Annex:

Reporting policy of maternal incidental findings detected by NIPT.

prepared by the BeSHG Prenatal Committee on 14.09.2023

approved by the College for Medical Genetics on 02.02.2024

1. General guidelines

In general, maternal incidental findings detected by NIPT are only reported when this is indicated by the BeSGH guidelines as found on the College for Genetics website[1]:

*NIPT good clinical practice guidelines

*Managing incidental findings detected by NIPT

2. List of possible maternal findings to report or not to report

A non-exhaustive list of possible maternal incidental findings can be found in the table below:

Maternal incidental finding	Chromosome region	Genes	To report?	Literature/remarks
4qter deletion	4qter		**NO**	Susceptibility locus; Strehle et al., 2012; Manolakos et al., 2013; Vona et al., 2014
SMN1, *SMN2* deletion	5q13.2	*SMN1 / SMN2*	**NO**	AR disorder, variable region not well interpretable on confirmatory CGH (technically unreliable/blacklisted region)
10qter deletion	10q25-qter		**NO**	Fragile site on 10qter: not clinically relevant (PMID 29493577 and 9660961); often mosaic in mother
HBB deletion	11p15.4	*HBB*	**NO**	Not to report in "high risk population" (cf. consult with clinical geneticist dd 17/12/2021)
GJB6 deletion	13q12.11	*GJB6 / GJB2*	**NO**	Discussed on prenatal consortium meeting dd 10/12/2020
15q duplication syndrome	15q11.2q13.1	*SNRPN / UBE3A*	**YES**	Risk factor for developmental delay and autism when maternally inherited (Aypar et al., AJMG, 2014; PMID 24975781)
HNPP **deletion**	17p12	*PMP22*	**YES**	Perinatal actions possible
CMT1A **duplication**	17p12	*PMP22*	**NO**	If it has not yet been diagnosed, it is a predictive test of a condition for which no preventive measures exist. Discussed with neurologists and presented on prenatal consortium meeting dd 17/09/2022.

Maternal incidental finding	Chromosome region	Genes	To report?	Literature/remarks
RCAD **deletion**	17q12	*HNF1ß*	**NO**	MIM # 137920. This deletion is associated with maturity onset diabetes of the young type 5 (MODY5), cystic kidney disease, renal dilatation, pancreas atrophy and liver abnormalities. In addition, Nagami et al. (2010) reported that the 17q12 deletion could be associated with developmental delay. However, the severity of expression is variable. Further ultrasound follow-up is recommended, with special attention to renal anomalies.
22q11 **deletion** syndrome - **proximal**	22q11.21q11.22	LCR A-B or A-D	**YES**	Burnside et al; 2015
22q11 **deletion** syndrome - **central**	22q11.21q11.22	LCR B-D or C-D	**NO**	Susceptibility locus; Burnside et al; 2015
22q11 **deletion** syndrome - **distal**	22q11.21q11.22	LCR C-E, D-E, D-F, E-F or E-H	**NO**	Susceptibility locus; Burnside et al; 2015
22q11 **duplication** syndrome - **proximal**	22q11.21q11.22	LCR A-B or A-D	**NO**	Susceptibility locus; Burnside et al; 2015
22q11 **duplication** syndrome - **central**	22q11.21q11.22	LCR B-D or C-D	**NO**	Susceptibility locus; Burnside et al; 2015
22q11 **duplication** syndrome - **distal**	22q11.21q11.22	LCR C-E, D-E, D-F, E-F or E-H	**NO**	Susceptibility locus; Burnside et al; 2015
IL1RAPL1 intragenic duplication	Xp21.3	*IL1RAPL1*	**NO**	Insufficient information on pathogenicity
STS deletion	Xp22.31	*STS*	**NO**	Phenotype is not considered to be severe. Potential benefit does not outweigh possible distress caused by reporting.
SHOX deletion	Xp22.33	*SHOX*	**NO**	Phenotype is not considered to be severe. Potential benefit does not outweigh possible distress caused by reporting
SHOX duplication	Xp22.33	*SHOX*	**NO**	
int22h1/int22h2-mediated Xq28 deletion syndrome	Xq28	*RAB39B*, *CLIC2*	**NO**	El-Hattab et al; 2015 (discussed on prenatal consortium meeting dd 15/06/2023)

3. Susceptibility loci

In accordance with the BeSHG guidelines, maternal incidental finding of a susceptibility locus will **NOT** be reported when detected by NIPT. The revised list of these susceptibility loci can be found on the College for Genetics website[1].

Remark: This list was originally intended for the analysis of invasive prenatal tests. For NIPT, the column 'return' is not applicable.

References

[1]College for Genetics website: https://www.college-genetics.be/fr/pour-les-professionnels/recommandations-et-bonnes-pratiques/guidelines.html

Version history

Version	Date prepared by BeSHG Prenatal Workgroup	Date approved by College of Medical Genetics	Updates
V2023	14.09.2023	02.02.2024	New document: no history available.