INVERSION PIPELINE

33,924 rare disease families

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Short read genome sequencing

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Inversions called by Manta

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Focus on 351 haploinsufficiency genes

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Prioritization with SVRare and manual review

47 strong SVs candidate reported

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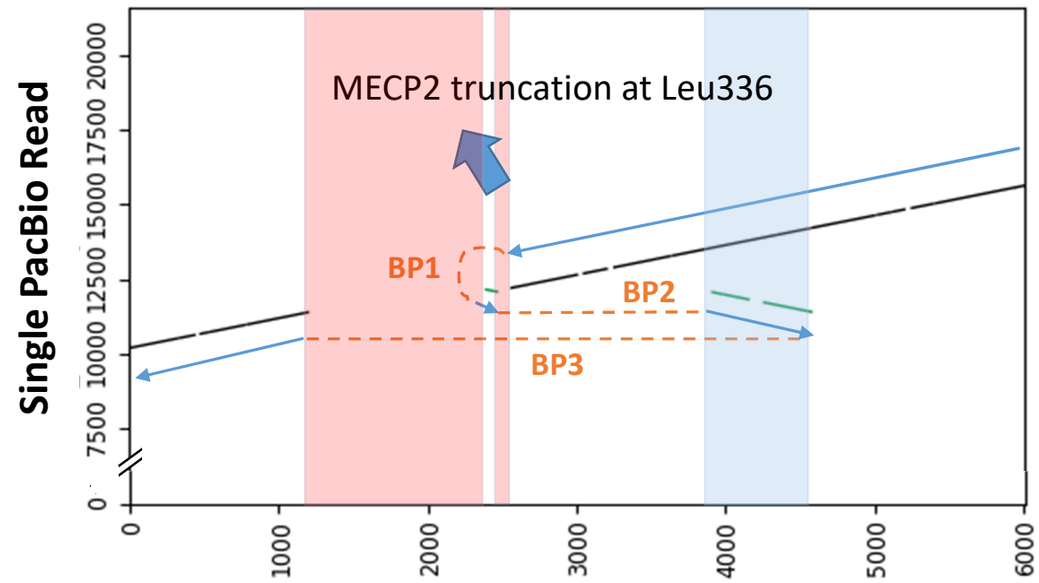
2 SVs are VUS

45 SVs considered likely diagnostic

VALIDATION

DNA validation of SVs

- Variety of orthogonal approaches (incl. retrospective exome analysis)
- Long-read sequencing for 2 ambiguous SVs altered clinical interpretation



RNAseq supported diagnosis in 6 cases

- Effects included expression outlier, allelic imbalance, truncation, fusion-gene creation and exon skipping
- Genes affected were *DYRK1A, APC, KMT2B, MLH1, PHEX* and *PTEN*