



## From Bench To Bedside

Academia slows the search for cures.

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Now that President Obama has almost all of his top science picks in place—from the Department of Energy to the FDA—the lack of an appointee for director of the National Institutes of Health is standing out like a creationist at an evolution conference. I hope the delay means Obama has grasped the need for, and the difficulty of finding, a powerful director who can get beyond the rhetoric about moving discoveries out of the lab and make it a reality. That hasn't happened yet, six years after a much-ballyhooed NIH "road map" declared such bench-to-bedside research a priority and vowed to reward risk-taking, innovative studies, not the same old incremental research that has produced too few cures.

NIH has its work cut out for it, for the forces within academic medicine that (inadvertently) conspire to impede research aimed at a clinical payoff show little sign of abating. One reason is the profit motive, which is supposed to induce pharma and biotech to invest in the decades-long process of discovering, developing and testing new compounds. It often does. But when a promising discovery has the profit potential of Pets.com, patients can lose out.

A stark example is the work of Donald Stein, now at Emory University, who in the 1960s noticed that female rats recovered from head and brain injuries more quickly and completely than male rats. He hypothesized that the pregnancy hormone progesterone might be the reason. But progesterone is not easily patentable. Nature already owns the patent, as it were, so industry took a pass. "Pharma didn't see a profit potential, so our only hope was to get NIH to fund the large-scale clinical trials," says Stein. Unfortunately, he had little luck getting NIH support for his work (more on that later) until 2001, when he received \$2.2 million for early human research, and in October a large trial testing progesterone on thousands of patients with brain injuries will be launched at 17 medical centers. For those of you keeping score at home, that would be 40 years after Stein made his serendipitous discovery.

The desire for academic advancement, perversely, can also impede bench-to-bedside research. "In order to get promoted, a scientist must publish in prestigious journals," notes **Dr. Bruce Bloom, president of Partnership for Cures, a philanthropy that supports research.** "The incentive is to publish and secure grants instead of to create better treatments and cures." And what do top journals want? "Fascinating new scientific knowledge, [not] mundane treatment discoveries," he says.

**Case in point: in research supported by Partnership for Cures,** scientists led by David Teachey of Children's Hospital of Philadelphia discovered that rapamycin, an immune-suppressing drug, can vanquish the symptoms of a rare and sometimes fatal children's disease called ALPS, which causes the body to attack its own blood cells. When Teachey developed a mouse model to test the treatment, he published it in the top hematology journal, *Blood* in 2006. But the 2009 discovery that rapamycin can cure kids with ALPS? In the 13th-ranked journal. The hard-core science was already known, so top journals weren't interested in something as trivial as curing kids. "It would be nice if this sort of work were more valued in academia and top journals," Teachey says.

Berish Rubin of Fordham University couldn't agree more. He discovered a treatment for a rare, often fatal genetic disease, familial dysautonomia. Given the choice of publishing in a top journal, which would have taken months, or in a lesser one immediately, he went with the latter. "Do I regret it?" Rubin asks. "Part of me does, because I'm used to publishing in more highly ranked journals, and it's hurt me in getting NIH grants. But we had to weigh that against getting the information out and saving children's lives."

Not all scientists put career second. One researcher recently discovered a genetic mutation common in European Jews. He has enough to publish in a lower-tier journal but is holding out for a top one, which means identifying the physiological pathway by which the mutation leads to disease. Result: at least two more years before genetic counselors know about the mutation and can test would-be parents and fetuses for it.

With these forces in play, NIH has to push back even harder to make translational research a priority. When Stein applied for NIH funding in the 1980s and 1990s, "people didn't believe that a pregnancy hormone could help patients recover from brain injury," he says. "People said it was too simple." And when he, too, tried to publish in top journals, the papers were rejected in large part because all he was reporting was success in treating people, not the mechanism or physiological pathway that constitutes the sexy science that wins plaudits. Teachey could not get NIH funding either. Reviewers said the work was too translational—and this was *after* the NIH road map professed love for translational research. It will take an NIH director of almost mythic proportions to turn around this ship.