Clusters of stem cell–derived cardiac muscle cells model how the heart may respond to a new drug.

positives and false negatives, Gintant notes.

Better ways to predict how heart muscle will behave would allow drug developers to advance more candidates into trials and maybe avoid large-scale, late-phase ECG studies. Some drug companies and academic labs are already exploring whether channels other than hERG are good predictors of arrhythmia risk. They have also begun developing more realistic models of the human heart in a dish, using induced pluripotent stem (IPS) cells—reprogrammed adult cells capable of differentiating into many types of cells. The challenge now is to turn that new science into a well-validated, standard set of tests.

The CiPA initiative, a partnership between FDA and several agencies and consortia, including Health Canada, the European Medicines Agency, and Japan's National Institute of Health Sciences, is an attempt to do just that. One group within CiPA is investigating seven channels (including hERG) known to regulate heart rhythm to find which combination of channel-blocking tests might best predict safety. A second team is refining a computer model of the human ventricle's electrical behavior; it will turn ion channel data into estimates of arrhythmia risk. A third is testing how well clusters of IPS-derived heart muscle cells mimic the behavior of the adult heart when exposed to various drugs. Some predict that this stem cell approach, after much refining, could even eliminate the need to test individual ion channels.

In a first round of validation last year, academic and industry labs blindly exposed IPS-derived cells to eight different compounds. Data across study sites “looked surprisingly similar,” says Joseph Wu, a cardiologist and stem cell biologist at Stanford University in Palo Alto, California, who led one of the testing efforts.

A second round of FDA-funded tests for a set of 28 compounds began this month. By the end of next year, CiPA collaborators intend to propose the complete assay—a three-part process combining ion-channel assays, computer simulation, and IPS-derived cells—to a group within ICH that could choose to revise the 2005 standard.

Even with this new set of tools, companies may still decide that a compound that acts on multiple cardiac ion channels is too risky to pursue, says Icilio Cavero, a retired cardiovascular pharmacologist and safety consultant to drug companies who is based in Paris. And it will take more than these initial 28 compounds to prove that IPS-derived cells can be reliable safety predictors. “The idea [of CiPA] is beautiful,” Cavero says, but “new things scare everybody.”

## RESEARCH MISCONDUCT

### Duke fraud case highlights financial risks for universities

Whistleblower alleges doctored data were used to secure $200 million in grants from NIH and other federal agencies by a former colleague of Potts-Kant. It accuses the researcher, her former supervisor, and the university of including fraudulent data in applications and reports involving more than 60 grants worth some $200 million. If successful, the suit—brought under the federal False Claims Act (FCA)—could force Duke to return to the government up to three times the amount of any ill-gotten funds, and produce a multimillion-dollar payout to the whistleblower.

The Duke case “should scare all [academic] institutions around the country,” says attorney Joel Androphy of Berg & Androphy in Houston, Texas, who specializes in false claims litigation. It appears to be one of the largest FCA suits ever to focus on research misconduct in academia, he says, and, if successful, could “open the floodgates” to other whistleblowing cases.

False claims lawsuits, also known as qui tam suits, are a growing part of the U.S. legal landscape. Under an 1863 law, citizen whistleblowers can go to court on behalf of the government to try to recoup federal funds that were fraudulently obtained.

### Holding universities liable for research fraud

Whistleblowers have a mixed record of success in False Claims Act (FCA) lawsuits against research universities that involve allegations of scientific misconduct. Highlights from selected cases:

<table>
<thead>
<tr>
<th>YEAR</th>
<th>WHISTLEBLOWER</th>
<th>DEFENDANT</th>
<th>ALLEGATIONS</th>
<th>OUTCOME</th>
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<tbody>
<tr>
<td>2009</td>
<td>Taryn Resnick, former employee</td>
<td>Weill Medical College of Cornell University</td>
<td>In grants totaling $14 million, researcher Lorraine J. Gudas falsified data, failed to disclose other funding, and misapplied funding.</td>
<td>College settled for $2.6 million, plus attorneys’ fees and expenses.</td>
</tr>
<tr>
<td>2012</td>
<td>Daniel Feldman, fellowship program participant</td>
<td>Weill Medical College of Cornell University  and psychiatrist Wilfred van Gorp</td>
<td>Misuse of research training grant; deviated from submitted plan.</td>
<td>Defendants paid $887,714, plus $602,898.63 in attorneys’ fees and expenses.</td>
</tr>
<tr>
<td>2012</td>
<td>Kenneth Jones, researcher</td>
<td>Brigham and Women’s Hospital, Massachusetts General Hospital, and researchers Marilyn Albert and Ronald Killiany</td>
<td>Including falsified data in application for Alzheimer’s disease research grant.</td>
<td>Failed; whistleblower ultimately lost at trial.</td>
</tr>
<tr>
<td>2014</td>
<td>Terri King, former associate professor</td>
<td>University of Texas Health Science Center</td>
<td>Falsifying research data.</td>
<td>Failed; U.S. Supreme Court upheld lower court ruling that the public university was exempt from FCA liability.</td>
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Winners can earn big payoffs, getting up to 30% of any award, with the rest going to the government. Whistleblowers filed a record 75+ FCA cases in 2013, and last year alone won nearly $600 million. The U.S. government, meanwhile, has recouped more than $3.5 billion annually from FCA cases in recent years.

Relatively few of these cases have targeted research universities (see box, p. 977); many allege fraud in health care or military programs. But that’s changing. The FCA “is increasingly being used to target alleged fraud in a diverse array of industries, including research and academia,” says attorney Suzanne Jaffe Bloom of Winston & Strawn LLP in New York City. Although recent court rulings suggest public universities may have some protection from qui tam suits because they are government entities, private institutions do not. Eleven private universities, including Duke, are among the top 25 recipients of federal funding for academic science over the past decade.

The Duke case centers on allegations made by biologist Joseph Thomas, who, according to court documents, joined Duke’s cell biology department in 2008. In 2012 Thomas moved to the pulmonary division, where Potts-Kant worked under William Michael Foster investigating how pollutants affect the body’s airways. After Potts-Kant was placed on leave in 2013, the pulmonary division conducted an investigation of the data produced by Foster’s lab, according to the lawsuit. (Duke has not released the results of the investigation.) Investigators analyzed raw data, recalculated results, and reran experiments, according to the suit. Thomas, who says he participated in the review, claims that other reviewers and pulmonary division staff told him that Potts-Kant doctored nearly every experiment or project in which she participated. Sometimes, the suit alleges, she hadn’t exposed mice to the right experimental conditions or run the experiments at all. Other times, Thomas alleges, Potts-Kant had run the experiments but altered the data, tweaking them to match the hypothesis or boost their statistical significance.

Thomas, who no longer works at Duke, alleges that Foster and others at Duke were aware of concerns raised about Potts-Kant’s work even before the investigation began. There were obvious red flags, he contends. For example, she spent far less time completing a research task than required by an equally experienced researcher. And at least one outsider had raised questions about her data at a scientific meeting. But the university withheld the scope of what it knew from federal funding agencies as it filed reports on existing grants and applied for new ones, the lawsuit alleges.

Specifically, Thomas alleges that since 2006 Duke received at least 49 grants worth $82.8 million from the National Institutes of Health (NIH), the Environmental Protection Agency, and other agencies “that were directly premised on and/or arose from the research misconduct and fraud of Potts-Kant and/or the Foster lab.” And he alleges that the doctored data helped other institutions win 15 additional grants, worth $120.9 million, from NIH. (Those grants involved using the Duke lab for some research tasks.)

Foster did not respond to requests for comment on the case. Thomas—who is represented by his brother John Thomas of Gentry Locke LLP in Roanoke, Virginia—would not comment, and Potts-Kant could not be reached. In a statement, Duke spokesperson Michael Schoenfeld says that officials learned of the “discrepancies” in Potts-Kant’s data only after her embezzlement was discovered in 2013. “Even though the full scope of Ms. Potts-Kant’s actions were not known at the time, Duke notified several government agencies in June 2013 about the matter and immediately launched a formal scientific misconduct investigation, as required by federal law,” he stated. “Since then, Duke has provided extensive information to the government regarding the grants in question, and we will continue to cooperate with their investigation.” (The government has not joined the case, but could later.)

An attorney not associated with the case says it may face obstacles. Although the high number of retractions suggests that Thomas can meet the FCA’s requirement that “falsity” exists, it may be more difficult to show that the inclusion of fraudulent data was key to winning the grants, another essential aspect of an FCA case, says Torrey Young of Foley & Lardner LLP in Boston. “An important concept,” she says, is that “you can have research misconduct without having a false claim.”

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#### SCIENCE POLICY

**Congress faces a lengthy science to-do list**

#### 2017 spending to be delayed

**By Science’s News Staff**

Congress returns next week from a 7-week summer break with a lengthy list of unfinished business, some of great interest to the U.S. research community—and just a few weeks to tackle it. Lawmakers aren’t likely to pare that list by much before they leave next month to campaign in advance of the 8 November elections. They might give some issues a second look after the election, however, when they return for a lame duck session after the country has picked a successor to President Barack Obama and a new Congress.

The one big responsibility Congress can’t shirk is passing some kind of spending bill to keep the government running for the 2017 fiscal year, which begins on 1 October. But Republicans, who control both the House of Representatives and the Senate, don’t agree on whether to abide by an existing spending pact made with Obama, or to modify it to increase the defense budget and cut domestic programs. As a result, legislators this month are expected to put off a decision by temporarily extending 2016 spending levels into 2017 with a so-called continuing resolution (CR). The CR likely will fund the government through late December, allowing lawmakers to wait until they know whether they will be dealing with Hillary Clinton or Donald Trump before devising a final 2017 spending plan.

Practically speaking, a CR means the budgets of federal research agencies will be frozen: Administrators won’t be able to start new programs or benefit from the spending hikes envisioned in some preliminary appropriations bills等着 final action. They include a hefty proposed increase for the National Institutes of Health (NIH), another big boost for a NASA mission to a jovian moon, a new Coast Guard icebreaker that would enhance polar research, and a third mid-sized research vessel for the U.S. academic fleet. A CR also would leave
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Alison McCook

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