SCIENTIFIC MISCONDUCT

Former star surgeon’s disgrace rocks Swedish science

Investigations into the Paolo Macchiarini scandal highlight misconduct and institutional failings

By Gretchen Vogel

What seemed a coup has turned into a nightmare for Sweden’s most prestigious university, the Karolinska Institute (KI). In 2010, KI and its associated hospital in Stockholm managed to recruit star surgeon Paolo Macchiarini, who had made international headlines when he implanted artificial windpipes into patients. With his groundbreaking tissue engineering work, KI leaders hoped he would propel the university to the top of a hot field.

Instead, Macchiarini has plunged Swedish science and KI into their most serious misconduct scandal in decades, with allegations ranging from faking scientific data to subjecting patients to a risky procedure without the necessary approvals, in at least two cases leading to their deaths. Over the past 2 weeks, four investigations have released their damning findings. One confirms that Macchiarini committed misconduct, and the other three paint an unflattering image of the roles KI and the hospital have played in the affair. The entire episode “is a sad failure of the academic community to take care of its own mistakes,” says Hans Rosling, a retired international health professor at KI.

The case has already led to a wave of resignations and dismissals, both at KI and the Nobel Assembly, the august body of 50 KI professors that selects the winners of the Nobel Prize in Physiology or Medicine. But restoring trust won’t be easy. A recent survey by a leading Swedish polling company found that KI’s reputation had plunged as a result of the scandal.

Macchiarini created artificial tracheae to help patients with a missing or damaged windpipe. He “seeded” them with a patient’s own stem cells, hoping the cells would proliferate and cover the artificial scaffold to create a fully functional organ. But the implants didn’t work. Two of his Stockholm patients died; a third has been in intensive care since 2012. Several Russian recipients died as well.

In 2014, colleagues from the hospital asked KI to investigate possible misconduct in Macchiarini’s papers and in the ethics and consent documents for the surgeries. The recipients were not as seriously ill as Macchiarini claimed, they said, and his descriptions of patients’ improvement after surgery were falsified. KI officials asked Bengt Gerdin, a retired professor of surgery at Uppsala University in Sweden, to investigate. Gerdin found that the allegations had merit, but KI stood by its wunderkind: In August 2015, then-Vice-Chancellor Anders Hamsten said that Macchiarini’s rebuttal to the report was convincing and dismissed the charges.

The case was rekindled in January by a three-part TV documentary that painted a troubling picture of Macchiarini’s treatment of patients in Sweden and Russia and the way KI had handled the allegations. After the final episode aired, KI announced it would cut ties with Macchiarini when his contract ended in November and asked the Swedish Central Ethical Review Board (CEPN) to reinvestigate the misconduct charges. It also commissioned an independent investigation into its own role, as did the hospital. In March, the university disciplinary board decided it had learned enough about Macchiarini’s conduct to fire him.

The hospital’s report was made public...
on 31 August, and KI’s own report a few days later. Both concluded that Macchiarini should never have been hired; administrators ignored “strikingly negative” references from Macchiarini’s previous employers as well as irregularities in his CV. Once he was on board, the reports found, loose oversight allowed him to skirt ethical regulations. “There was a stunning lack of interest in learning more about his work before extending his contract,” said Sten Heckscher, a former president of Sweden’s Supreme Administrative Court who headed the KI investigation.

In response to the reports, Swedish Minister for Higher Education and Research Helene Hellmark Knutsson fired the country’s chancellor in charge of all public universities, Harriet Wallberg-Henriksson, who was KI’s vice-chancellor when Macchiarini was hired. The minister also dismissed all remaining KI board members who were active during Macchiarini’s tenure. (Five board members had already stepped down.) Nobel Assembly leaders asked Wallberg-Henriksson and Hamsten to resign.

Meanwhile, a CEPN report issued on 9 September found scientific misconduct in a paper on rat esophagus implants that Macchiarini published in *Nature Communications* in 2014. Among other problems, the panel found no data to support the claim that the recipient animals had recovered and gained weight. (The journal says it’s investigating.) As *Science* went to press, the agency was about to release another report, on papers describing the artificial scaffolds. Conclusions about two key *The Lancet* papers describing successful human implant surgeries are expected later this year.

Macchiarini, who faces criminal inquiries, including possible manslaughter charges, did not respond to *Science’s* requests for comment last week. Swedish television, however, reported on 5 September that he again denied any wrongdoing.

Swedish scientists are left wondering how things went so terribly wrong. Macchiarini was exceptionally persuasive, notes Anders Ekbom, a clinical epidemiologist at KI. In January, *Vanity Fair* reported that Macchiarini had told an NBC news producer with whom he had an affair that he had treated many world leaders, including two popes; he also convinced her that Pope Francis would marry them. Rosling says the *Vanity Fair* story helped KI leadership see that they, too, had been deceived: “It pinpointed that there was a deep personality problem with Macchiarini.”

Another part of the problem, according to the KI report, was “a growing fixation on excellence” at the university and “the aspiration to close the gap between research and its application in healthcare.” The fixation is natural, Rosling says: “There is nothing more wasteful and boring than mediocre research. We need spectacular new research findings.” He says. But although hiring Macchiarini may have been understandable, he says, “the serious thing here is the failure to rectify the mistake.”

Ekbom hopes the dismissals and resignations will give KI a fresh start. “If something good comes out of it—better routines, better safety—the net outcome after this drama will be a better Karolinska,” Gerdin adds. “That is what we hope.”

### Cystic fibrosis foundation opens drug discovery lab

**Funded by a drug royalty bonanza, lab seeks novel ways to target mutations**

By Bijal P. Trivedi

The Cystic Fibrosis Foundation (CFF) is once again breaking new ground. In 2000, with little beyond symptomatic relief available for the inherited, life-threatening condition, the Bethesda, Maryland–based foundation hired a biotech company to develop more effective treatments. The move, unprecedented for a disease advocacy organization, paid off in two new drugs, the first to target the molecular root of the disease. But there is still no cure, and cystic fibrosis (CF) patients continue to die—467 in the United States alone in 2014. So on 19 September, the foundation is setting another precedent by officially opening its own independent laboratory in Lexington, Massachusetts, to speed drug development, funded primarily from the success of the two drugs it helped bring to fruition.

The goal of the new CFF Therapeutics Lab, says Preston W. Campbell III, the foundation’s CEO and president, is to generate and share tools, assays, and lead compounds, boosting its partners’ chances of finding treatments. Frustration with academic technology transfer agreements was a key motivation, he notes. University-based researchers funded by the foundation have to seek approval from their institution’s legal department before sharing assays, cells, or any intellectual property, a hurdle that can take a year to negotiate. “This was killing us,” Campbell says, “[but] if we created our own laboratory, we could focus on the things we wanted to focus on, we could also share them freely.”

Margaret Anderson, executive director of FasterCures, a Washington, D.C.–based think tank and arm of the Milken Institute, believes other disease philanthropies will be watching the experiment. “I’m excited ... and I would venture to say that the disease foundation community is going to be excited about it, too.”

CF, which afflicts 30,000 people in the...
Former star surgeon's disgrace rocks Swedish science

Gretchen Vogel

Science 353 (6305), 1193-1194.
DOI: 10.1126/science.353.6305.1193