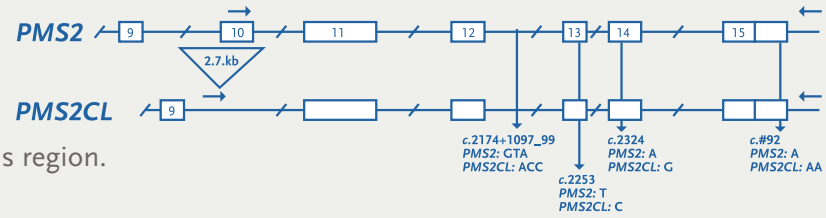
Not all genetic tests are created equal

PMS2 and Lynch syndrome

Why is *PMS2* analysis technically challenging?

PMS2 (exons 12–15) and *PMS2CL* (exons 3–6) sequences are almost exactly the same.

Only when using the gold standard method (Vaughn *et al*) including LR-PCR followed by Sanger sequencing and MLPA (when necessary), can a lab appropriately disambiguate variants in this region.



Using NGS data, Invitae was able to disambiguate 25% more variants when MLPA was not informative.

25% MORE VARIANTS

How common are variants in this region?

26% of Invitae's pathogenic and likely pathogenic PMS2 variants were in exons 12–15

PMS2 is low penetrance and therefore not all cases have a striking family history. For patients outside criteria, most PMS2 variants were detected through **larger cancer panels**.

40% of these patients did not meet the criteria for Lynch syndrome testing

What's the clinical impact?

- Potential to miss a lynch syndrome diagnosis
- Potential to misdiagnose lynch syndrome

INVITAE

How does your lab compare?