Growing Kidneys from Scratch

Tissues from the early stages of renal development may offer new hope to the numerous patients awaiting access to a limited number of donor kidneys. Many thousands of lives have been saved in the nearly 50 years that have passed since the first successful kidney transplant; however, the demand for these organs remains considerably higher than the supply, resulting in a waiting list several times larger than the number of patients who will actually receive a new kidney in a given year.

The kidney derives partly from pluripotent stem cells that are induced to develop into nephrons, the tubules that act as filtering units in the kidney. These immature kidney precursors have shown considerable promise as potential transplant substrates. Now, in a recently published *Nature Medicine* article (3 January 2003), researchers at the Weizmann Institute (Rehovot, Israel) present data indicating that human and porcine embryonic kidney precursors can, following transplantation into mouse hosts, successfully grow and differentiate into partially functional nephrons.

Transplant viability depended on the developmental age of the graft; adult kidney tissue failed to develop, and whole-kidney transplants from late-stage (10- to 14-week human or 6- to 8-week pig) embryos gradually became necrotic. Far more successful were transplanted whole kidneys from early-stage or kidney fragments from late-stage gestational donors.

Such transplants exhibited growth and development of tubular and glomerular structures, and immunostained against mouse PECAM, an endothelial protein, indicating that host blood vessels were vascularizing the transplanted kidney tissue. The transplants also proved capable of producing dilute urine, indicating that they were carrying out rudimentary filtration. Importantly, the researchers found that transplants derived from early-stage human and porcine donor tissue were largely resistant to immune system rejection both in immunocompetent host mice and in mice whose immune systems were 'humanized' by injection with human immune cells.

These results suggest the possibility that embryonic tissue may provide a valuable transplant substrate for kidney replacement; more importantly, the use of porcine embryonic kidney precursors could offer an easy and abundant alternative to their scarcer and more controversial human-derived counterparts.

–M.E.

faster than conventional high-yield mammalian cell culture systems.

A group led by Katsutoshi Yoshizato of Hiroshima University in Japan transfected silkworm eggs with a cDNA construct consisting of a portion of the human collagen gene linked to the gene for enhanced green fluorescent protein (EGFP). The green fluorescence in the silk glands and cocoons served as a marker for expression of the transgene. The researchers were then able to separate the collagen from the silk protein using a relatively simple chemical extraction (*Nature Biotechnology*, January).

Many current methods for the production of medically useful proteins are complicated, expensive, and require specialized facilities; as such, the demand for such therapeutic proteins generally exceeds the supply. In contrast, the optimization of silk manufacturing over hundreds of years has led to its easy, inexpensive implementation throughout the world. Aside from these benefits, therapeutic proteins produced by an insect such as *B. mori* also carry a considerably reduced risk for transmission of infectious agents, compared with transgenic animals or mammalian cell culture systems.

—T.S.