POLICY

Puerto Rico's statistics agency in jeopardy

Reorganization could threaten reliable, independent data about the island, critics say.

BY GIORGIA GUGLIELMI

JOE RAEDLE/GETTY

Changes loom for body that handles statistics such as hurricane damage.

Puerto Rico's senators last week approved a plan to overhaul an independent statistics agency tasked with coordinating the collection and analysis of crucial data on the island. The reorganization will wreck the US territory's ability to produce credible data about itself, including updated estimates of the death toll from last year's Hurricane Maria, critics of the plan say.

The decision paves the way for the restructuring of several government agencies, including the Puerto Rico Institute of Statistics (PRIS). To make it official, policymakers must now approve legislation dismantling the laws that established PRIS. Under Governor Ricardo Rosselló's plan to streamline government agencies, first introduced in January, PRIS would become an office in the Department of Economic Development and Commerce, which would contract the institute's duties to private companies.

But some fear that privatizing official statistics isn't in the island's best interests. "The private companies are going to be chosen by the government and we don't know how independent their leaders are going to be," says Mónica Feliú-Mójer, director of communications and science outreach at Science Puerto Rico, a non-profit group based in San Juan.

Another worry is that private companies might not distribute their data freely, or provide access to information on how they collected and analysed the numbers, says Steve Pierson, director of science policy at the American Statistical Association in Alexandria, Virginia.

Since PRIS began operating in 2007, it has worked to improve the quality of government agencies' statistics: the institute trains statisticians in new methodologies, ensures that data collection and analysis meet international standards and helps the agencies to make their data publicly accessible.

PRIS has improved tracking of Puerto Rico's mortality rate, and it established a fraud-prevention system related to the US Medicaid health-insurance programme, saving the government millions of dollars.

But Rosselló disputes the agency's effectiveness. PRIS "has failed in establishing efficient data gathering procedures that produce reliable statistics", says Alfonso Orona, the governor's principal legal counsel. He says that outsourcing data collection and analysis will help to address this.

It's likely that lawmakers will approve the legislation that would officially dismantle the institute, says Roberto Rivera, a statistician at the University of Puerto Rico at Mayagüez. Puerto Ricans are grappling with many issues, including the aftermaths of last year's hurricanes and a series of education and labour reforms, so PRIS is not a priority, he says. "If there's not enough pressure on the government, they'll get their way." ■

THERAPEUTICS

Promising cancer drug hits snags

Physicians struggle to identify which patients are likely to respond to cutting-edge therapy.

BY HEIDI LEDFORD

Cancer specialists in the United States had high hopes last year when they gained approval for a new approach to treatment: a drug that targeted certain tumours regardless of where they first appeared in the body.

But clinicians and researchers are struggling to put that plan into practice. Although the drug itself works well against a variety of tumour types, there have been problems with some of the tests used, which identify suitable tumours on the basis of certain molecular markers.

On 15 April at the American Association for Cancer Research annual meeting in Chicago, Illinois, researchers and representatives from the US Food and Drug Administration (FDA) will discuss how best to tackle the issue. "If you get a false negative result, you're not going to give that patient the therapy, which is terrible," says Zsofia Stadler, an oncologist at the Memorial Sloan Kettering Cancer Center in New York City. "That's why there's such a debate."

The drug in question, pembrolizumab (Keytruda), works by firing up the body's immune responses against tumours. First approved by the FDA in 2014 to treat melanoma, it has since been given the go-ahead to treat a handful of other cancers, including lung cancer.

But last year, researchers reported that patients whose tumours had a disabled DNA-repair system also responded to the drug, regardless of where the tumour originated ▶

(D. T. Le *et al. Science* **357**, 409–413; 2017). Damaged DNA can yield mutant proteins, which the immune system could target as potential invaders. Scientists think that this increases the chances that immune cells unleashed by pembrolizumab will find and attack the tumour.

In May 2017, the FDA allowed pharmaceutical giant Merck of Kenilworth, New Jersey, to market pembrolizumab to people with advanced-stage cancer who had any solid tumour with that particular DNA-repair defect. "This is absolutely a breakthrough approval," says Razelle Kurzrock, an oncologist at the University of California, San Diego. "We have seen some dramatic responses in our patients."

But the three kinds of test commonly used to look for DNA damage arising from that defect can produce conflicting results, says Heather Hampel, a genetic counsellor at the Ohio State University in Columbus. One relies on PCR, a process that amplifies specific regions of the genome; a second looks for certain proteins; and a third relies on DNA sequencing. "Which is the best? Is any positive on any test sufficient?" Hampel says. "Does that mean you should try them all? No one wants to miss a patient who might benefit from pembrolizumab."

And there are signs that some of the tests might work better in certain tissues than in others, says Shridar Ganesan, a physician and cancer researcher at the Rutgers Cancer Institute of New Jersey in New Brunswick. PCR assays, for example, look for changes in certain regions of DNA called microsatellites. Particular microsatellites might be more prone to damage in some tissues than in others, he says.

Stadler notes that the degree to which the DNA changes might also vary from tissue to tissue: colon cancers tend to accumulate many mutations, whereas tumours in the adrenocortex generally have fewer. That can lead to a false negative result in tissues with fewer mutations, she says.

"Which is the best? Is any positive on any test sufficient? Does that mean you should try them all?"

Similar complications might arise for some future tissue-agnostic drug approvals, particularly those based on DNA-repair defects. This could include drugs called PARP inhibitors, which are approved in the United States for breast and ovarian cancers caused by mutations in either of two genes involved in DNA repair: *BRCA1* or *BRCA2*. Researchers are looking at whether PARP inhibitors might also work in any solid tumour that carries similar DNA-repair defects, even if they aren't caused by *BRCA1* or *BRCA2* mutations. There are multiple tests available for identifying the patterns of DNA damage in such tumours, says Hampel.

Evidence has also been building that the overall number of mutations in a tumour could indicate how likely it is to respond to immunotherapies such as pembrolizumab. Tests for this might also be complex, notes Stadler.

Eventually, some of these issues will be ironed out, says Michael Overman, an oncologist with the University of Texas MD Anderson Cancer Center in Houston, as researchers gather data on which tests work best in which cancers. But the FDA was wise to move forward with the approval rather than wait for more evidence to sort out the issues with the molecular marker tests, he says. "There are still a lot of open questions, but the therapy works exceptionally well," he says. "It was the right thing to do." ■

CORRECTIONS & CLARIFICATIONS

The News story 'Alzheimer's study zeroes in on enigmatic protein' (*Nature* **555**, 567–568; 2018) misstated the radioactive marker that will be used in the tau scans. It is GTP1, not GPT1.

The News story 'Copyright reforms draw fire from scientists' (*Nature* **556**, 14–15; 2018) should have made it clear that when Vanessa Proudman talked of "that process" she was referring to how institutional repositories deal with copyright violations.