The apa-sequencing Documentation

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Preface

This documentation is intended to describe the apa-sequencing[1] project.

Objective

Primary aldosteronism (PA) is the most common cause of secondary hypertension and is more common than primary hypertension in causing secondary diseases such as stroke, myocardial infarction, heart and renal failure. It is caused by inappropriately increased, partially autonomous synthesis and secretion of the steroid hormone aldosterone with consequent increased renal and intestinal sodium and water reabsorption and increased potassium secretion. The most common causes are a unilateral benign adrenal tumour (aldosterone-producing adenoma, APA) or bilateral aldosteronism. In recent years, the molecular mechanisms leading to autonomous aldosterone production have become the focus of increasing scientific attention. It has been shown that approximately 95% of all APAs have somatic mutations in known disease genes, mainly affecting ion channels and transporters: About 40% have *KCNJ5* (e.g. [Choi et al., 2011]) mutations; *CACNA1D* is the second most commonly affected gene (about 20%; e.g. [Scholl et al., 2013]). Other less common somatic mutations include mutations in the ATPases *ATP1A1* and *ATP2B3* and the gene encoding b-catenin, *CTNNB1*.

Methods

Sample selection and preparation

Archived formalin-fixed paraffin-embedded (FFPE) material was selected from individuals with primary aldosteronism.

[1] https://github.com/scholl-lab/apa-sequencing

Targeted Sanger sequencing for known mutations

Analysis of high-throughput sequencing data

We implemented a comprehensive workflow for aligning, calling variants, and annotating sequencing data. The raw sequencing data files were obtained from the sequencing provider in FASTQ format. The BWA (Burrows-Wheeler Aligner) tool was used to align the sequences to the hg38 the reference genome. The GATK (Genome Analysis Toolkit) was used for variant calling. We used SnpEff and SnpSift to perform annotations. The GitHub repository contains detailed instructions as well as the complete codebase.

Results

Conclusion

Outlook

References

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