Bioinformatics for translational benefit

“visualisation and web based tools bring sequence data to the clinic”

NHMRC Emerging Researcher Grant - Pitch

Dr Miles Benton

2017/07/28

Motivation

identification of known or novel pathogenic variants

- found among a host of common and rare polymorphisms
- identification of clinically relevant variants is time consuming
    - large potential for analysis induced false negatives
- larger datasets (WES/WGS) contain **thousands** to **millions** of variants
- aggravated by complex conditions/disorders
    - multitudes of genes / mutations responsible for symptoms or important for treatment

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I'm an emerging researcher (3 years out from PhD)

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paywalls

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NO software readily accessible and user-friendly for end users 'on the ground'

Significance

current methods fall into either:

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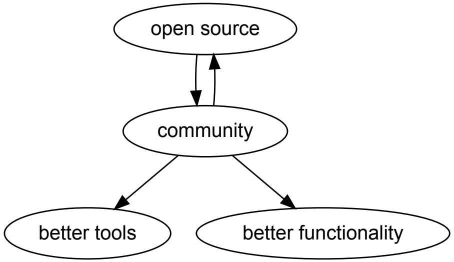
Accessible, flexible, powerful, and ... free



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address shortfall in current methods

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cloud integration and deployment options

Team members on this submission

Dr Miles Benton - Principal Investigator (emerging investigator)[1]

Prof Lyn Griffiths[1]	AI (*Human Genetics*)
A/Prof Rod Lea[1]	AI (*Genome Informatics*)
Dr Robert Smith[1]	AI (*Diagnostics*)
Prof Greg Gibson[2]	AI/Mentor (*Integrative Genomics*)

[1] CDA, MM, IHBI, QUT
[2] Georgia Tech, USA

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[*] *if you are not familiar with the commandline*

To 95% of people these are just really large complex text files

- no easy interaction
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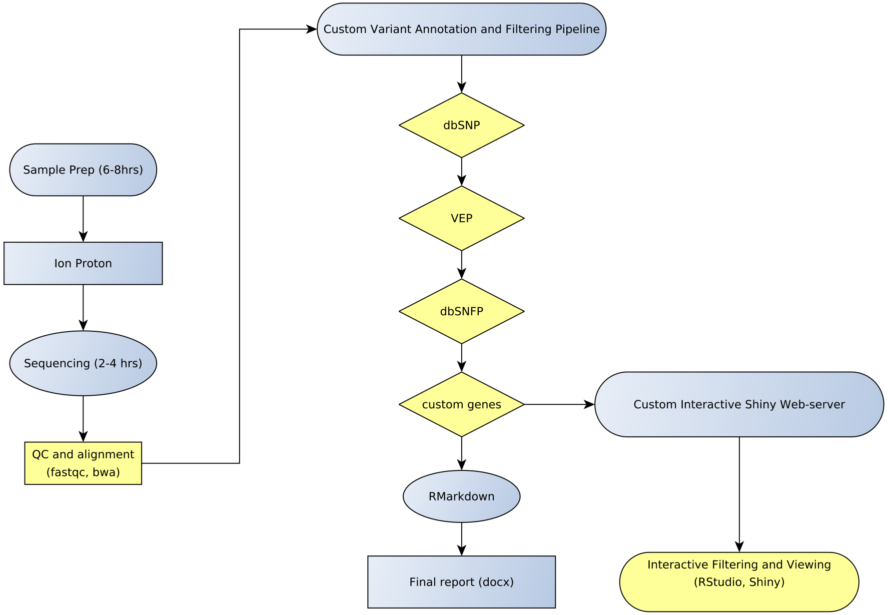
variant filtering process is complicated**

[**] *even if you **are** familiar with the commandline*

A large number of people still do this manually...
...this is what computers are for!

Progress to date

WESTARC - live demonstration


Custom Variant Annotation and Filtering Pipeline
dbSNP
VEP
dbSNFP
custom genes
Custom Interactive Shiny Web-server
RMarkdown
Final report (docx)
Interactive Filtering and Viewing (RStudio, Shiny)
Sample Prep (6-8hrs)
Ion Proton
Sequencing (2-4 hrs)
QC and alignment (fastqc, bwa)

Research Design

Develop a series of modules, each achieving a specific task:

- initial QC and sequence alignment

  + including functionality for structural variation (routinely overlooked)

- VCF annotation and manipulation

  + currently only accessible to 'advanced' users

- simple interactive 'base' fontend (i.e. WESTARC)

  + include database interfacing

- Additional analysis interface

  + phenotype, case/control, sample comparison ...

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Distribute:

- GitHub, docker, & online cloud server (Amazon S3)

Expected outcomes

> *simple, scalable and robust method for the annotating and categorising genetic variants enabling more rapid and effective analysis of potentially pathogenic variants*

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A fully operational suite of software 'modules':

- integrate into an easy-to-use workflow
- can handle all forms of sequence data
- open-source / free to use and develop

Deployment of an user friendly app version / suite of apps:

- integration with existing databases
- cloud deployment
- docker integration

Direct to consumer:

- putting the 'power' back in the hands of those that matter