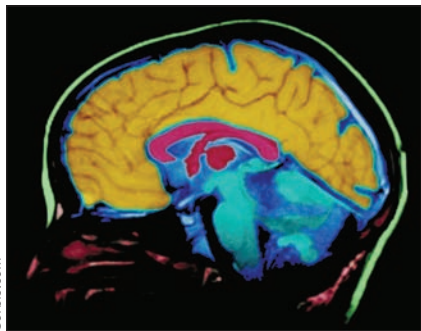


## BENCH TO BEDSIDE

## Breaking down the blood–brain barrier

Although the blood–brain barrier protects the brain from harmful substances in the blood, it also prevents potentially beneficial drugs from reaching the brain. One solution for improving drug delivery to the brain is to remove the blood–brain barrier from the equation altogether.

Soshana Behrstock and colleagues recently did this by implanting cells in the brain that are engineered to produce a chemical (*Gene Ther* 2005;doi:10.1038/sj.gt.3302679). These cells, which are derived from human fetal brain tissue, produce a protein called glial cell line-derived neurotrophic factor (GDNF). Behrstock and colleagues found that implantation of the engineered cells can help alleviate symptoms of Parkinson's disease in animal models.



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GDNF was chosen because it prevents dopamine neuron loss and has shown promise in relieving symptoms of Parkinson's disease in clinical trials (*J Neurosurg* 2005;102:216-22). However, since GDNF does not cross the blood–brain barrier, it must be administered directly to the brain with a

complex catheter and pump system.

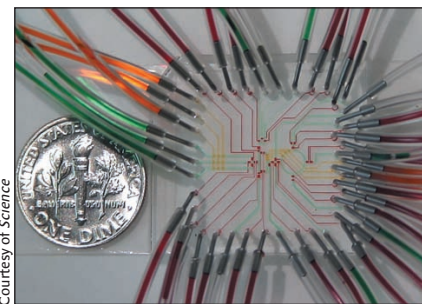
In their search for an alternate delivery system, Behrstock and colleagues modified human neural progenitor cells so that they would secrete GDNF. These cells were then implanted into the striatum of rats and elderly primates. Over time, the engineered cells not only survived but also migrated and released GDNF; the scientists also found new nerve fibre growth in animals who received the GDNF-secreting cells.

The implanted GDNF-producing cells did not cause tumours in any animals, an important result if such implantations are ever to be used in human clinical trials. However, further research is needed to learn how to control the levels of GDNF produced by the cells. Nevertheless, with the blood–brain barrier blocking around 70% of drug entry into the brain, the new strategy may help get some drugs to where they are needed most.

### A PET mini-chip

Microfluidics, a field that deals in part with creating miniature systems for mixing liquids and gases, is likely unfamiliar to most physicians. Nevertheless, microfluidic technology may revolutionize the field of medical imaging.

Positron electron tomography (PET) is an imaging technique that employs radioactive compounds to build images of the human body, and it is currently used in diagnosing disease like cancer and Alzheimer's dementia and in guiding the choice of interventions. PET often involves radioactively labeled sugar molecules like fluorodeoxyglucose (FDG), which are injected into patients; the tissues in which the molecules appear on imaging indicate rates of cellular metabolism, which often change



Courtesy of Science

with disease. Over 1 million doses of FDG were made in the United States in 2004. However, making radioactive compounds is expensive.

In an effort to overcome costs, Chung-Cheng Lee and colleagues recently turned to microfluidics to produce radioactive molecules for PET (*Science* 2005;310:1793-6): they designed a stamp-sized chip made up of miniature fluid channels, chambers and valves, all of which are controlled by a computer.

The PET mini-chip — which looks like an integrated circuit (see photograph) — uses pumps to deliver small volumes of the components needed to make radioactive FDG (e.g.,  $^{18}\text{F}$  and FDG). All of the chemical reactions are performed inside the chip as liquid flows through it. The production process normally takes over an hour, but it takes only 14 minutes in the mini-chip. Moreover, the mini-chip makes enough FDG to be used in human studies.

The mini-chip can be envisioned as a miniature chemical factory that is capable of quickly producing the compounds needed for PET scans. Since it can be redesigned to make alternative compounds, the mini-chip may one day spur the design of new compounds to help refine the imaging of disease. — Compiled by David Secko, Vancouver

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