Billions of dollars for research at stake in health-reform case

In April, shortly after the US Supreme Court had wrapped up three days of hearing arguments regarding the constitutionality of the country's 2010 Patient Protection and Affordable Care Act (PPACA), President Barack Obama noted that without the law "you cannot have a mechanism to ensure that people with preexisting conditions can actually get health care." But concerns as to the fate of the law go beyond hospital care. Several newly created biomedical research agencies and billions of dollars in funding will take a blow if the Supreme Court strikes down not only the mandate that individuals purchase insurance but possibly the entirety of the more-than-2,000-page law.

"Researchers ought to be concerned about the PPACA because the controversy could seriously hamper the progress we've made in the last few years," says Jerry Krishnan, who teaches medicine and public health at the University of Illinois College of Medicine at Chicago and also chairs the US Food and Drug Administration's pulmonary drug advisory committee.

The parts of the law affecting research include a rule stating that, beginning next year, providers must disclose research contracts to patients, including those with pharmaceutical companies, and a mandate that, from 2014 forward, insurers must cover clinical trial participation for beneficiaries of their health plans. Without the latter, many patients may lack the opportunity to participate in clinical trials and may lack access to experimental, but sometimes life-saving, medicine. The new law also created the Cures Acceleration Network, a grant program within the US National Institutes of Health (NIH) that, dependent on appropriations through Congress, could fund up to $500 million in projects per year to turn basic scientific discoveries into treatments. In addition, the PPACA pays particular attention to breast cancer, directing the NIH to conduct research on new screening methods, prevention and early detection of the disease in young women.

Funding of the Patient Centered Outcomes Research Institute—a nongovernmental body based in Washington, DC designed to improve personalized health care through understanding variation in treatment responses—also hangs in the balance. The PPACA established a funding stream for the institute that would dedicate up to $4 billion over ten years. Experts applaud the comparative effectiveness efforts that this institute will identify and reject the notion that it will stifle research. "Some believe that will deter pharmaceutical companies from making 'me too' drugs, but do you really think a manufacturer is not going to invest a billion dollars in doing something new?" says Freeman Farrow, a health law expert at DePaul University College of Law in Chicago.

There is worry, however, that if the entire PPACA is struck down, certain regulatory structures will be thrown into disarray. For example, the PPACA allows for generic versions of biologic drugs after 12 years of patent protections—a move that the industry supported, because the Obama administration had originally proposed shortening the exclusivity period to just seven years. And healthcare reform imposes up to $4 billion in new fees on drug and device manufacturers through 2018. "Of course, manufacturers also stand to gain millions of dollars in new revenue as a result of the expansion of coverage," says Topher Spiro, managing director for health policy at the Center for American Progress, a left-leaning think tank in Washington, DC.

A decision by the Supreme Court on the case, including whether the PPACA is an unconstitutional expansion of congressional power under the federal interstate commerce clause, is expected in June.

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favorable when the data were pooled. The company is now seeking a meeting with the US Food and Drug Administration to discuss the next steps.

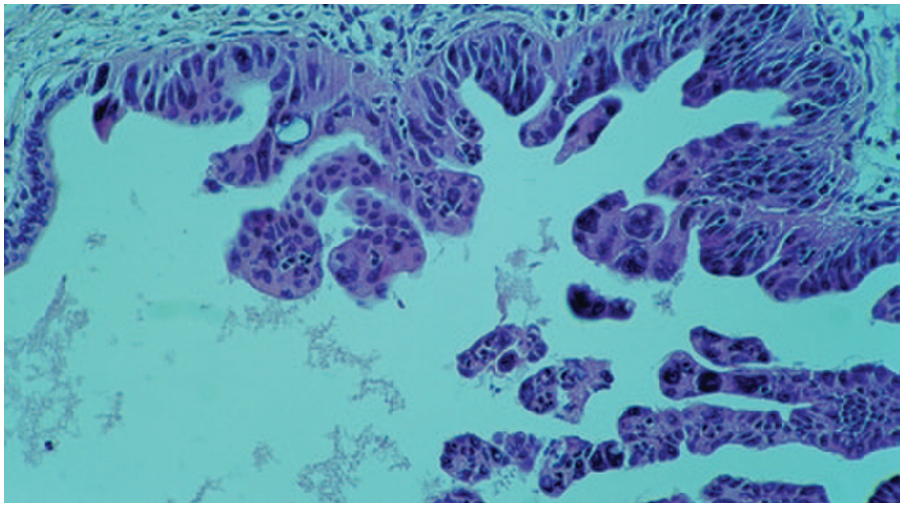
Going pro

Other cancer-killing prodrugs moving forward include Proacta's PR-104 and Allos Therapeutics' RH-1. Similar to TH-302, these drugs are converted into toxic molecules in hypoxic cells to make powerful DNA-damaging agents; oxygen inhibits this process, leaving most healthy cells untouched. Proacta is currently recruiting participants for a phase 2 study involving people with acute myeloid leukemia, and Colorado's Allos—which was acquired last month by Spectrum—recently finished a phase 1 trial testing its drug in subjects with advanced solid malignancies.

According to Martin Brown, a radiation oncologist at the Stanford University School of Medicine in California and a founding scientist at Proacta, these prodrugs could be used to treat "a very wide spectrum of tumors." However, he cautions that "there's absolutely no point in giving these drugs, which are bound to have some toxicities, to patients who don't have hypoxic tumors."

To that end, Wilson and his colleagues have been looking for molecular biomarkers that might help identify the people most likely to benefit from hypoxia-targeted therapy. Earlier this year, his team showed that a compound called 2-nitroimidazole EF5, which is currently in clinical development as a signpost of hypoxia, also flagged the enzymes that convert prodrugs into their active forms (*Clin. Cancer Res.* **18**, 1684–1695, 2012). "We are making real progress," Wilson says, "and the field is poised for major advances in the near future."

Melinda Wenner Moyer



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Elemental solution: Threshold Pharmaceuticals' drugs trialed for pancreatic cancer (shown here).