Healthcare Innovations
How practice has changed

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Identifying integrations of clinical gene therapy vectors with isling

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The problem:

Viral vectors are a critical part of gene therapy applications, and verifying the the safety of every viral vector is an important precursor to the clinical application of gene therapies. To identify potential genotoxicity from integrations of gene therapy vectors we developed isling, a software tool that identifies integration junctions in next-generation sequencing data.
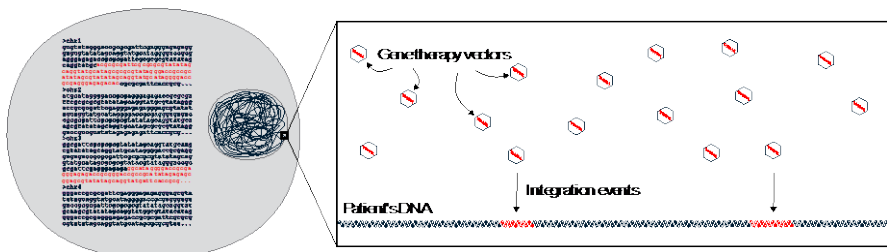
Isling identifies integrations by finding chimeric reads in sequencing data.
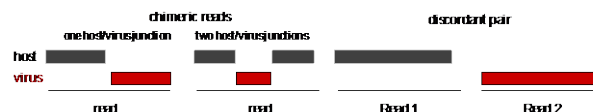
How good is isling at finding integrations?

Isling was benchmarked on simulated data containing integrations of wild-type Adeno-associated virus 2 (AAV2) or a recombinant AAV gene therapy vector (rAAV). Isling performed better than four other viral integration tools[1,2,3,4].

The Jaccard statistic measures the amount of overlap between simulated and identified integrations, with 1 being perfect overlap


The true positive rate (TPR) indicates the fraction of missed events, and the positive predictive value (PPV) indicates the fraction of false positives. These were calculated by measuring the distance between simulated and identified events, and vice versa.
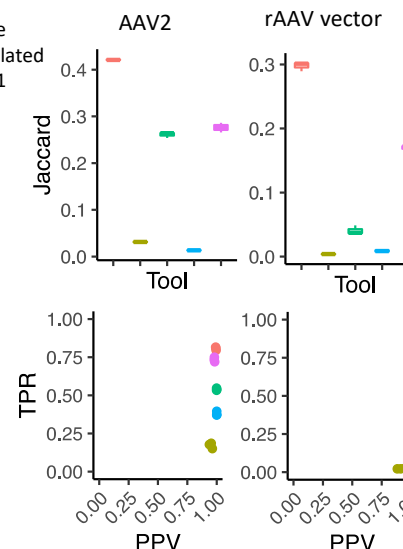
tool: ● isling ● Polyidus ● Seeksv ● ViFi ● VSeq–Toolkit

Isling was also compared against the other tools on a whole-genome sequencing dataset from liver cancer patients, and contained 22 validated hepatitis B virus integrations[5]. Isling found the most integrations.
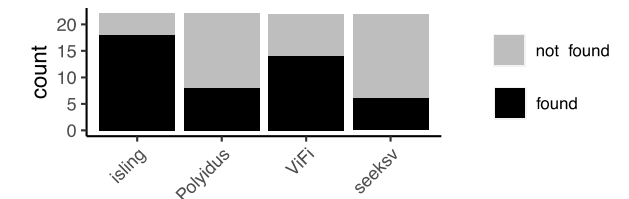
What can isling be used for?

Isling is an accurate, fast tool for identifying integrations of both gene therapy vectors and wild-type viruses. Use-cases include:

- Characterising genotoxicity of gene therapy vectors in pre-clinical work and clinical trials
- Comparing integration behaviour of wild-type viruses and their vectorized equivalents

References:
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4. Afzal et al . Mol. Ther. Methods Clin. Dev. 17, 752–757 (2020).
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