

Blood group genotype in determination of feto-maternal red blood cells incompatibility status: Experience of the French National Center for Perinatal Hemobiology (CNRHP)

N.R. DA SILVA(1), OUDIN O. (1), SAULET P. (1), OGER M. (1), C. ROUILLAC-LE SCIELLOUR(2), M. MENU(3), Y. COLIN(4), C. LE VAN KIM(4), J.P. CARTRON(4), Y. BROSSARD(1), A. CORTEY(1), B. CARBONNE(1), A. MAILLOUX(1)

(1) Centre National de Référence en Hémobiologie Périnatale (CNRHP), AP-HP St Antoine, PARIS, FRANCE ; (2) Laboratoire Central CHI Poissy-Saint Germain en Laye, POISSY, FRANCE ; (3) Institut Jacques Boy, REIMS, FRANCE ; (4) Institut National de la Transfusion Sanguine, PARIS, FRANCE

Background: Hemolytic disease of the fetus and newborn (HDFN) is a significant cause of fetal and neonatal death. The French "Centre National de Référence en Hémobiologie Périnatale" (CNRHP) is dedicated to biological and clinical diagnosis and treatment of feto-maternal red blood cells incompatibilities.

Aim: Review of the molecular biology tools used in determining of the feto-maternal incompatibility status over one year in our reference center.

Methods: To identify fetuses at risk for HDFN, our laboratory uses 3 types of analysis :

- Paternal zygosity of *RHD* locus from blood cells to determine the potential risk of incompatibility in the next pregnancy in allo-immunized woman with (Chiu RW *et al.*, Clin Chem., 2001, 47 : 667-72).
- Non invasive fetal *RHD* genotyping from maternal blood sample of allo-immunized and non immunized woman to guide the prophylaxis and follow-up (Rouillac-Le Sciellour *et al.*, TCB, 2007, 14 : 572-7).
- Invasive fetal *RHD*, *RHE*, *RHC/c*, *Kell* genotyping from chorionic villus or amniotic cells in allo-immunized or non immunized woman (Aubin JT *et al.*, Br J Haematol., 1997, 98 : 356-64; Le Van Kim C *et al.*, Br J Haematol., 1994, 88 : 193-5; Tax MG *et al.*, Transfusion, 2002, 42 : 634-44.; Lee S *et al.*, Blood, 1995 (85) :912-6).

Fetal genotype results were compared with the phenotype of the red blood cells of the babies at birth.

Results:

1)For genetic counseling for future pregnancies of allo-immunized woman with anti-D, 18 determination of the paternal zygosity at the *RHD* locus were done. 14 fathers were found homozygous *RHD/RHD* and 4 fathers were found heterozygous *rhD/RHD*.

2)To determine fetal *RHD* status,

1378 non invasive fetal *RHD* genotype from maternal blood were done: 192 from allo-immunized anti-D woman (142 positive fetuses, 48 negative and 2 undetermined) and 1378 from non allo-immunized woman (847 positive fetuses, 323 negative and 16 undetermined).

286 invasive fetal *RHD* genotype from chorionic villus or amniotic cells were done: 9 from allo-immunized anti-D women (7 positive fetuses and 2 negative) and 277 from non allo-immunized women (182 positive fetuses, 94 negative and 1 undetermined).

3)To determine fetal *RHE* status, 2 invasive fetal *RHE* genotype from amniotic cells of allo-immunized anti-E woman were done (1 positive and 1 negative fetuses).

4)To determine fetal *RHC* status, 1 invasive fetal *RHC* genotype from amniotic cells of allo-immunized anti-C woman was done (positive fetus).

5)To determine fetal *RHc* status, 2 invasive fetal *RHc* genotype from amniotic cells of allo-immunized anti-c woman were done (1 positive and 1 negative fetuses).

6)To determine fetal *Kell* status, 16 invasive fetal *Kell* genotype from amniotic cells were done (7 positive fetuses and 9 negative).

Conclusion: Molecular biology is a powerful tool to diagnose a feto-maternal red blood cells incompatibility and allows to legitimize a costly and heavy specific antenatal monitoring. In non immunized *RHD*-negative pregnant woman, it allows to rationalize prophylaxis indicated only for women expecting a *RHD*-positive baby.