

Independent, Third-Party Studies Evaluating the Efficiency of the Twist Human Core Exome Kit for Target Sequencing

Twist Bioscience combines proprietary probe design algorithms with highly accurate and scalable probe production to offer uniquely efficient target enrichment products. In 2018, Johns Hopkins University and CeGaT GmbH both independently compared the performance of the Twist Human Core Exome Kit with other commercially available exome enrichment protocols. Here, we summarize their findings, both of which demonstrate that the Twist Human Core Exome Kit is superior in the generation of higher-quality data at lower sequencing cost than its competitors.

Both publications are available at the links below or upon request from Twist Bioscience.

COMPARISON OF WHOLE EXOME CAPTURE PRODUCTS – COVERAGE & QUALITY VS COST (JOHNS HOPKINS UNIVERSITY, 2018)

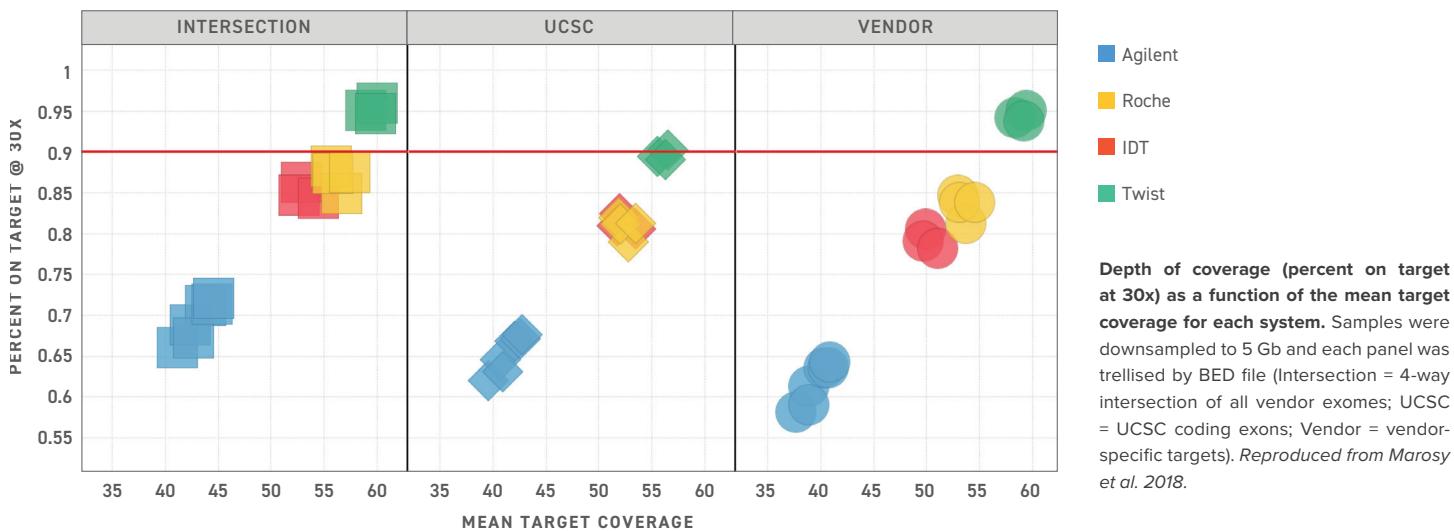
Researchers at John Hopkins University evaluated four commercially available whole exome target enrichment protocols for relative uniformity, coverage, and cost of

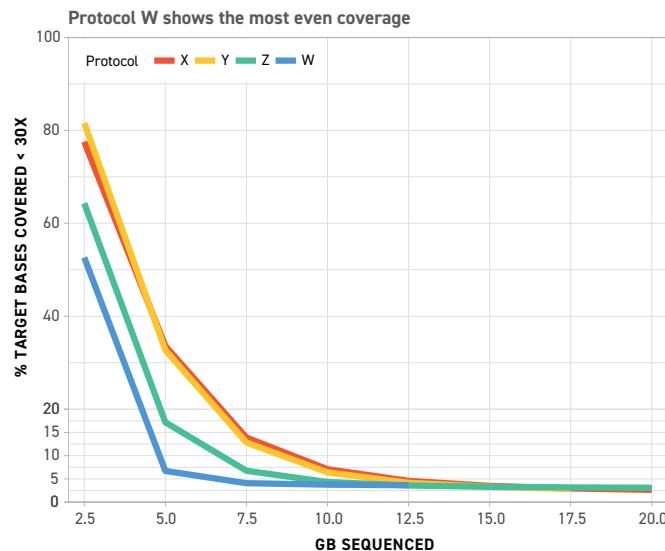
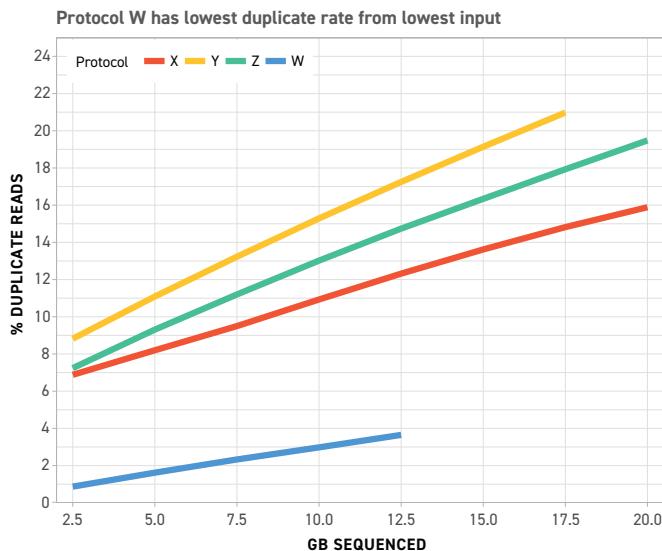
sequencing required to achieve 90% on target at various depths of coverage (Marosy et al. 2018). The products evaluated were:

- SureSelect Human All Exon v7 (Agilent Technologies)
- xGEN Exome Research Panel v1.0 (Integrated DNA Technologies)
- Prime Exome (Roche Sequencing)
- Human Core Exome (Twist Bioscience)

All products were applied to HapMap samples according to the vendor's instructions.

The data showed Twist offered superior uniformity and the lowest duplication and GC/AT dropout rates among the four systems evaluated. Though overall sequencing requirements vary by project, the confident calling of germline mutations often requires ~90% of bases to be seen 30 times (30x). In this analysis, only Twist achieved >90% coverage 30 times across all the exome sets evaluated (see figure below), demonstrating the Twist kit includes targets that build a robust exome.





ON THE QUEST FOR A MORE PRECISE EXOME (CEGAT GMBH TECH NOTE)

CeGaT GmbH (2018) also independently assessed the uniformity, specificity, and complexity offered by a similar set of exome enrichment protocols:

- Protocol X: SureSelect Human All Exon V6 (Agilent Technologies, used as the benchmark)
- Protocol Y: SureSelect Human All Exon V7 (Agilent Technologies)
- Protocol Z: xGEN Exome Research Panel v1.0 (Integrated DNA Technologies)
- Protocol W: Human Core Exome (Twist Bioscience)

PROTOCOL	X	Y	Z	W
Targeted Region [Mb]	38	36	39	33
Design efficiency [%]	64	72	76	90
Bait/Probe type	RNA	RNA	ssDNA	dsDNA
Input DNA (ng)	1000	1000	100	50
Pre-hybridized library	750	750	500	187.5

In this comparison, the same human DNA source was used with all enrichment procedures, which were carried out according to each vendor's protocol. Reads were downsampled to approximate equivalent sequencing.

CeGaT determined that the Twist Human Core Exome Kit (Product W) exhibited the highest efficiency with the lowest input requirements. It also presented more efficient read usage and higher library complexity, as reflected in the extremely low duplicate rate of <5% at 12 Gb sequencing output. In contrast, the other protocols resulted in more than three-fold that rate. As a result, the Twist protocol, "could achieve higher coverage than other protocols at the same sequencing output" (CeGaT 2018).

Moreover, the Twist Human Core Exome Kit had the fewest regions with coverage less than 30x, meaning the other protocols would "require much more sequencing in order to reach 30x coverage on most targets" (CeGaT 2018).

CeGaT determined the Twist protocol had, "the lowest input requirement, a high on-target rate, lowest duplicate rate, highest sequencing coverage, lowest underrepresented regions, and high uniformity of coverage" (CeGaT 2018).

SUMMARY

Two independent, third-party investigations compared the performance of the Twist Human Core Exome Kit with other exome enrichment protocols. Each study used independent metrics to assess performance, and data from both studies showed that the Twist Human Core Exome Kit was superior to its competitors in its ability to generate high-quality data at lower sequencing cost. Twist's efficient probe design "results in a high on-target rate that provides unprecedented coverage at minimal sequencing" (CeGaT 2018).

REFERENCES

Marosy B, Gearhart J, Craig B, Doheny KF (2018) Comparison of whole exome capture products — coverage & quality vs cost, ASHG 2018 PgM Nr 1795 (poster) (www.cidr.jhmi.edu/nih/ASHG2018_ExomeComparison_FINAL.PDF)

CeGaT GmbH (2018) Tech Note: On the quest for a more precise exome (www.cegat.de/web/wp-content/uploads/2018/06/Twist-Exome-Tech-Note.pdf)

TRADEMARKS

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