
 - Rare coding/splice site
- 2 SNV Exome filtering**
Variants that are:
 - Rare de novo
 - Rare coding/splice site in known genes
 - Known pathogenic
 - Rare truncating
 - Unique coding/splice site
- 3 CNV Panel filtering**
Variants that are:
 - In other affected family members
 - Known pathogenic
 - Rare and large CNVs
 - In known associated disease genes
 - In recessive disease genes
- 4 CNV Exome filtering**
 - As in (3) but genome-wide

