

DYNAMIC CHANGES IN MICROCHIMERISM FROM A WOMAN'S OWN MOTHER AND FETUS IN PERIPHERAL BLOOD MONONUCLEAR CELLS DURING PREGNANCY

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Objective: Fetal-maternal cell trafficking during pregnancy results in the long-term persistence of small populations of fetal cells in the mother and maternal cells in her progeny, called microchimerism (Mc). Dynamic changes in Mc may occur in pregnant women as a result of either pregnancy-associated changes in the maternal immune system, or the active transfer of fetal cells across the placenta. Higher levels of Mc may contribute to pregnancy complications as suggested by studies of fetal Mc in skin (pruritic eruptions of pregnancy) and plasma (preeclampsia). We asked whether quantities of maternal Mc (MMc, from a pregnant woman's own mother) and fetal Mc (FMc) increase in peripheral blood mononuclear cells (PBMC), CD4+, and CD8+ subsets with advancing gestation.

Methods: Peripheral blood was obtained from women pre-pregnancy, during each trimester of pregnancy, and postpartum. PBMC were isolated and T cell subsets (CD4+, CD8+) obtained by magnetic bead sorting. DNA samples were also obtained from the fetus at delivery (cord blood), subjects' mother, and prior children. Genetic polymorphisms were typed in the major histocompatibility complex, glutathione S transferase, and antithrombin III gene loci. A panel of quantitative PCR assays targeting non-shared genetic polymorphisms was employed to quantify MMc and FMc in PBMC and CD4+/CD8+ subsets. A quantitative PCR assay targeting DYS14, a Y-chromosome target, was also used to quantify FMc if the fetus was the first boy. DNA quantities were reported as the DNA genome equivalent number of microchimeric cells per million host cells (gEq/mil).

Results: A total of 30 pregnancies (28 women) were studied for MMc and 25 pregnancies for FMc. Overall, mean levels of MMc and FMc in PBMC were similar with the exception of higher quantities of MMc in the third trimester and relatively higher FMc postpartum: pre-pregnancy 0.0 vs. 0.0 gEq/mil, first trimester 0.4 vs. 1.2 gEq/mil, second trimester 2.2 vs. 3.5 gEq/mil, third trimester 33.8 vs. 2.5 gEq/mil, and postpartum 1.8 vs. 7.7 gEq/mil for mean MMc and FMc respectively. Levels of MMc in PBMC were as high as 650 gEq/mil in the third trimester. The frequency of positive PBMC samples tended to increase with gestation and postpartum: pre-pregnancy 0% vs. 0%, first trimester 7% vs. 25%, second trimester 13% vs. 21%, third trimester 20% vs. 31%, and postpartum 25% vs. 35% for MMc and FMc respectively. In a logistic regression model, the odds ratio of a positive PBMC sample for MMc increased 1.57 for each increase in gestational period ($p < 0.05$). MMc was detected in no CD4+ (0/42, 0%) and in rare CD8+ (1/31, 3%) subsets, while FMc was frequently detected in both CD4+ (5/21, 24%) and CD8+ (5/13, 38%) subsets.

Conclusions: Surprisingly, mean quantities of MMc were higher than FMc during pregnancy. Extrapolating from the highest quantity of MMc detected, 0.07% of a pregnant woman's cells in her PBMC were from her own mother. PBMC samples were also more frequently positive for Mc postpartum, which for FMc may be the result of increased cell trafficking during childbirth. The discrepancy between frequent detection of FMc and near absent MMc in CD4+ and CD8+ subsets may reflect the different circumstances under which each type of Mc was acquired. Further studies are indicated to investigate interactions between microchimeric cells and the host, particularly in late pregnancy, and whether higher levels of Mc might be associated with adverse pregnancy outcomes.