MEDICINE

The Bunny Chip

The drug industry could slash its costs, and spare millions of furry creatures, with a chip that mimics a living organism.

By Amanda Schupak

Rabbit and its best friend: the tiny Hurel chip.

THOMAS BROENING FOR FORBES

DRUG RESEARCHERS MUST hack their way through tens of thousands of chemical candidates to find one blockbuster drug. Every toxic or ineffective molecule they rule out brings them closer to their goal. But it takes, on average, $800 million and 14 years to develop a drug and win Food & Drug Administration approval. Regrettably, some 30 million rabbits, mice and other creatures are sacrificed each year for pharma's sake.

"Drug development is a very inefficient process," says Gregory Baxter, a molecular biologist and cofounder of Hurel Corp. in Beverly Hills, Calif.

Baxter thinks he can save drug companies tens of millions of dollars and six months or more of delay—not to mention spare them the ire of animal lovers—with his company's curious product, the Hurel. Part silicon, part animal, the Hurel is a microchiplike wafer with several chambers lined with live mammalian cells from the liver, heart, lungs or other organ systems (extracted either from animals or from

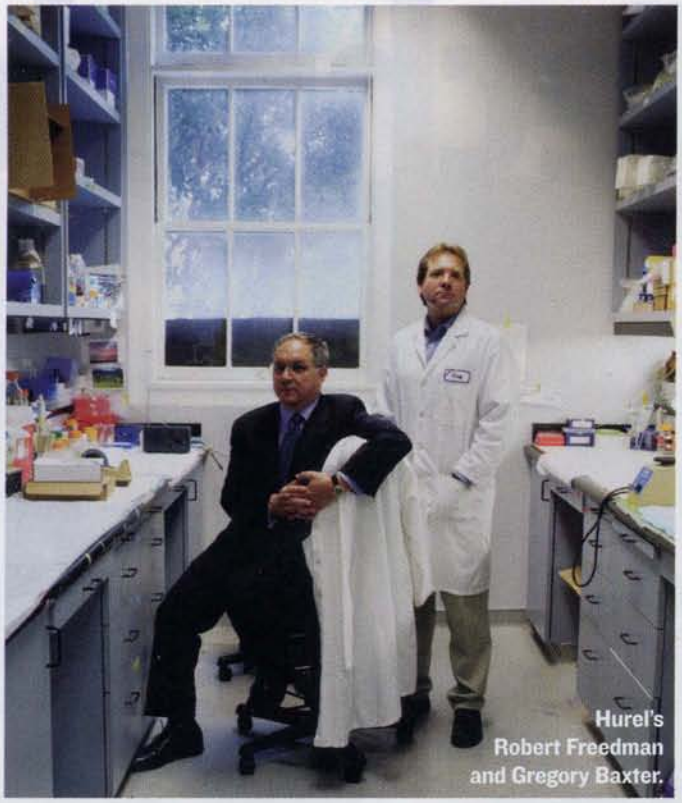
lab-grown cell lines). An external pump moves a candidate drug molecule through the Hurel's compartments, which are connected by a network of channels as narrow as 20 micrometers.

The Hurels mimic in vitro the complex physiology of mammals. Within hours of injecting a drug into a Hurel, a lab researcher can determine if a drug might be toxic or ineffective in the body of an animal—or a human—averting the costly leap from cellular screenings to lengthy animal trials.

It's a leap drugmakers would desperately like to avoid: To get one drug approved by the FDA, a pharma company puts 250 candidates into animal testing, at a cost of $250 million. Baxter estimates that screening drug candidates with the Hurel chip before animal tests would help researchers identify 20% of those molecules typically doomed to fail and eliminate them early, saving $50 million. Cutting down a proportionate number of drugs that go into human trials would save another $88 million. Moreover, Hurels lined with human cells may someday be used in personalized medicine, allowing doctors to concoct effective and safe drug combinations for, say, a cancer patient, by using the patient's own cells and a biopsy of the tumor.

In early 2004 Hurel Chief Executive Robert Freedman contacted 12 large drug companies to form a yearlong collaboration to refine and validate the Hurel technology. The first to sign up was Johnson & Johnson Pharmaceutical Research & Development in June 2005. "This actually could replace early animal screening studies for pharmacokinetics," says Alfred Tonelli, a vice president of preclinical development at J&J PRD. The Hurel, he says, could be "a model that's better than animals, more human-relevant."

Freedman and Baxter are also talking to consumer products companies looking to get out of animal testing. Happy news to Mary Beth Sweetland, research director at People for the Ethical Treatment of Animals. "These technologies take us from cruel, crude animal tests into real science," she says. "Only these companies are going to get the numbers [of animals killed] down."



Hurel's Robert Freedman and Gregory Baxter.

The first Hurels are expected to hit the market in late 2006, designed to fit into the high-speed chemistry screening equipment used in most labs. Hurel says it can manufacture them for under $100 apiece by injection molding or embossing the intricate fluid channels out of plastic. Current prototypes are made from silicon etched under plasma gas.

The Hurel originated at the nanofabrication facility at Cornell University as a collaboration between the 45-year-old Baxter and 58-year-old biomedical engineer Michael Shuler. Baxter arrived at Cornell in the spring of 1997 with a background in microfluidics; on his second day there he met Shuler, who was doing toxicology testing with a Rube Goldbergian system of beakers and tubes. Baxter suggested they try miniaturizing the beaker works. Within minutes the two were scribbling down ideas, and at the end of their second meeting they had a device in mind: an animal-on-a-chip.

In 1999 they started testing a prototype, focusing on a common complication in pharmaceutical testing. "The chemical you start out with, or the drug, isn't the chemical that ends up interacting with the target," says Baxter. Body chemistry often gives drugs a new form, which can be toxic or even deadly. Simple test tube experiments often cannot predict these changes. Baxter and Shuler set out to show that their chip could.

They took naphthalene, the smelly ingredient in mothballs, and ran it through a three-chambered chip containing a rat's lung and liver cells and an empty compartment representing the rest of the body. Naphthalene is harmless in its natural state, yet it is toxic to mammals once metabolized by the liver. The naphthalene-infused fluid was pumped first through the lung chamber, then split between the liver and cell-less "other" compartment. Then the divergent paths rejoined, and the fluid began its course again. After a few hours, analysis using fluorescent dyes showed high rates of cell death in the lung compartment: The chip had metabolized the naphthalene, which then poisoned the lung cells. (Control tests without liver cells showed no damage.) Baxter and Shuler demonstrated how a harmless compound could become harmful in the body—without using a body at all. Since then they have completed successful proofs of concept with 15 different compounds, including the muscle relaxant Dantrolene and the chemotherapy medication tegafur.

Hurel Corp. got its start in 2002, when Robert Freedman, a venture capitalist in California, heard Baxter speak about the device and was instantly impressed: "Like they said in the movie: He had me at 'hello.'" Freedman's firm, Athena Capital, invested more than half a million dollars to license the technology from Cornell and file additional patents. (Shuler still sits on Hurel's scientific advisory board.)

"It's an easily usable tool, it's widely applicable, and it's disposable," says Freedman. The Hurel is so simple, he says, "it's just like a Bic pen." F

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