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The Globally search for a Regular Expression and Print matching lines (GREP) strategy: an innovative reanalysis strategy combining bibliographic monitoring with fast GREP directly applied to a massive genomic database to rapidly improve diagnosis

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Abstract

Purpose: Exome sequencing has a diagnostic yield ranging from 25% to 70% in rare diseases and regularly implicates genes in novel disorders. Prospective data reanalysis has demonstrated strong efficacy in improving diagnosis, but poses organizational difficulties for clinical laboratories. We applied a reanalysis strategy based on intensive prospective bibliographic monitoring, and directly applied the Globally search for a Regular Expression and Print matching lines (GREP) command-line to a massive ES database. **Methods:** For 18 months, we submitted daily the same 5 keywords of interest ((*intellectual disability*, (

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neuro)developmental delay, (neuro)developmental disorder)) to PubMed, to identify recently published, novel disease-gene associations, or new phenotypes in genes already implicated in human pathology. We used the Linux GREP command-line and an in-house script, to collect all variants in these genes from our 5459 exome database. **Results**: We *grepped* 128 genes and collected 56 candidate variants in 53 individuals. We confirmed causal diagnosis for 19/128 genes (15%) in 21 individuals, and identified variants of unknown significance for 19/128 genes (15%) in 23 individuals. Altogether, we confirmed pathogenicity in 21/2875 undiagnosed affected probands (0.7%). **Conclusion**: The GREP command-line is efficient, and less tedious than complete periodical reanalysis. It is an interesting reanalysis strategy to improve diagnosis.

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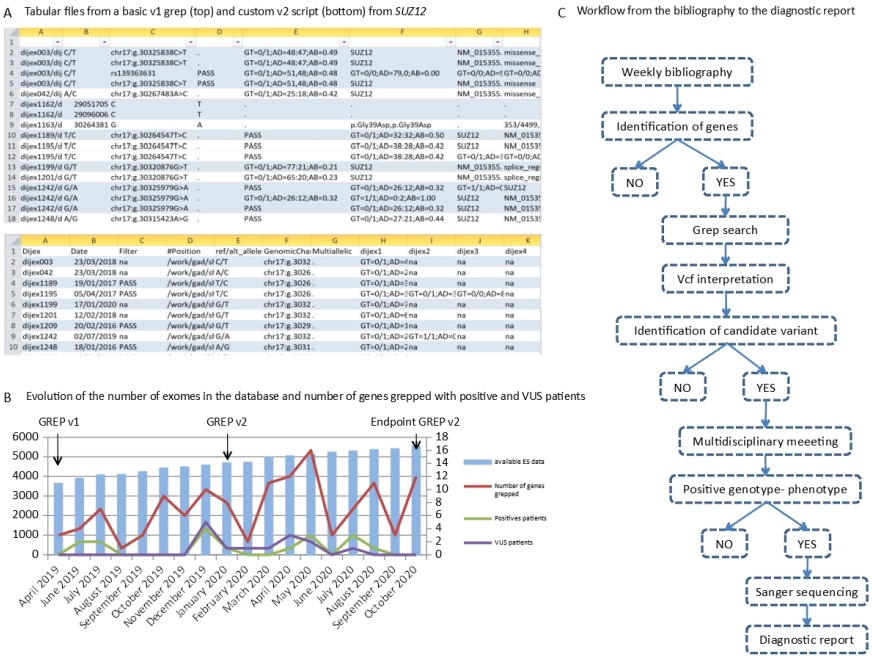
`GREP_final.docx` available at https://authorea.com/users/464395/articles/559305-the-globally-search-for-a-regular-expression-and-print-matching-lines-grep-strategy-an-innovative-reanalysis-strategy-combining-bibliographic-monitoring-with-fast-grep-directly-applied-to-a-massive-genomic-database-to-rapidly-improve-diagnosis



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Workflow and version of the GREP reanalysis strategy with number and class of identified variants, genes and individuals in the expanding exome database