Nomination bungle leaves CIRM leadership in limbo

The architect of California's \$3 billion stem cell agency is set to keep his job for a little longer. Bob Klein—the man who co-wrote the ballot initiative that created the California Institute for Regenerative Medicine (CIRM) and then served as the agency's only chairman for the past six years—was reelected by its board of directors in a near-unanimous vote last month, meaning he will stay in his post for another six months while the organization regroups in its search for a suitable successor.

State officials tasked with nominating his replacement had originally tapped current vice-chairman Art Torres as well as Alan Bernstein, executive director of the New York-based Global HIV Vaccine Enterprise as possible successors. But Bernstein, a Canadian national, was forced to pull out of the race at the beginning of December because of a state law requiring the head of a public agency to hold US citizenship, and Torres, a former state senator, withdrew his nomination a week later. As a result, Klein effectively became a shoo-in for the post.

Under the terms of the agency's statute, the board members' reappointment of Klein means he could serve as chairman for another six-year term. But the board also passed a motion calling on Klein to find a

No exit: Klein stays a little longer.

replacement and step down within 180 days, if not sooner.

"I'm going to be aggressively trying to find a replacement," Klein told *Nature Medicine*. "Going forward here, we're going to have the time to go through a process to define the criteria" for the next chairman. Klein insists that he didn't intend to remain chairman and has agreed to stay on an unpaid, temporary basis.

Not everyone was happy with this scenario. In a strongly worded letter sent two days

before the board's vote, state controller John Chiang urged the CIRM board members to delay their decision and start anew with fresh nominees. "It is clear that the current selection process is fundamentally flawed," Chiang wrote. "The taxpayers who provide the funds for CIRM must be assured that the chair and vice chair are selected in an open, transparent process—not through a backroom deal or by default because a deal has fallen apart."

"This path that they've gone down is a face-saving path for Klein, who screwed up this election by trying to manipulate it and tap his own successor," says John Simpson, stem cell project director of the Santa Monica, California-based advocacy group Consumer Watchdog. "He needs to let go and let the board step up and exercise its oversight responsibilities without constantly trying to pull the strings."

Bernstein's name is not necessarily off the table. According to Klein, the 1978 attorney general decision ruling the requirement of US citizenship for holding public office may be unconstitutional. The state attorney general's website states that such opinions "have been accorded 'great respect' and 'great weight' by the courts," but they do not technically define the law.

Elie Dolgin

Conference brings Asia-Pacific research funding scheme closer

For several years, the idea of a multinational funding scheme to support research in the Asia-Pacific region has been brewing. Finally, at the biannual Australian Health and Medical Research Congress late last year, policymakers publicly discussed the merits and challenges of such a venture for the first time.

The congress in Melbourne, convened by the Australian Society for Medical Research (ASMR), attracted about 1,500 delegates from 18 countries. Dignitaries at the November event included Australia's minister for mental health and aging and the acting consul-general of Japan.

Alison Butt, who held the post of ASMR president until the congress, says that with the numbers of scientists in countries such as China overtaking numbers in the US, the Asia-Pacific region should combine forces to nurture the growth of local medical research.

"The Society feels that there are enormous benefits to collective schemes that will fund projects that combine the region's scientific resources and capabilities," she says. "We have evidence for economic gains in health and

medical research that extend from reducing disease burden and associated healthcare costs to minimizing work absence. There's also a case to be made in ensuring there's a critical mass of appropriately trained scientists to meet industry demands." The EU's Framework Programme funding scheme is held up as one potential model of multinational collaboration. The Framework Programme, now in its seventh iteration, has a budget of €50 billion (\$66 billion), of which a little bit less than 10% is allocated for health research. The 27 EU member nations commit approximately 3% of their GDP to the scheme, on average.

The scale of funding for the proposed Asia Pacific Health and Medical Research Funding Union (APHMRFU) was not discussed in detail, but it would most likely be pegged to a percentage of GDP. ASMR plans to issue a statement and will begin preparing a proposal for the Asia Pacific Parliamentary Forum in early 2012.

"Asia's population is aging more rapidly than in the rest of the world; in some countries the number of people over 65 is increasing at 3% per year—twice the rate in most Western

Drug developers explore vitamin D benefits without the vitamin

Late last year, the US Institute of Medicine released a report stating that research claiming any benefits from vitamin D beyond building strong bones is “inconsistent and inconclusive.” Although inert vitamin D supplements have yet to prove their worth, new research is increasingly showing that active analogs of the molecule can help fight a number of diseases, including cancer and chronic kidney failure.

Physicians already prescribe one such drug—calcitriol, an active form of vitamin D first synthesized in the 1970s—to treat rickets, psoriasis and vitamin D deficiencies sometimes seen with kidney disease.

But there is a drawback to calcitriol: high doses can lead to a surfeit of calcium in the blood, a condition known as hypercalcemia. So investigators have been working to develop other vitamin D analogs that minimize this risk while maximizing the benefits.

Over the past two decades, various labs have synthesized thousands of such analogs with molecular structures that differ slightly from calcitriol. “Analogues have been tweaked at every possible chemical ‘intersection,’” says Donald Trump, chief executive of the Roswell Park Cancer Institute in Buffalo, New York.

Some of the analogs have been designed to bind the receptor less tightly, although this compromises their efficacy. Another way to make better vitamin D drugs would be to

develop analogs that have a different half-life in the blood or by finding coactivators of the receptor that only function in certain tissues, says Glenville Jones, a biochemist at Queen's University in Kingston, Ontario, and an author on the IOM's vitamin D report.

To date, clinical research on calcitriol and its analogs has focused mainly on treatment of cancer. In 2002, a company called Novacea (now Transcept) developed a formulation of calcitriol called DN-101. The drug seemed to work well in a phase 2 clinical trial of patients with prostate cancer—those who received the drug plus chemotherapy survived longer and had fewer side effects than those who received chemotherapy alone (*J. Clin. Oncol.* 25, 669–674, 2007). But DN-101 faltered in the phase 3 trial, which was subsequently halted in November 2007.

More recent trials have also failed to meet expectations. This past July, researchers from the MD Anderson Cancer Center in Houston reported that their vitamin D analog ILX23-7553 failed to provide the result they'd hoped for in a phase 1 trial of patients with solid tumors (*Invest. New Drugs*. doi:10.1007/s10637-010-9492-5, 2010).

“So far, no clinical trial has been so positive that it has caused a sea change in cancer treatment,” Jones says.

Still, several companies are working on

The sunny side: vitamin D stimulates cells.

new vitamin D analogs. At the Symposium on Molecular Targets and Cancer Therapeutics in Berlin this past November, researchers from the Georges Pompidou European Hospital in Paris reported that one analog of vitamin D caused a promising drop in levels of prostate-specific antigens in a phase 2 trial involving 54 men who had prostate cancer that was resistant to hormone therapies.

Meanwhile, the Toronto-based company Receptor Therapeutics has developed its own special formulation of calcitriol—Onco-D102—and plans to test whether it can enhance survival in people with cancer when combined with standard chemotherapy. “There’s still a lot of skepticism,” says Joseph Elliot, the chief executive of Receptor Therapeutics. But “we think we can get it right.”

Cassandra Willyard

countries. And Asia is usually the origin of infectious disease pandemics,” says Colin Blakemore, former head of the UK's Medical Research Council who holds appointments at Oxford University in the UK and A*STAR (Singapore's Agency for Science Technology and Research). “These are just a few of the areas in which everyone could gain from collaborative research efforts.”

Prerequisite discussion

Bob Williamson, secretary for science policy at the Australian Academy of Science, believes that requiring cross-country collaborations such as those required by the EU's Framework Programme should also be a prerequisite for a proportion of APHMRFU grants.

“They force the best scientists from countries who have not traditionally participated in science at the highest levels to work together in the international arena,” Williamson says.

Enric Banda, president of Euroscience, an organization similar to the American Association for the Advancement of Science, says that this aspect of the EU's Framework Programme has been successful. But he points to the European Research Council, formed in 2007, which bases its decisions purely on scientific excellence, as another possible funding mechanism,

saying “the ideas and priority areas that are being funded aren't politically motivated; the researchers are involved in the decision making.”

Mechanisms aside, the Asia Pacific region lacks an EU-style political center, which may be a potential barrier to the formation of the proposed APHMRFU, particularly when it comes to financing.

The problem of co-funding international grant schemes is evidenced by the Human Frontiers Science Program (HFSP), conceived by Japan and founded in 1989. Its aim of funding intercontinental cross-disciplinary teams is similar to the proposed APHMRFU, but it has a narrower scope and different agenda, giving room for coexistence.

Japan expected that many countries would join and share the cost. Indeed thirteen individual countries and the EU now fund the HFSP. Australia, which joined in 2004, contributes approximately 1% of the \$60 million budget. Japan, however, remains the primary contributor—currently providing just over half of the total funds.

Given this history, Butt explains that the new APHMRFU venture “has to be truly inclusive and collaborative to succeed; it cannot be driven by a single nation.”

Branwen Morgan