Whole genome analysis of chordoma

4th International Research Workshop

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- MGH

Chordoma Foundation
Forme Fruste Tumour Profiling

- TFRI/CIHR
- David Huntsman

“Clinically and pathologically homogenous tumour types, presumed to be driven by a limited number of genetic events”

- FOXL2
  Granulosa Cell Tumour of the Ovary

- ARID1A
  Endometriosis associated Ovarian Ca

- DICER1
  Sex cord stromal tumour

- CIC
  Oligodendroglioma

- Chordoma, Epithelial sarcoma, GI carcinoids
### Update on BCCA sequencing of chordoma specimens

<table>
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<tr>
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<th>Whole Transcriptome Sequencing</th>
<th>Exome Sequencing</th>
<th>Whole Genome Sequencing</th>
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Farzad Jamshidi
“Holy Trinities”

- WGSS - Tumour
- WGSS - Normal
- WTSS - Tumour
Metrics of WGSS

Tumour coverage = 60X
Normal coverage = 30X

• Single Nucleotide Variants
• Copy Number Variants
• Fusion/Translocations
# Somatic SNVs in matched T/N pairs

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<th>Sample ID</th>
<th># non-synonymous variants in coding region (&gt;0.8)</th>
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*Classifier Probability score >0.8*
APOLLOH is a hidden Markov model (HMM) for predicting somatic loss of heterozygosity and allelic imbalance in whole tumour genome sequencing data.

Model Features
- **SC** = Spatial Correlation
- **CN** = Copy Number Aware
- **SP** = Stromal Parameter

Modified Figure 2. Ha et al., Genome Res 2012.
deFuse: An Algorithm for Gene Fusion Discovery in Tumor RNA-Seq Data

Andrew McPherson¹,², Fereydoun Hormozdiari², Abdalnasser Zayed¹, Ryan Giuliani¹, Gavin Ha¹, Mark G. F. Sun¹, Malachi Griffith³, Alireza Heravi Moussavi¹, Janine Senz¹, Nataliya Melnyk¹, Marina Pacheco⁴, Marco A. Marra³, Martin Hirst³, Torsten O. Nielsen⁴, S. Cenk Sahinalp², David Huntsman¹,⁴, Sohrab P. Shah¹,⁴,⁵⁺

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Feature-based classifiers for somatic mutation detection in tumour–normal paired sequencing data

Jiarui Ding¹,², Ali Bashashati¹, Andrew Roth¹, Arusha Oloumi¹, Kane Tse³, Thomas Zeng³, Gholamreza Haffari¹, Martin Hirst³, Marco A. Marra³, Anne Condon², Samuel Aparicio¹,⁴ and Sohrab P. Shah¹,²,⁴,⁺

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MeDIP/MRE- Sequencing

40440 – WTSS/Exome/MeDIP/MRE
Profiling of chordoma methylome and correlation with gene expression

Martin Hirst
Summary

- Tumours with homogenous histology/clinical behaviour may be driven by limited number of genetic events
- Completion of 5 matched pairs of chordoma exomes
- Completion of 2 sets of chordoma “holy trinities”
- Ongoing methylome analysis
  - Relatively small number of somatic mutations
  - No recurrent mutations identified in 5 matched exomes
  - WGSS revealed numerous fusion events