



**Karolinska
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Department of Clinical Science and Technology

Maternal microchimerism

AKADEMISK AVHANDLING

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ABSTRACT

Microchimerism refers to one individual harboring cells or DNA at a low level that derive from another individual. The most common source is pregnancy when cells from the fetus and the mother pass the placenta bidirectionally, and give rise to maternal microchimerism (cells from the mother in the fetus) and fetal microchimerism (cells from the fetus in the mother). The cells persist in the individual, at least until middle-age. Several hypotheses have addressed the consequences of harboring semiallogeneic cells. Both maternal and fetal cells within the host are associated with certain autoimmune diseases, as inducers of the disease but also as repairers of already injured tissue. Furthermore, inducing fetal-maternal tolerance during pregnancy seems to be an important purpose of the cell-trafficking. Observations from the transplantation field yield that this effect may be long lasting.

In paper I, we examined the presence of maternal cells within different cellular subsets in tissues from eleven 2nd trimester fetuses. Seven fetuses presented with maternal microchimerism. The cells were widely spread in different tissues and found in both normal fetuses and fetuses with trisomy 21. The cells were of mature immunological and hematopoietic stem cells character.

Paper II aimed to examine maternal microchimerism in healthy children's tonsils and adenoid by a quantitative PCR assay. We found maternal microchimerism in four of 20 children. The children were between four and six years old and harbored maternal cells in the tonsils and/ or adenoid at levels that ranged from 2×10^{-2} to 7.1×10^{-5} . The same children were also positive for maternal cells in peripheral blood.

In paper III, we investigated the association between maternal microchimerism in peripheral blood and systemic lupus erythematosus. In the study, 32 nulligravida women with SLE were included. Seventeen brothers of the women and additional 12 unrelated males constituted healthy controls. Two patients and one control appeared with maternal cells in peripheral blood. The result indicates no correlation between maternal microchimerism in blood and SLE (P-value = 0.65). At a follow up, the same individuals tested negative 16 years after the first draw date.

The purpose of paper IV was to evaluate the cellular subset and frequency of maternal cells in umbilical cord blood following vaginal deliveries and caesarian sections, when the time of umbilical cord clamping was known. We included 44 babies from normal term pregnancies who were delivered vaginally (24) and by caesarian section (20). Five of 44 (11%) of the umbilical cord blood samples contained maternal microchimerism. The positive fractions were total DNA, CD34+ and CD56+. Four of the five positive samples were from caesarian sections and one was from a vaginal delivery. The positive samples were from deliveries with a mean clamping time of 37 seconds compared to 54 seconds in the negative group.

Overall, we have shown that maternal cells are common in fetuses, infants and children. Their nature is of mature immunological and hematopoietic stem cell character. There is no correlation between the autoimmune disorder SLE, and maternal microchimerism.