

haplotypes genome-wide. Reflections on how to use this information in the diagnostic laboratory are lacking.

#### Methods

Here we present the clinical outcome of 164 embryo transfers following PGD for monogenic and/or chromosomal disorders using haplarithmis. Given that (1) our main aim is selection against the genetic disorder that occurs in the family and (2) embryo selection is performed on day 3 biopsied material, we opted for a relaxed aneuploidy testing model, according to which only embryos carrying viable trisomies and trisomies of meiotic origin are excluded from transfer. Embryos were approved for transfer based on (1) the haplotype in the region of interest, (2) genome-wide copy number profile and (3) embryo morphology at the blastocyst stage.

#### Results

From January 2015 until December 2016, 164 embryos had been transferred in 152 single and 6 double embryo transfers. This led to 44 singleton and 2 twin pregnancies which gives a pregnancy rate of 30% per embryo transfer. Interestingly, 38 embryos with one or more aneuploidies had been included in the transfers, 6 of which gave rise to a clinical pregnancy and resulted in the birth of 4 healthy babies and 2 ongoing pregnancies.

#### Conclusions

Haplarithmis allows the distinction of meiotic and mitotic trisomies enabling the use of embryos that would have otherwise been discarded as inappropriate for embryo transfer. With regard to pregnancy outcome, our data show an improved pregnancy rate per embryo transfer in case of chromosomally normal embryos (33% versus 15.8%). Importantly, a remarkable 15.8% of the aneuploid embryos seem to be leading to normal pregnancies and life births, stressing the value of correct interpretation of detected aneuploidies on day 3. Both findings underline the added value of genome-wide based haplotyping used in preimplantation genetic diagnosis.

### 3.P10

#### Rare Autosomal Trisomies detected through NIPT a relevant secondary incidental finding

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After the discovery of circulating cell free fetal DNA, non-invasive prenatal testing (NIPT) for Down syndrome was permitted by massively parallel sequencing technologies with low-pass whole genome sequencing. Since 2015, we have been performing NIPT using a pangenomic strategy with a semiconductor sequencer (H+ Consortium) and WISECONDOR for data analysis.

After 1000 tests, we have identified 20 trisomies 21, 1 trisomy 18 all confirmed after invasive testing, no trisomy 13 and 6 other autosomal aneuploidies. A trisomy 15 was suspected for a

45 years-old patient. Amniotic fluid karyotype was normal but molecular testing demonstrated maternal uniparental heterodisomy for chromosome 15 (Prader-Willi syndrome) leading to termination of the pregnancy while ultrasound scans were normal. 4 patients had a NIPT profile suspicious of trisomy 16. Patients were informed considering potential consequences on fetal growth during the last trimester and complications leading to intrauterine fetal death (ACLF Guidelines). None of them had an invasive test but two pregnancies are still ongoing. The two others were complicated by intrauterine growth delay for the first one and preeclampsia for the second one with respective births at 34 and 27 weeks of gestation. Postnatal karyotype was normal in both cases with mosaic placental trisomy 16 demonstrated for the only placenta sample available. Finally, a trisomy 8 was suspected for a 42 years old patient who refused invasive testing considering normal ultrasound scans and was later lost to follow-up. With 6 cases over 1000 tests, we are close to the attended 0.7% all-chromosome confined placental aneuploidy probability based on chorionic villus sampling data. Ideally, all observations should be confirmed postnatally on a placental sample. Herein we stress the interest of a pangenomic strategy and the role of cytogeneticists facing situations experienced with chorionic villus sampling.

### 3.P11 Microarray

#### Incidental X Linked Findings A female fetus with a gain in the DMD gene

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In prenatal diagnosis, chromosomal microarray analysis (CMA) has not yet fully replaced conventional cytogenetic but has rapidly become the recommended genetic test in pregnancies with ultrasound abnormalities. This methodology allows the identification of pathogenic small copy number variation (CNVs) in 5-10% of pregnancies with ultrasound abnormalities and a normal karyotype, increasing the diagnostic yield. However, this increased resolution can also result in the detection of incidental findings.

Here we report a fetus referred for prenatal diagnosis due to skeletal dysplasia. Affymetrix Cytoscan HD chromosome microarray analysis was performed and a 204 kb gain was detected at Xp21.1 region (chrX: 31993622\_32191110 [GRCh37]) in a female fetus, encompassing the intron 44 of the DMD gene, for the largest gene transcript. Nevertheless, if we considered the smaller transcripts it encompasses exon 1. The gain was maternally inherited.

The DMD gene is involved on Becker muscular dystrophy, Cardiomyopathy, dilated, 3B and Duchenne muscular dystrophy. Intron 44 is a preferential breakpoint in about 30% of all DMD deletions, being the DMD transcript NM\_004006.2 responsible for dystrophin expression in the skeletal muscle.

The FGFR3 gene sequencing revealed the presence of the c.1118A > G, p.Y373C mutation associated to Thanatophoric Dysplasia, type 1 (TD1) justifying the ultrasound abnormalities.

With this case, we reinforce that the discovery of CNVs in prenatal CMA goes beyond the correlation with the CNV and the ultrasound abnormalities. Incidental findings can also have a larger impact to the family clinical managing, even if not for the ongoing pregnancy for the reproductive future of the couple.