Brilliance and Precision:
From Surgery to *In utero* Transplantation

As a gifted pianist in high school, Assistant Professor of Surgery Tippi MacKenzie, MD, spent every Saturday studying music at Juilliard. This musical training was good preparation for her current work as a researcher and surgeon.

"When you're playing the piano, you work out the details in a difficult passage until it's perfect," she said. "It's the same with science. If there's an issue with your experiment, you can't just sweep it under the rug. You tackle that problem." With a smile, she added, "The technical fine motor skills also come in handy as a surgeon."

Now a fetal and pediatric surgeon in the Fetal Treatment Center, MacKenzie performs open and minimally invasive procedures on fetuses with severe congenital anomalies. She also conducts research aimed at transplanting stem cells *in utero* to treat a variety of diseases. This approach would take advantage of the fetal immune system, which is still flexible enough in the early second trimester to incorporate foreign cells without rejecting them.

The *in utero* stem cell strategy could someday be used to cure blood disorders that can be diagnosed prenatally, such as sickle cell anemia and immunodeficiencies. It also could prove effective in infants receiving organ transplants after birth. For example, a fetus with a kidney abnormality may need a transplant when it is born. Even if a parent can donate a kidney, the baby will need immunosuppressant drugs for life to reduce the risk of organ rejection. "If we were able to tolerize the fetus *in utero* to a particular donor, we would then be able to do the kidney transplant after birth and not need to give immunosuppression," she said. "Tolerance induction is the Holy Grail of any sort of transplantation."

In utero stem cell transplantation also holds promise for such disorders as muscular dystrophy, which currently has no cure. "We've discovered that when you inject stem cells into a fetus, the transplanted cells actively migrate throughout the body," said MacKenzie. "There is a much greater likelihood of cells going to different muscle groups and helping them, compared to in adults, where cells tend to stay where they were injected."

While stem cell transplantation has been successful in fetuses with severe combined immunodeficiency (SCID) – because these fetuses lack a sufficient immune system and there is more space in the bone marrow for the new cells to settle – the technique has yet to work for other diseases.

With an eye toward developing such treatments, MacKenzie and her mentor, Abul Abbas, MBBS, chair of the Department of Pathology, are studying the fetal immune system. Using a syringe thinner than a human hair, MacKenzie injects blood stem cells into the livers of fetal mice. One question she is currently pursuing is to what extent the mother's immune system affects tolerance induction in her unborn child, and whether it is more important to match transplanted cells to the fetus or the mother.

MacKenzie's research could potentially help stem cell transplant patients of any age. "Unless the stem cell comes from the patient, you're going to have to deal with your recipient's immune system," she said. "Our work into understanding the immunology of stem cell transplantation has implications for when these wonderful stem cells are finally taken to patients."

Although her life is busy, MacKenzie still makes time to play her Steinway grand, which she had shipped to San Francisco when she was recruited to UCSF in 2007 after training at Children's Hospital of Philadelphia, Brigham and Women's Hospital in Boston and Stanford Medical School. She is married to John MacKenzie, MD, a radiologist at Stanford. They have 2 daughters, Emma, 8 and Katharine, born April 12, 2009.

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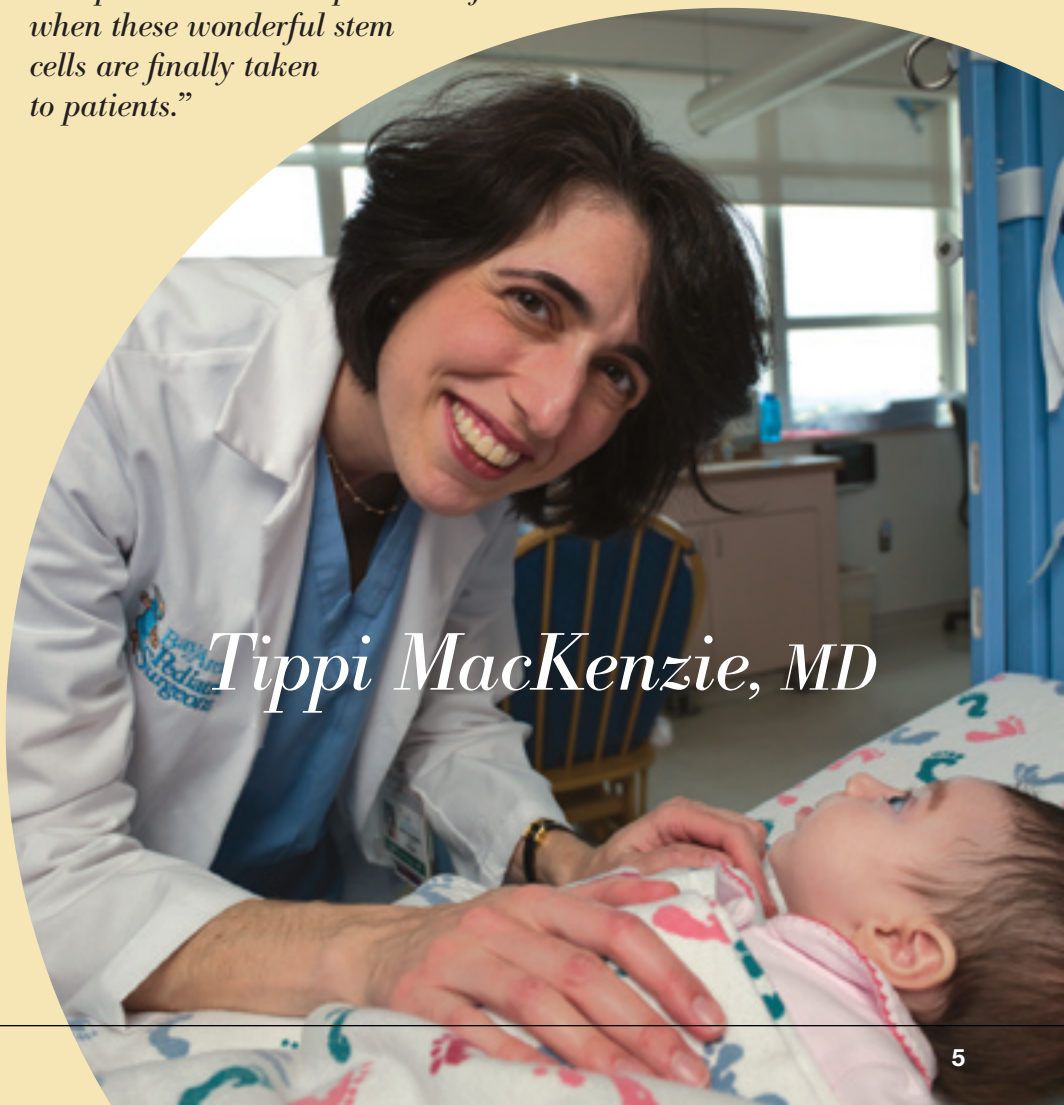

Tippi MacKenzie, MD