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People often ask why structural variants (SV) are so important and why $BNGO is laser focused on revolutionizing the way they are detected in the clinic. Doesn't the success of $PACB and $ILMN show that sequencing and the small variants it detects are what matters?

Let's look at what happens in the industrialized world when a doctor orders a genome to be analyzed. If a child has a suspected genetic disease, medical guidelines recommend successive testing rounds until a pathogenic variant is found or all techniques have been exhausted. $BNGO

Before we go into detail, let's start by pointing out that this NEVER involves long-read whole genome sequencing by $PACB or Nanopore. Never, nowhere. Those are niche sequencing technologies for reference genome projects but not practical for the clinic. $BNGO

Long-read sequencing COULD matter in the clinic in the future if they get cost down & throughput significantly higher. As comparison, a whole genome w/ $PACB HiFi takes several days per patient per sequencer. Unusable in the clinic. Each Saphyr can run 96 patients per week! $BNGO

The tests start with chromosomal microarray (CMA), karyotyping, and then repeat expansion testing, single gene or gene panel testing, and whole exome sequencing. This long and expensive process still leaves 50% of children undiagnosed. $BNGO

CMA, the 1st test for genetic disease, only finds duplications & deletions tens of thousands to millions of basepairs long. Studies show that #Saphyr detects 100% of the variants seen by CMA, but also much smaller variants that take out single genes. $BNGO https://t.co/GVk2u9fhlh

CMA can not identify genes or parts of chromosomes that moved around, or if their orientation has been inverted. To detect those variants, the doctor orders karyotyping. It is a slow, manual, and difficult process where chromosomes are studied under a microscope. $BNGO

Karyotyping only detects variants that are millions of basepairs in size! Studies have shown that #Saphyr can detect 100% of the variants detected by CMA, but also many much smaller variants that can cause disease. $BNGO https://t.co/GVk2u9fhlh

The human genome is full of repeats, and these repeats can expand or contract to cause a variety of mostly neurological or muscular disorders. CMA or karyotyping can not detect those repeat changes, so individual tests need to be ordered for each gene. $BNGO

#Saphyr can detect about a dozen repeat expansion disorders at once, including for Fragile-X Syndrome, and several clinical labs in the U.S. already offer Saphyr-based tests for a repeat contraction disease FSHD1. $BNGO

#Saphyr finds the variants found by CMA and karyotyping and many repeat tests combined in a single, fast, automated assay. On top of that, it diagnoses another 18-25% of patients who do not get a diagnosis using these traditional methods. $BNGO https://t.co/1Iw1F1tbgx

#Cancer is even more complicated. As tumors grow, they accumulate mutations. Different cells in the #tumor have different variants. If you sequence this as you would for genetic disease, you average all of them out and see little to nothing. $BNGO

That's why you need to collect really high coverage. If you have a lot of data you can find variants present in a low fraction of the cells. #Saphyr can map a tumor at 1600x. With $PACB HiFi this would take weeks per tumor. That's why long read seq isn't used in the clinic. $BNGO

For many #cancers and certainly blood cancers such as #leukemias, medical guidelines also prescribe testing for SVs. Karyotyping is performed, and depending on country and disease CMA and a number of FISH tests as well. FISH tests for only a single SV at a time. $BNGO

Studies have shown that #Saphyr can detect all variants identified by CMA, karyotyping, and FISH combined in #leukemias. No sequencing platform like $ILMN or $PACB has shown to have that capability. $BNGO https://t.co/Uo6ndi6Xf7

So to summarize all of this: it's not $BNGO vs $PACB or $ILMN. They can do much that we can't do and vice versa. It's $BNGO vs many decades-old technologies used in thousands of clinics all around the world that sequencing has failed to replace, and #Saphyr can.