Breaking New Ground

Surgeon Maria Siemionow sees ever-growing promise for transplant patients postsurgery

MARIA SIEMIONOW ROSE TO INTERNATIONAL PROMINENCE IN 2008 as the lead surgeon on the first near-total face transplant in the U.S., a 22-hour procedure performed at Cleveland Clinic. She later published an inspiring autobiography that recounts the landmark event (see "The Road to Cleveland Clinic," right). And while Siemionow is committed to groundbreaking procedures as the clinic's director of plastic surgery research and microsurgery training, she's equally excited about investigating drug therapies to aid transplant patients after surgery.

The technical skill required to perform composite allograft surgery — the medical term for a transplant involving skin, nerves, blood vessels, and bone — is considerable, but the biggest challenges involve recovery following the procedure. Ensuring that a patient's immune system does not reject the transplant is critical.

Generally, transplant recipients take immunosuppressant drugs for the rest of their lives. "They do the job, but they also have a lot of side effects and cause damage to the body of the organ recipient," says Siemionow, the first U.S. physician to receive Institutional Review Board approval to perform facial transplantation surgery. Existing therapies selectively deplete T-cells, a type of white blood cell responsible for immune reactions, making the transplant viable but leaving the patient susceptible to serious side effects, including infections, diabetes, and lymphoma.

Currently Siemionow is researching the possibility of shorter-term drugs that have fewer side effects. Her lab has developed protocol with an antibody that selectively blocks T-cell receptors. The result, Siemionow hopes, will be reduced susceptibility to serious infections. Plus, the antibody is short-acting, which speeds the recovery of the patient's suppressed immune system from months or years to weeks.

Siemionow's lab has tested the new antibody in composite transplants involving experimental models. Animals that received the antibody for a week accepted the transplants with no further immunosuppressants necessary. The antibody is ready for clinical trials in kidney transplants, and might allow physicians to eventually wean patients off immunosuppressant drugs. Siemionow also believes the antibody will produce fewer side effects than current drugs.

As for the future, Siemionow is experimenting with a new cell-based therapy using chimeric cells — which fuse donor and recipient genes — to aid transplant recipients. "We are actually fusing the cells of the donor and the cells of the recipient and using these fused cells as a supportive therapy with the transplant, but that's still in the preclinical, laboratory stage," says Siemionow, with a hint of excitement. — *Sheila Callahan*

The Road to Cleveland Clinic

In her memoir, *Face to Face* (Kaplan, 2009), Dr. Maria Siemionow tells the story of her groundbreaking career, recounting her studies at the renowned hand clinic at the University of Louisville and her research at the Cleveland Clinic on immunosuppressant drugs.

Describing early efforts in plastic surgery, Siemionow tells of a surgeon in Renaissance Italy who rebuilt ravaged noses by grafting forearm skin to patients' faces. However, modern advances still don't guarantee success. Patient screening is vital, she says. For example, the first hand transplant recipient, unwilling to maintain the immunosuppressants, had the hand amputated within two years.

In Siemionow's lab, a white rat with a dark transplanted face exemplifies the promise of new therapies. After a short course of immunosuppressants, he tolerated the transplant without further drugs. — *S.C.*

GREG RUFFING (SIEMIONOW)