Detection of reciprocal translocations using short read sequencing

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Background
Breeding candidates
Karyotype screening
0.4% abnormal karyotype
- Trisomy
- Mosaicism
- Reciprocal translocations (RT)

Material
Reference genome animal
23x coverage
paired end
short reads
Control animals (n=10)
20-30x coverage
paired end
short reads
RT cases (n=6)
30x coverage
paired end
short reads

Objective
Identify reciprocal translocations detectable with karyotyping using short read paired end sequencing
To replace karyotype screening when sequencing breeding candidates becomes a (cost efficient) routine

Methods
Sequence alignment: Sus Scrofa build 11.1
Detection: discordant pairs (DP) & split reads (SR)
Software: Delly (detection), Jbrowse (visualization)
Basic filtering: contigs, low quality, imprecise
Final filtering: mapping quality, read support, reciprocal breakpoint present
Using reference & control animals: genome build problems, common issues (e.g. repeats)
Visual inspection: normal reads present; forward DP & reverse SR left; reverse DP & forward SR right

Conclusions
- Reciprocal translocations detectable using short read sequence
- Software outputs many false positive translocations – but they can be identified as false

Results
Pig 1, 2, 3, 5: reciprocal translocation detected
Pig 4: visual inspection debatable
Pig 3 & 4 full sibs, and relative of Pig 1 - same RT
Pig 6: nothing passed visual inspection – false neg.

<table>
<thead>
<tr>
<th></th>
<th>PIG1</th>
<th>PIG2</th>
<th>PIG3</th>
<th>PIG4</th>
<th>PIG5</th>
<th>PIG6</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT chr</td>
<td>2,4</td>
<td>6,8</td>
<td>2,4</td>
<td>2,4</td>
<td>7,14</td>
<td>1,16</td>
</tr>
<tr>
<td>Delly out</td>
<td>73,923</td>
<td>96,378</td>
<td>85,597</td>
<td>94,223</td>
<td>94,683</td>
<td>78,946</td>
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<tr>
<td>Basic fil</td>
<td>1,127</td>
<td>1,426</td>
<td>1,185</td>
<td>1,175</td>
<td>1,503</td>
<td>1,116</td>
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<tr>
<td>Final fil</td>
<td>30(15)</td>
<td>56(28)</td>
<td>34(17)</td>
<td>38(19)</td>
<td>68(34)</td>
<td>44(22)</td>
</tr>
<tr>
<td>Visual insp</td>
<td>1(2,4)</td>
<td>1(6,8)</td>
<td>1(2,4)</td>
<td>1(2,4)</td>
<td>1(7,14)</td>
<td>FN</td>
</tr>
</tbody>
</table>

To do:
- Automate visual inspection
- Test specificity using (additional) controls
- Confirm breakpoints with PCR