O16: Clinical Implementation of NIPT – Results from 4000 pregnancies

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Non-invasive prenatal testing (NIPT) for fetal aneuploidy detection is increasingly being offered in the clinical setting following studies demonstrating high sensitivities and specificities for trisomies 21, 18 and 13 detection. However, a baseline false positive and false negative rate remains.

We introduced an analysis pipeline which addresses some of the technical as well as the biologically-derived causes of error. Importantly, it differentiates high z-scores due to fetal trisomies from those due to local maternal CNVs causing false positives.

In addition to detection of the common autosomal aneuploidies in pregnancies at high risk, we also detect common aneuploidies in the low risk group. Furthermore, values indicative for trisomy were also observed for other chromosomes, as were segmental imbalances. Two of the trisomies were confirmed to be mosaic, one of which contained a uniparental disomy cell line. Since placental trisomies pose a risk for low grade fetal mosaicism as well as uniparental disomy, we propose that genome wide non-invasive aneuploidy detection is improving prenatal management.

Following routine clinical analysis of over 4000 prospective pregnancies we found test failure rates of only 0.6% upon first sampling (due to poor quality) and a success rate upon resampling of 82.6%. In 4 cases a poor quality score was observed upon second sampling, suggestive of a biological cause. One of those pregnant women with reproducible abnormal NIPT results received a follow-up MRI investigation which revealed a mediastinal mass. Subsequent cytogenetic investigations of biopsied material allowed for diagnosis of early-stage nodular sclerosis Hodgkin lymphoma (NSHL) in the pregnant woman. We show that a genome-wide analysis can lead to a better clinical management.