# My mother's keeper

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**A two-way street:** Mom and child both appear to trade cells that cross through the placenta

At various stages in life, children break away from their mothers—they cross the street alone for the first time, wave goodbye from the yellow school bus, and eventually leave home all together. But the mother-child bond is enduring—and not just on an emotional level. During pregnancy, the placenta acts as a two-lane highway, allowing bits and pieces of biological material to flow between a mother and fetus. Decades after giving birth, mothers might still be carrying around a small fraction cells and DNA donated by their children, and their children may, in turn, harbor cells and DNA from their mothers. Researchers are just beginning to understand the health implications of this biological trade and to explore ways of harnessing it for practical purposes.

The enduring presence of a mother's cells in her children, referred to as maternal microchimerism, seems to have both good and bad effects, explains Lee Nelson of the Fred Hutchinson Cancer Research Center in Seattle. Scientists suspect that a mother's cells gain access to the fetus via the placenta, and the small percentage of those cells lingering in the tissues after birth may contribute to some autoimmune diseases. Nelson's team found maternal cells lurking in the hearts of infants who died of cardiac failure caused by neonatal lupus. They suspect that the immune system of the growing fetus attacks the maternal cells (*Lancet* **362**, 1617–1623; 2003). In some cases, however, a mother's cells might help regenerate diseased tissue. It turns out that children with type 1 diabetes tend to have higher-than-average numbers of maternal cells dwelling in the blood and pancreas. "There are indications that in the pancreas these cells might be serving a repair function," says Kathleen Gillespie of the University of Bristol, who is currently leading an autopsy study of pancreatic maternal cells in diabetic and nondiabetic children.

## A mixed bag

Fetal microchimerism, which refers to fetal cells or DNA surviving in the mother, also seems to be a mixed bag. Studies conducted by Nelson's lab have implicated fetal cells in autoimmune diseases such as scleroderma, which erodes the connective tissue and causes hardening of the skin and internal organs.

Meanwhile, women with certain autoimmune diseases, including multiple sclerosis and rheumatoid arthritis, experience a temporary remission during pregnancy. Scientists speculate that fetal microchimerism might have a role. A study by Nelson's lab linked high levels of fetal microchimerism during pregnancy to pronounced decreases in rheumatoid arthritis symptoms (*Immunol. Invest.* **37**, 631–644; 2008). It could be that the fetal cells somehow cause a shift in the pregnant woman's immune system so that it better tolerates foreign tissues, such as the growing fetus, and in doing so also make the immune system less reactive to her own tissues.

Preliminary data suggests that fetal microchimerism may even offer mothers ongoing protection against breast cancer, perhaps because the presence of foreign cells keeps the immune system in a heightened state of alert for malignant cells (*Cancer Res.* **67**, 9035–9038; 2007). The exact mechanisms of these effects remain unclear.

As a growing community of researchers strives to understand the role of microchimerism in health, others are harnessing it to develop noninvasive prenatal tests.

A team from Howard Hughes Medical Institute and Stanford University recently published a study suggesting that a blood test using fetal DNA might detect Down's syndrome and other chromosomal abnormalities in pregnant women (*Proc. Natl. Acad. Sci.*, doi:10.1073/pnas.0808319105; 2008). In Europe, many medical centers are already using fetal DNA in maternal blood to test for gender and rhesus D status (a blood-typing characteristic) as early as seven to eight weeks into pregnancy.

In the US, at least two companies have launched tests using fetal DNA in maternal blood—Biocept in San Diego and Lenetix near New York. Currently, US doctors rely on invasive prenatal tests, such as amniocentesis and chorionic villus sampling, which are done later in pregnancy and may cause miscarriage in up to 1% of women. Not only are DNA blood tests safer, they are potentially more cost effective, notes Farideh Bischoff of Baylor College of Medicine in Houston. For doctors to begin ordering these tests and insurance companies to begin covering them, there must be clinical trials showing they are effective, says Bischoff, who also directs translational research and development at Biocept.

The ultimate goal, Bischoff says, is to use DNA blood tests not just for early gender identification and blood typing but also for detecting a broad array of genetic disorders.

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