Introduction of the Illumina VeriSeq v2 NIPT Solution at TDL Genetics

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Introduction

Introduction of the Illumina VeriSeq v2 NIPT Solution at TDL Genetics including a comparison of data from the UK and international general risk population and a higher chance English NHS Fetal Anomaly Screening Programme population.

Objectives

- To describe the workflow in our high throughput, ISO 15189 accredited laboratory for processing samples for Non-invasive prenatal testing (NIPT).
- To review the overall performance of the Illumina VeriSeq v2 NIPT solution to include turn-around time and pass rates.
- To compare the higher probability data statistics generated from UK and international general risk population referrals, and a higher chance English NHS Fetal Anomaly Screening Programme (FASP) population.

Method

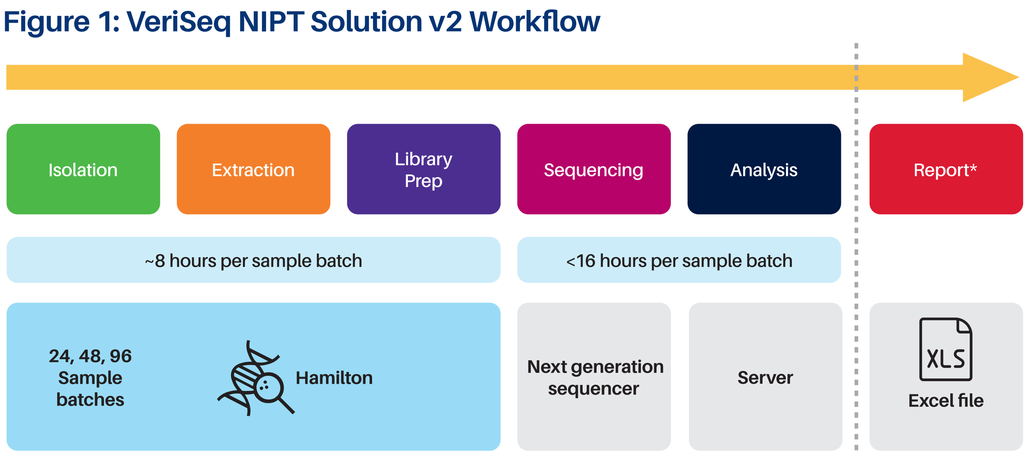
TDL Genetics have provided an NIPT service since 2012, initially by referral to the US, before introducing it in-house in 2014 following a technology transfer process. We converted to the Illumina VeriSeq v2 NIPT solution in 2023.

Implementation of the Illumina VeriSeq v2 NIPT solution involved a period of training by Illumina which covered the practical and scientific aspects of the NIPT process. Internal verification was then performed, initially using artificial plasma provided by Illumina, followed by our internal verification using stored plasma from consented patients.

Equipment was purchased to enable processing of up to 192 samples per day. This consists of two VeriSeq NIPT MicroLab STAR liquid handling robots, two high speed centrifuges (one refrigerated), two spectrophotometers, three Illumina Next Seq 550Dx Next Generation Sequencers and two servers for data analysis and storage.

The VeriSeq NIPT Solution v2 workflow provided by Illumina (Figure 1) outlines the steps of the process. The timescale for sample processing has been demonstrated to be accurate. In our laboratory, the high sample numbers received ensures that there is no delay due to batching of samples and we process 24, 48 and 96 sample batches to ensure maximum flexibility, enabling very fast turnaround times to be achieved.

Figure 1: VeriSeq NIPT Solution v2 Workflow



*Note: the output of analysis is the NIPT report which is an Excel file.

Samples are processed and results reported six days a week, Monday to Saturday. There are seven staff employed to run the NIPT service including two HCPC registered Clinical Scientists. The service is consultant led by Consultant Medical Geneticist (FRCP, FRCPCH) and Consultant Clinical Scientist (FRCPath) staff, and managed by PhD clinical scientists each having over 25 years genetics experience.

The NHS Fetal Anomaly Screening Programme (FASP) added NIPT to the existing screening pathway for Down syndrome, Edwards syndrome and Patau syndrome in 2021 as part of an evaluative roll out. NIPT is an option for women with a higher chance combined or quadruple test screening result of between 1 in 2 and 1 and 150 for trisomy 21, 18 or 13.

Women are eligible for NIPT via the FASP pathway from ~12-14 weeks (after receiving a higher chance serum screening result) up to a gestation of 21+6 weeks. Women are eligible from 10 weeks gestation via the private pathway.

Figure 2: Higher Probability Result Data (FASP and Private samples)

Final test results for samples that have passed. For samples that were repeated, only the most recent result is displayed.
(Data from 15/09/2023 - 07/06/2024)

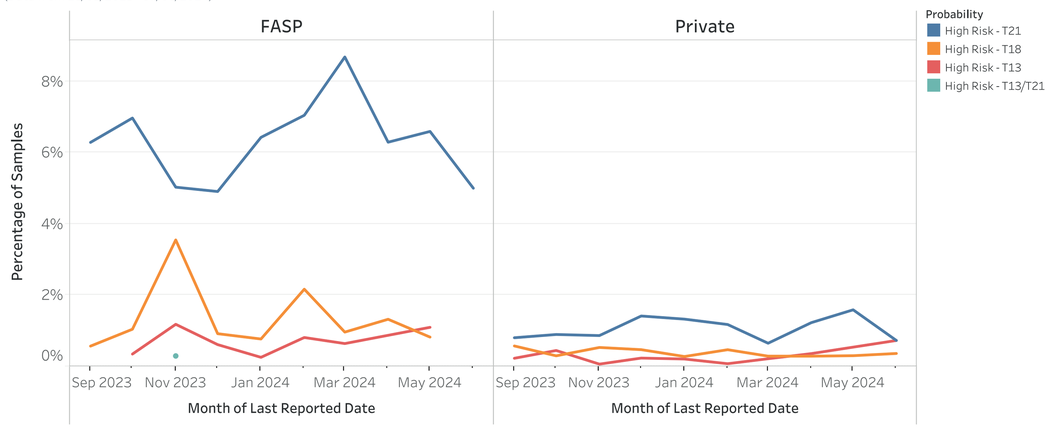


Figure 3: VeriSeq NIPT Higher Probability Result Data

The percentage of samples with high probability results are plotted in colour whilst the number of samples received for each age group are displayed as grey bars.
(Data from 15/09/2023 - 07/06/2024)

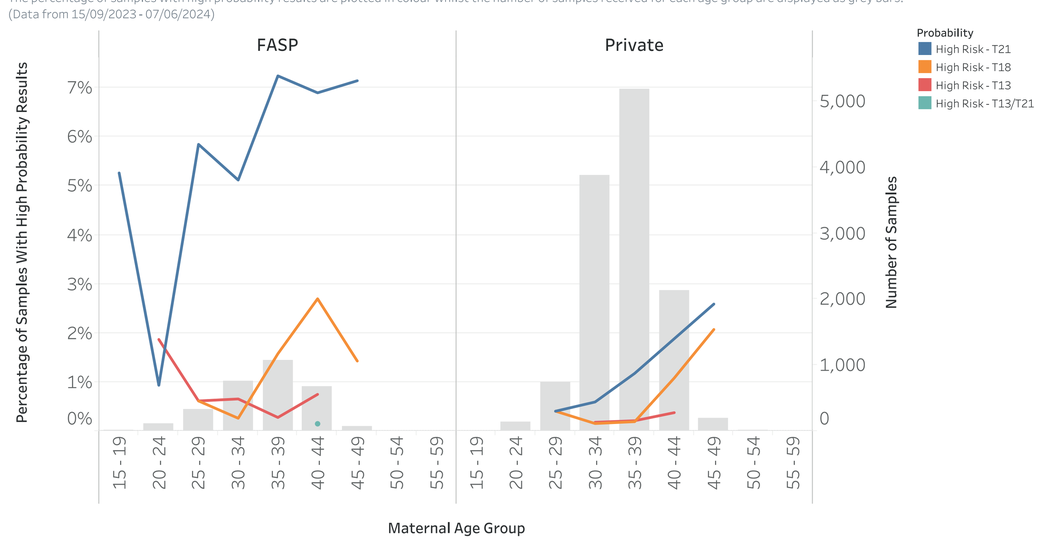
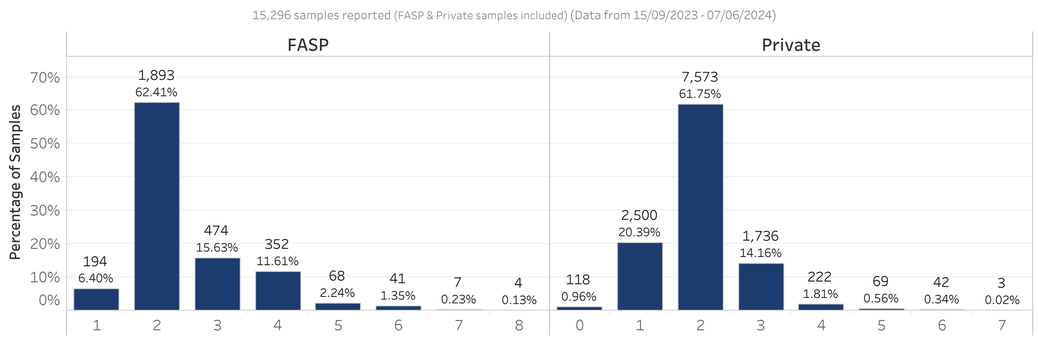


Figure 4: VeriSeq NIPT Turnaround Times

15,296 samples reported (FASP & Private samples included) (Data from 15/09/2023 - 07/06/2024)



Mean TAT		Overall NIPT Pass Rates	
FASP	Private	FASP	Private
2.54 Days	2.03 Days	98.89%	99.44%

NIPT FASP testing is performed at three laboratories in England who meet the NHS England criteria required to provide this. Laboratories must be accredited by the UK Accreditation Service (UKAS) and participate in the external quality assessment for NIPT provided by GenQA. Additional performance criteria are monitored and data are returned to NHS England on a monthly basis.

These data are being reviewed to assess the performance of NIPT in this higher chance group. The data presented in this poster represents data generated from our laboratory over 7.5 months of the three year evaluative roll out. Therefore these data are a small subset of the overall data collected by NHS England including outcome data.

Data collated from all samples processed were analysed to determine the pass rate, turnaround time (in calendar days), average gestation and result generated.

A comparison of the data from the general risk population (private referrals) and the English NHS FASP population was performed.

Samples were processed within the same laboratory using the same equipment for both the private general risk pathway and the NHS FASP pathway.

Samples received from patients via the private pathway are at the patient's request through their doctor and do not need to meet specific risk categories.

Results

- Initial data from >15000 samples analysed show 80% of samples were reported within 2 days and 95% within 3 days (Figure 4).
- The positivity data shows a higher chance result was generated in 8.1% of FASP samples (6.2% for Trisomy 21, 1.3% for Trisomy 18 and 0.56% for Trisomy 13) (Figures 2 and 3).
- For the general risk private referral population the overall higher chance rate was 1.68% (1.09% for Trisomy 21, 0.38% for Trisomy 18 and 0.21% for Trisomy 13) (Figures 2 and 3).
- The average gestation for samples received in the FASP group was 14+2 weeks and in the private group it was 12+5 weeks.
- The effect of increased maternal age can be seen in the general risk population but not the FASP group (Figure 3).

Conclusions

The Illumina VeriSeq v2 NIPT assay allows rapid testing of maternal blood samples for common aneuploidy with the majority of results generated in 2 days.

In our laboratory a low redraw rate of 0.6% was obtained. This is consistent with data reported by 1-3.

In our laboratory, the higher chance population (determined by combined or quadruple test result of 1 in 2 to 1 in 150) had higher chance NIPT result rates ~4.8 x higher than in the general risk population.

1. Pertile MD, Flowers N, Vavrek D, *et al*. Performance of a paired-end sequencing-based non-invasive prenatal screening test in the detection of genome-wide fetal chromosomal anomalies. Clin Chem. 2021;67(9):1210-1219. doi: 10.1093/clinchem/hvab067.
2. Borth H, Teubert A, Glaubitz R, *et al*. Analysis of cell-free DNA in a consecutive series of 13,607 routine cases for the detection of fetal chromosomal aneuploids in a single center in Germany. Arch Gynecol Obstet. 2021;303:1407-1414. doi: 10.1007/s00404-020-05856-0.
3. Eiben B, Borth H, Kutur N, *et al*. Clinical experience with noninvasive prenatal testing in Germany: analysis of over 500 high-risk cases for trisomy 21, 18, 13, and monosomy X. Obstet Gynecol Rep. 2021;5:1-7.

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