Avidity sequencing: Novel technology that expands possibilities of NGS applications

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Background:

Avidity sequencing employs advanced chemistry that separates processes of the nucleotide detection and controlled incorporation with more accurate base calling and reduction of the concentration of the key reagents to the nanomolar scale compared to sequencing by synthesis. In order to separate these two processes in avidity sequencing framework an incorporation 3' blocked but unlabeled nucleotide takes place first and then is followed by a binding of a complementary labelled nucleotide to the subsequent base in the template for base identification. Nucleotide identification is enhanced by multivalent ligands on the dye-labelled cores that form polymerase-polymer-nucleotide complexes. Avidity sequencing uses an accumulated strength of multiple affinities of individual noncovalent binding interactions, which can be achieved when multivalent ligands tethered in close proximity simultaneously bind to their target. Avidity sequencing routinely surpasses base calling error rate of one error per 10000 base pairs (Q40) and demonstrates high accuracy of a sequencing through homopolymers. Avidity sequencing was performed on the AVITI commercial system manufactured by Element Biosciences. This benchtop system has dual-flow cells with maximum output of 600 gigabases in two independent runs. It utilizes rolling circle amplification which minimizes the propagation of PCR errors and index hopping. AVITI platform can be used for the various applications including single-cell sequencing, whole genome sequencing and cell free DNA sequencing. Unprecedentedly accurate base calling at a nanomolar concentration of key-reagents significantly reduces prices of the sequencing. Recently announced first commercial Q50 kit capable of generating 100-fold higher accuracy than currently available products.

Conclusion:

This technology will empower research investigations into cancers, rare diseases, and other complex genetic variants.