What pushes scientists to lie? The disturbing but familiar story of Haruko Obokata

https://www.theguardian.com/science/2015/feb/18/haruko-obokata-stap-cells-controversy-scientists-lie

The spectacular fall of the Japanese scientist who claimed to have triggered stem cell abilities in regular body cells is not uncommon in the scientific community. The culprit: carelessness and hubris in the drive to make a historic discovery.

John Rasko and Carl Power

The year 2014 as one of extremes for Haruko Obokata. A year of high highs and even lower lows. Barely 30 years old, she was head of her own laboratory at the Riken Center for Developmental Biology (CDB) in Kobe, Japan, and was taking the male-dominated world of stem cell research by storm. She was hailed as a bright new star in the scientific firmament and a national hero. But her glory was short-lived and her fall from grace spectacular, completed in several humiliating stages.

Obokata shot to prominence in January 2014 when she published two breakthrough articles in Nature, one of the world's top science journals. She and her colleagues had demonstrated a surprisingly simple way of turning ordinary body cells – she used mouse blood cells – into something very much like embryonic stem cells. All you need to do is drop them into a weak bath of citric acid, let them soak for half an hour and – presto! – you have washed away their developmental past. They emerge like cellular infants, able to multiply abundantly and grow into any type of cell in the body, a superpower known as pluripotency. This was a much faster and easier way to reprogram cells than the one pioneered, back in 2006, by another Japanese scientist, Shinya Yamanaka. Moreover, Obokata's method seemed much less likely to damage the cells or, worse still, make them cancerous.

Because Yamanaka had won a Nobel Prize, journalists wondered whether Obokata would soon get one herself. And because she was a young woman, they also needed to know how she decorated her laboratory (she painted it pink and yellow and stuck cartoons everywhere), what she wore at work (not a lab coat but a cooking apron – a *kappogi* – which her grandmother had given her) and what she did after hours (fed her pet turtle, took baths, shopped and went on dates).

But Obokata had little time to enjoy success. Within days of her two Nature papers being published, disturbing allegations emerged in science blogs and on Twitter. Some of her images looked doctored, and chunks of her text were lifted from other papers. Riken soon began an investigation and, on 1 April, announced its findings: Obokata was guilty of scientific misconduct.

Public shaming soon followed. The news media, having built her up, was more than happy to tear her down. A tearful Obokata faced a gruelling press conference, broadcast live on TV. Standing amongst a battery of microphones, strobe-lit with camera flashes, she apologised, bowed, answered questions, bowed, apologised some more, and bowed.

Obokata apologised for many things that day. She apologised for "insufficient efforts, ill-preparedness and unskilfulness", for errors of methodology and sloppy data management. They were all, she said, "benevolent mistakes", due to her youth and inexperience. But she denied fabricating her results and was shocked that the Riken investigators would say that she "sorely lacks not only a sense of research ethics, but also integrity and humility as a scientific researcher". Above all, she maintained that her Stap ("stimulus-triggered acquisition of pluripotency") cells really do exist.

However, the existence of Stap cells grew ever more doubtful. Despite the apparent simplicity of Obokata's method, no one else was able to make it work. Initially her collaborators stood firmly by her, but one by one they relented and asked Nature to retract the articles. Finally, in June, so too did Obokata. And with the retraction came the most damning piece of evidence yet: genetic analysis showed that the Stap cells didn't match the mice from which they supposedly came. Through her lawyer, Obokata said she couldn't understand how that was possible. But the obvious, and rather depressing, explanation is that her so-called Stap cells were just regular embryonic stem cells that someone had taken from a freezer and relabelled.

Some complain that Riken made a scapegoat of Obokata in order to contain the crisis. True, it cleared her senior co-authors of dishonesty; however, it gave them a brutal drubbing for not properly checking her work. Riken also admitted that its whole system of oversight had failed and promptly set about overhauling the CDB from top to bottom, stripping away half of its 500-odd staff, renaming it and installing a new management team.

One of those singled out for criticism was Yoshiki Sasai, deputy director of Riken and Obokata's supervisor. A well-respected stem cell scientist, Sasai was, in his own words, "overwhelmed with shame". In early August, after a month in hospital for depression, the 52-year-old committed suicide in a stairwell at a research facility opposite the CDB, leaving behind three farewell notes. The one he addressed to Obokata contained this plea: "Be sure to reproduce Stap cells."

Indeed, Riken offered Obokata an opportunity to honour Sasai's dying wish. Rather than fire Obokata, Riken decided to keep her on, allowing her – under very strict supervision – to help a team of researchers reproduce her work. That way, the efforts at verification would not lack Obokata's expertise and would have the best possible chance of success. In December, however, after eight months of effort, the verification team admitted defeat and Obokata, claiming to be "extremely perplexed" by these results, at long last resigned.

The year ended with Riken's final report on the matter. It found that Obokata had falsified and fabricated data, that her so-called Stap cells were actually embryonic stem cells, and that the mixup was probably not accidental – though it lacked definitive proof that Obokata had committed this mortal sin of science.

And just like that, Obokata had joined the ranks of some very distinguished biomedical fraudsters.

Hwang Woo Suk, for instance. In 2004, this charismatic, square-jawed scientist from Seoul National University became the pride of South Korea when he claimed he had created the first human embryonic stem cells by means of cloning. His smiling face was on the front page of newspapers worldwide, and Koreapost issued a commemorative stamp in his honour. Since cloning is a form of cellular reprogramming, Hwang's work generated the same kind of excitement as Obokata's. Both promised the holy grail of regenerative medicine: patient-specific stem cells capable of repairing any damaged tissue or organ in the body. But an investigation by Hwang's university proved his results were as bogus as Obokata's. None of his 11 "cloned" stem cells matched their supposed donors.

Over the past century, the "wet lab" (where scientists carry out biological experiments) has seen more than its share of scandal. Indeed, modern cell science emerged from a terrible debacle.

The man in the middle of it all was Alexis Carrel, a brilliant and rather dapper Frenchman working at the Rockefeller Institute in New York. Carrel discovered that, if you remove some cells from the body, sit them in a nutritious broth and handle them correctly, they can not only survive, but thrive and multiply. Also, if you take some cells from one culture, you can start a new one and, with that, a third, and so on. The importance of this technique – know as cell "passaging" – can't be overstated. With it, Carrel literally opened a new era in cell research. Unfortunately, he did so with an experiment that, while earning him international superstardom, proved to be a complete and utter train wreck.

On 17 January 1912, Carrel removed a chick embryo from its egg and cut out a small fragment of its still-beating heart with the aim of keeping it alive as long as possible. He had hardly begun this experiment when he announced to the world that his chicken heart culture was immortal, that immortality belonged potentially to all cells, and that death was only the consequence of how cells are organised in the body. In other words, the secret of eternal life is within us all, an attribute of our basic biological building blocks. It captured the public's imagination and was soon accepted by the scientific community.

Carrel and his assistants kept – or claimed they had kept – that culture alive for 34 years, which is five times longer than the average chicken. For many years, around 17 January, journalists wrote birthday stories on the chicken heart and wondered how large it would have grown had Carrel nurtured every one of its ever-multiplying cells. (According to calculations, it swiftly dwarfed the Earth and filled up the entire solar system.)

The problem was, no one else could keep a cell culture alive indefinitely. Lab after lab tried and failed, decade after decade. Because Carrel was a giant in the field of cell research and a Nobel Prize winner, few dared to doubt him. Scientists blamed themselves when their cells died. They assumed that they lacked the master's skill, that his lab had higher standards than they could reach, that they had somehow exposed their cells to infection or failed to keep them properly nourished. We now know that the reverse was true. Other researchers probably couldn't duplicate Carrel's results because they weren't incompetent or dishonest enough.

It was only in the mid-60s – half a century after Carrel established his chicken heart culture – that the dogma of cell immortality came crashing down. That's when Leonard Hayflick, an ambitious young researcher at the Wistar Institute in Philadelphia, discovered that ordinary body cells have a finite life span – or, more precisely, an average number of times they can multiply in vitro. This is their Hayflick number. For chickens, it is 35. In other words, a population of chicken cells can double about 35 times before they die, which usually takes several months.

By the time Hayflick proved this, Carrel was long dead and his "immortal" chicken cells discarded. Which means that we know Carrel's most famous experiment was a sham, but not why. If it was fraud, it was one of the most outrageous cases in the history of science. However, the cause may have been carelessness rather than dishonesty. Carrel and his staff used "embryonic juice" as a culture medium and, if they prepared it badly, it might have contained live chick cells. In that case, instead of just feeding their culture, they re-seeded it. It's an easy enough mistake, but to make it consistently enough to keep their chicken heart cells alive for 34 years suggests an astonishing degree of negligence.

Reproducibility is one of the cornerstones of modern science. Unless an experiment can be repeated again and again by different researchers, each time yielding similar results, it can't be said to prove anything much. At least that's the theory. Carrel's chicken heart experiment shows how far science can stray from the scientific method. And the fault doesn't just lie with Carrel and his laboratory. The entire scientific community shares some of the blame because it upheld the dogma of cell immortality for more than 50 years despite the fact that it was based on a single, sensational, irreproducible experiment.

By contrast, the speed of Obokata's undoing should make us feel more confident about the ability of science to correct itself. As soon as she announced the creation of Stap cells, other researchers tried to make their own and, when they failed, wanted to know why. Without doubt, the standards of cell science have improved since Carrel's day. Biomedical research is more strictly regulated, and wet lab procedures better established. The internet has also played its part, making it faster and easier for scientists to compare notes and spot errors.

But before we start to congratulate ourselves on the ever-upwards path of science, we should bear in mind that most experiments are never reproduced. There are simply too many of them. Besides which, researchers often don't have much interest in repeating the work of others. Scientists may be truth-

seekers, but they generally prefer new truths. They want to be the first to make a discovery. That's where all the glory lies; that's how to get a name for yourself, attract more funding and advance your career. Confirming – or failing to confirm – someone else's discovery is unlikely to get you very far. It's unlikely to even get you into print since science journals tend to favour novel research.

Not only are most experiments not reproduced, most are probably not reproducible. This statement will shock only those who have never worked in a wet lab. Those who have will already suspect as much.

A few years ago, Glenn Begley put this suspicion to the test. As head of cancer research for pharmaceutical giant Amgen, he attempted to repeat 53 landmark experiments in that field, important work published in some of the world's top science journals. To his horror, he and his team managed to confirm only six of them. That's a meagre 11%. Researchers at Bayer set up a similar trial and were similarly depressed by the results. Out of 67 published studies into the therapeutic potential of various drugs (mostly for the treatment of cancer), they were able to reproduce less than a quarter.

The Amgen and Bayer studies were too small to tell us how bad the problem really is, but they do illustrate something that biomedical researchers already know in their heart of hearts: reproducibility is the exception rather than the rule. There are probably many reasons for this. Apart from outright fraud, there are all those "benevolent mistakes" that scientists make more or less unwittingly: poor experiment design, sloppy data management, bias in the interpretation of facts and inadequate communication of results and methods. Then, of course, there is the devilish complexity of reality itself, which withholds more than it reveals to the prying eyes of science.

All of which should have provided Obokata with plenty of cover. Aside from her lack of "integrity and humility as a scientific researcher", what did she do wrong? Assuming that she falsified not only her data but the very existence of Stap cells – and it's difficult to believe otherwise – why didn't she succeed?

Two obvious reasons spring to mind. First, unbelievable carelessness. Obokata drew suspicion upon her Nature papers by the inept way she manipulated images and plagiarised text. It is often easy to spot such transgressions, and the top science journals are supposed to check for them; but it is also easy enough to hide them. Nature's editors are scratching their heads wondering how they let themselves be fooled by Obokata's clumsy tricks. However, we are more surprised that she didn't try harder to cover her tracks, especially since her whole career was at stake.

Second, hubris. If Obokata hadn't tried to be a world-beater, chances are her sleights of hand would have gone unnoticed and she would still be looking forward to a long and happy career in science. Experiments usually escape the test of reproducibility unless they prove something particularly important, controversial or commercialisable. Stap cells tick all three of these boxes. Because Obokata claimed such a revolutionary discovery, everyone wanted to know exactly how she had done it and

how they could do it themselves. By stepping into the limelight, she exposed her work to greater scrutiny than it could bear.

But perhaps hubris is the wrong term. While some stem cell researchers may indeed possess that "vaulting ambition" characteristic of Shakespeare's tragic heroes, from what we have read and witnessed firsthand, scientific fraud rarely springs from a heroic, all-or-nothing decision. It is more like a bad habit you acquire, a gentle slope you descend without realising how deep you're getting.

It all starts with a temptation, one that every scientist faces and to which quite a few succumb. (In anonymous surveys, almost 2% of scientists actually admitted to falsifying data at least once in their careers, and about 14% had witnessed others doing so.)

Imagine it: you have sunk many long hours into your experiment, growing, manipulating and testing cells in various ways, all with a certain hypothesis – a hunch – in mind. You really want to prove that your hunch is right, that the money invested into your work was well spent, and that you aren't just frittering your life away in a white coat, in a white room, under fluorescent lights. And of course, you want to get ahead in a competitive field, where the pressure to perform can be intense. But you get your results and they are disappointing. You can see straightaway what the data should look like and how, with just a tweak, you can improve them. All you need to do is count something a little creatively, shift a point on a graph or touch up an image. If you get rid of the original data, no one will ever be the wiser. And maybe your hunch is right anyway. Surely it is. You will find more proof – *real* proof – sooner or later if you just keep looking.

But once you start fiddling with the facts, it's hard to stop. In part, that's because you have done some reality-testing and discovered just how easy it is to fool your colleagues. In part, too, you have enjoyed their admiration and your improved chances of being published, promoted and otherwise funded. Maybe you even enjoyed the risk. But things get progressively more complicated. You are now expected to build on your past success, which means adding fiction upon fiction while making sure that the whole contrivance fits neatly together. And as your project thrives, more people will climb on board, and you will have to micromanage their contributions and their perceptions of what is going on. The upside is that their good reputations will lend your work added credibility. The downside is that you will have more eyes peering over your shoulder.

It seems that Obokata was adept at playing this game. She recruited some highly respected figures in the field of cloning and stem cell research and handled them so well that, when questions were first raised about her work, they immediately jumped to her defence, declaring that they had independently verified her work. That is probably what they believed. However, the subsequent investigation revealed that Obokata had always helped her Riken colleagues in their efforts at verification.

And what of Obokata's US colleagues? More particularly, what of Charles Vacanti, the chief co-author of the now-discredited Stap cell papers?

This charming, silver-haired midwesterner, who headed the anesthesiology department at Brigham and Women's Hospital in Boston, did almost as much to confuse the issue of replication as Obokata herself. From the start, Vacanti claimed that he had been able to create Stap cells, including human ones, though he offered no evidence. What he did offer, however, was his own special recipe, which he posted online in mid-March (around the time that Riken first declared Obokata guilty of misconduct), assuring the scientific community that if he could make Stap cells, anyone could.

Unfortunately, that humble boast backfired. No one else could get his recipe to work. Many hoped that Vacanti would toil night and day until he proved the existence of Stap cells, but instead, last September, he left Brigham for a year's sabbatical. Had he lost faith in Stap cells? Apparently not. As a parting gesture, Vacanti posted an improved recipe which, he said, "should increase the likelihood of success". So far, the new recipe seems no better than the old one.

Vacanti's role in this scientific debacle is especially intriguing because Stap cells originally sprang from his fertile imagination. For well over a decade, he had been working on a hunch that pluripotent stem cells exist in all mammalian tissue, ready to swing into action whenever needed. It was a big, bright, potentially career-defining idea which for a long time Vacanti couldn't sell. He lacked conclusive proof. He also lacked credibility. After all, he was not a stem cell scientist but an anesthesiologist and tissue engineer best known for grafting an artificial ear on to the back of a mouse (the infamous Vacanti earmouse).

Then, in 2008, Obokata joined his lab as a graduate student, bringing with her the skill set and credentials he sorely needed. Thus began a partnership that continued after Obokata returned to Japan. With her help, Vacanti repeated his earlier experiments and revised his hypothesis: mammalian tissue doesn't so much maintain a reserve of pluripotent stem cells; it creates them when put under stress by injury or disease. Stap cells were supposed to confirm this hunch, being the laboratory equivalent of stem cells spontaneously produced by the body.

Did Obokata begin cooking data in order to please her supervisor? Did Vacanti ever suspect that her results were too good to be true? Whatever the case, the Stap cell scandal is their monster child.

It makes you wonder why Vacanti hasn't been dragged over hot coals like Obokata and her Japanese colleagues, and why Brigham hasn't followed Riken's example by publicly flogging itself.

The answer is simple: in the US, investigations into scientific misconduct usually take place under a veil of secrecy. In all likelihood, Brigham has begun its own inquiry but, in stark contrast to the one carried out by Riken, we probably won't learn anything about it – even the fact of its existence – until after a verdict is reached.

The Stap cell case is not yet closed.

Whistleblower sues Duke, claims doctored data helped win $200 million in grants

http://www.sciencemag.org/news/2016/09/whistleblower-sues-duke-claims-doctored-data-helped-win-200-million-grants

By Alison McCook, Retraction Watch

On a Friday in March 2013, a researcher working in the lab of a prominent pulmonary scientist at Duke University in Durham, North Carolina, was arrested on charges of embezzlement. The researcher, biologist Erin Potts-Kant, later pled guilty to siphoning more than $25,000 from the Duke University Health System, buying merchandise from Amazon, Walmart, and Target—even faking receipts to legitimize her purchases. A state judge ultimately levied a fine, and sentenced her to probation and community service.

Then Potts-Kant's troubles got worse. Duke officials took a closer look at her work and didn't like what they saw. Fifteen of her papers, mostly dealing with pulmonary biology, have now been retracted, with many notices citing "unreliable" data. Several others have been modified with either partial retractions, expressions of concern, or corrections. And last month, a U.S. district court unsealed a whistleblower lawsuit filed 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. Winners can earn big payoffs, getting up to 30% of any award, with the rest going to the government. Whistleblowers filed a record 754 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, below); 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.

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:

YEAR	WHISTLEBLOWER	DEFENDANT	ALLEGATIONS	OUTCOME
2009	Taryn Resnick, former employee	Weill Medical College of Cornell University	In grants totaling $14 million, researcher Lorraine J. Gudas falsified data, failed to disclose other funding, and misapplied funding.	College settled for $2.6 million, plus attorneys' fees and expenses.
2012	Daniel Feldman, fellowship program participant	Weill Medical College of Cornell University and psychiatrist Wilfred van Gorp	Misuse of research training grant; deviated from submitted plan.	Defendants paid $887,714, plus $602,898.63 in attorneys' fees and expenses.
2012	Kenneth Jones, researcher	Brigham and Women's Hospital, Massachusetts General Hospital, and researchers Marilyn Albert and Ronald Killiany	Including falsified data in application for Alzheimer's disease research grant.	Failed; whistleblower ultimately lost at trial.
2014	Terri King, former associate professor	University of Texas Health Science Center	Falsifying research data.	Failed. U.S. Supreme Court upheld lower court ruling that the public university was exempt from FCA liability.

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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The Celebrity Surgeon Who Used Love, Money, and the Pope to Scam an NBC News Producer

http://www.vanityfair.com/news/2016/01/celebrity-surgeon-nbc-news-producer-scam

When Benita Alexander fell for celebrated doctor Paolo Macchiarini—while filming a documentary about him—she thought her biggest problem was a breach of journalistic ethics. Then things got really interesting.

Adam Ciralsky

“B—P 4 EVER”

Then NBC television producer Benita Alexander and Dr. Paolo Macchiarini glide toward the Doge’s Palace, on the left, and the Bridge of Sighs (visible beyond the pedestrian walkway), Venice, 2013. They met during the making of an NBC News special about the doctor’s work.
From the collection of Benita Alexander.

He’s the doctor who does the seemingly impossible, going where no other has yet dared.
—Meredith Vieira

I. A Most Interesting Man

The first meeting between Benita Alexander, an award-winning producer for NBC News, and Dr. Paolo Macchiarini, the famous transplant surgeon, took place at the bar at Boston’s Mandarin Oriental hotel. It was February 2013, shortly before Macchiarini would have his initial interview with Meredith Vieira for a two-hour NBC special called *A Leap of Faith.*

Macchiarini, 57, is a magnet for superlatives. He is commonly referred to as “world-renowned” and a “super-surgeon.” He is credited with medical miracles, including the world’s first synthetic organ transplant, which involved fashioning a trachea, or windpipe, out of plastic and then coating it with a patient’s own stem cells. That feat, in 2011, appeared to solve two of medicine’s more intractable problems—organ rejection and the lack of donor organs—and brought with it major media exposure for Macchiarini and his employer, Stockholm’s Karolinska Institute, home of the Nobel Prize in Physiology or Medicine. Macchiarini was now planning another first: a synthetic-trachea transplant on a child, a two-year-old Korean-Canadian girl named Hannah Warren, who had spent her entire life in a Seoul hospital.

Macchiarini had come to Vieira's attention in September 2012, when she read a front-page *New York Times* story about the doctor. She turned to Alexander, one of her most seasoned and levelheaded producers, to look into a regenerative-medicine story for television. With blue eyes and raven hair, Alexander seems younger than her 49 years. Though she brims with confidence, friends say she bears the scars of a turbulent childhood in Huntington Woods, Michigan. In her own telling, just shy of her 16th birthday, she returned home from a sleepover to discover that her mother had left the family. Two years later, her father, who by then had married a neighbor, asked her to pack up and leave. Alexander overcame her upbringing and in 1987 graduated magna cum laude from Wayne State University with a degree in journalism. She spent the early 1990s working at a string of local television stations and briefly taught journalism at her alma mater. After she met and married fellow reporter John Noel, the two moved to New York City, where she joined NBC's *Dateline.* In 2003, Alexander gave birth to a daughter, Jessina. Alexander and Noel divorced in 2009, and in 2012 she married a ballroom dance instructor named Edson Jeune. Over the years, Alexander has worked with NBC's top talent—Tom Brokaw, Matt Lauer, and Ann Curry, as well as with Vieira—and earned many accolades, including two Emmys as well as the Edward R. Murrow Award, the Alfred I. duPont-Columbia University Award, and the Society of Professional Journalists' Sigma Delta Chi Award.

Now Alexander sat across from Macchiarini at Bar Boulud, in the Mandarin Oriental. At the time, Alexander's first husband, Noel, was hospitalized with glioblastoma, an aggressive form of brain cancer, and she would in time begin sharing details about his condition—as well as about her dissatisfaction with her second marriage. "Having worked with so many patients who are terminally ill, Paolo was immensely helpful as far as helping me navigate my complicated emotions," she explained when I spoke with her this fall. He also suggested ways to talk about the matter with her daughter. "He was an amazing friend to me during that time, and a solid, reliable pillar of strength. He spent hours listening to me talk about it all and offering gentle advice." (Disclosure: I worked as a producer at NBC News from 2004 to 2009. I did not meet Alexander until I contacted her in 2015.)

SAVE THE DATE

Alexander in her Matthew Christopher wedding dress.

Photograph by Gina LeVay.

When Alexander and Macchiarini found themselves together in Illinois for a period of weeks in the spring of 2013—brought there by the NBC special—they met frequently for quiet dinners. The trachea transplant on Hannah Warren, the Korean-Canadian girl, was being performed at Children's Hospital of Illinois, in Peoria, and the procedure was fraught with risks, not least because Macchiarini's technique was still a work in progress even for adults. (Christopher Lyles, an American who became the second person to receive an artificial trachea, died less than four months after his surgery at

Karolinska.) “He’s a brilliant scientist and a great technical surgeon,” said Dr. Richard Pearl, who operated alongside Macchiarini in Illinois. Like others, Pearl described his Italian colleague as a Renaissance man, fluent in half a dozen languages. Another person, who would get to know him through Alexander, compared Macchiarini to “the Most Interesting Man in the World,” the character made famous in Dos Equis beer commercials.

In Peoria, Macchiarini’s medical magic appeared to have its limitations. Hannah Warren died from post-surgical complications less than three months after the transplant. Her anatomy “was much more challenging than we realized,” Pearl recounted. “Scientifically, the operation itself worked. It was just a shame what happened. When you’re doing something for the first time, you don’t have a textbook. It was the hardest operation I’ve ever scrubbed on.”

II. Crossing the Line

The personal relationship between Alexander and Macchiarini continued to blossom. In June 2013, they flew to Venice for what Alexander called “an incredibly romantic weekend.” Macchiarini bought her red roses and Venetian-glass earrings and took her on a gondola ride under the Bridge of Sighs. Like a pair of teenagers, they attached love locks to the Ponte dell’Accademia bridge, one of them bearing the inscription “B—P 23/6/13, 4 Ever.” Alexander told me that, “when he took me to Venice, we were still shooting the story … He always paid for everything … gifts, expensive dinners, flowers —the works. When it came to money, he was incredibly generous.”

It is a bedrock principle at NBC and every other news organization that journalists must avoid conflicts of interest, real or apparent. Alexander was not oblivious to this. “I knew that I was crossing the line in the sense that it’s a basic and well-understood rule of journalism that you don’t become involved with one of the subjects of your story, because your objectivity could clearly become compromised,” she told me. “I never once thought about him paying for the trip as him ‘buying’ me in some fashion, or potentially using money to influence me, because, from my perspective anyway … that just wasn’t the case. We were just crazy about each other, and I was falling in love.”

While Alexander insists that she tried to put the relationship on hold after Venice, she flew to see Macchiarini in Stockholm two weeks later. “Our nights were always spent together, and always romantic in one way or another,” she said. Macchiarini was in Stockholm to attend to Yesim Cetir, a 25-year-old Turkish woman whose artificial trachea had failed. As Swedish television later reported, “It has taken nearly 100 surgeries to support the cell tissue around the airpipes. Her breathing is bad, and to avoid suffocation, her respiratory tract must be cleansed from mucus every fourth hour. She has now been lying in the hospital for nearly 1,000 days.” NBC’s special would come to include skeptical commentary from Dr. Joseph Vacanti, who questioned the sufficiency of Macchiarini’s research, but Cetir’s post-operative complications were not mentioned.

By October 2013, when Macchiarini and Alexander flew to Europe for another romantic getaway, she had in her own mind reconciled her personal and professional behavior. “The story was basically done by the time we went to London. It was all little tweaking after that, nothing significant, and so I totally separated Paolo and work in my head,” she explained. “I was in love and because I had made a very personal decision to take a leap of faith for love, I never looked back.” Should she have informed her friend and mentor, Meredith Vieira? “I knew I was crossing the line at work,” Alexander said, “and I made a very conscious decision not to tell anybody else at work what I was doing.”

III. Breakthrough in Spain

Paolo Macchiarini was born in Switzerland to Italian parents and has spoken of having had a difficult childhood in Basel, where by his own account he felt like a perpetual outsider in school. He attended the University of Pisa, where he would earn a medical degree with a specialization in surgery. During his studies, Alexander recalled Macchiarini telling her, he had received a call from his father, who complained of feeling unwell. The aspiring doctor examined his father but could find nothing wrong and returned to the university. His father died shortly thereafter. It was a moment, Alexander said, that has forever haunted him. In 1986, Macchiarini started a family of his own, marrying an Italian woman, Emanuela Pecchia, with whom he had a daughter and a son.

Over time, Macchiarini developed a certain skepticism about his homeland. “After I had graduated and specialised in thoracic surgery,” he was quoted saying in *The Irish Times,* in 2008, “I wanted to enter university to continue my studies in that field. I was blocked, I was told not to apply for the job because the result, even before the interviews, had already been decided. There were the usual *raccomandati* [those with pull] in the queue in front of me.” The Italian system, he told the British medical journal *The Lancet* in 2012, “favours people who are linked to the politics or are sons of sons but not the merits. I knew that in other countries this was not the fact. So I left.”

In 1990 he traded Italy for America, where, according to his curriculum vitae, he did a fellowship in thoracic surgery at the University of Alabama at Birmingham. Macchiarini’s peripatetic studies continued in Besançon, France, where, according to his C.V., he earned a master’s of science and a Ph.D. in organ and tissue transplantation. According to another C.V., he earned a master’s in biostatistics in Alabama and a Ph.D. in life and health science in Besançon. All told, he had a distinguished medical pedigree.

He then plunged headlong into academia, starting in France, where according to his C.V.’s he joined the University of Paris—Sud with an “accreditation to Full Professor.” A full professor in Europe is comparable to what Americans call a tenured professor, meaning the individual in question has obtained the highest academic rank at a given institution and has been accorded the job protection and other benefits that go with it. But as Macchiarini told *The Lancet* in 2012, he was restless: “I think if you stay in a single place for your entire life you restrict your capacity…. In 10 years it came to a point

where I was adult, and I needed to go away to express my creativity." So in 2000 or 2001—depending on which C.V. one consults—he became a full professor at Hannover Medical School, in Germany. Even Germany seemed too confining for Macchiarini, and he moved to Spain, where in 2005, according to one C.V., he became a *professore ordinario,* a full professor, and where he would continue to maintain a residence.

Macchiarini's wide-ranging academic appointments seemed to prepare him well for his star turn. In June 2008, he performed a trachea transplant using a donor organ seeded with stem cells. The operation in Barcelona on a 30-year-old mother of two, Claudia Lorena Castillo Sanchez, was heralded in the press as the "dawn of the stem-cell revolution." By replacing cadaverous cells with autologous stem cells (that is, those harvested from the patient's bone marrow), the technique held out the promise of minimizing organ rejection and reliance on powerful immunosuppressive drugs. Macchiarini himself called the operation "a major achievement in the history of medicine."

The breakthrough in Spain caught the eye of officials back in Italy, who, concerned that the country was experiencing a brain drain, sought his return. A headline in *La Repubblica* summarized the turn of events neatly: ROSSI PHONES MACCHIARINI: "COME AND OPERATE WITH US"—referring to Enrico Rossi, then Tuscany's top health official, who would later become the region's president. Rossi lured Macchiarini back with a large and prestigious package: a state-sponsored laboratory, the chance to showcase his innovative surgical techniques at Florence's Careggi Hospital, and a full professorship at the university to which it is connected. Italian law, however, required proof of equivalency: in order to appoint a full professor without an open competition, the university had to show that the candidate had held an equivalent post—that is, a full professorship—at a comparable institution, whether in Italy or abroad.

Given his fame, his political connections, and his ample academic credentials, the star surgeon was regarded as a shoo-in, and in late 2009, Dr. Gian Franco Gensini, the dean of the faculty of medicine, assembled a special commission to, in the words of one participant, "rubber-stamp" Macchiarini's appointment. But in the end, Macchiarini never got the full professorship. He operated at Careggi for a few years and then moved on to posts at the Karolinska Institute and Kuban State Medical University in Russia.

IV. Paolo, Putin, and the Pope

Macchiarini proposed to Benita Alexander on Christmas Day 2013, Alexander said. In the months leading up to the airing of *A Leap of Faith,* in June 2014, Macchiarini and Alexander went on trips to the Bahamas, Turkey, Mexico, Greece, and Italy. They went on shopping sprees and ate their way through Michelin-starred restaurants. Macchiarini even took Alexander and her daughter to meet his mother at her home, in Lucca. "She cooked homemade gnocchi," Alexander recalled. Macchiarini's mother shared pictures from the family photo album while her son translated. Emanuela Pecchia, the

woman whom Macchiarini had married years earlier, lived only a short distance away. When Macchiarini informed Alexander, during a dinner cruise later that summer, that his divorce had finally come through, she recounted, he gave her an engagement ring.

Macchiarini could be secretive at times. After his Christmas proposal, he told Alexander that he could not stick around for New Year's because he was on call for what, she said, he termed an "emergency V.I.P. surgery." When she pressed him for details, he swore her to silence before telling her, as she recalled, that he was part of a "highly classified group of doctors from around the world who cater to the world's V.I.P.'s." She said Macchiarini over time revealed that he had operated on Bill and Hillary Clinton, Emperor Akihito of Japan, and President Obama. People who spent time with the couple said they heard Macchiarini talk about his high-level connections. An NBC colleague, Alisha Cowan-Vieira (no relation to Meredith Vieira), recalled, "I saw a lot of text messages between Benita and Paolo, and she would say, 'OMG, look what he just told me.' The texts would say, 'I just left a meeting with PF [Pope Francis]' or with Bill Clinton or the Obamas."

Shortly after NBC aired *A Leap of Faith,* Alexander met Meredith Vieira for lunch at the Modern, an airy restaurant at the Museum of Modern Art. In the dining room overlooking the Abby Aldrich Rockefeller Sculpture Garden, with its works by Miró, Matisse, and Picasso, Alexander said, she told her boss for the first time about her relationship with Paolo and that it had begun while the story was still in production. She said that, while she preferred to keep their conversation private, Vieira was taken aback. "I perfectly understand her reaction," Alexander said. "There's no two ways about it. I crossed the line." A source close to Vieira confirmed that Alexander disclosed the relationship at this lunch but, by this account, had assured Vieira that it began only after production wrapped.

In the months that followed, the doctor and his fiancée began planning their wedding in earnest. They set a date for July 11, 2015, in Rome. But their desire to marry in the Catholic Church was complicated by the fact that she is Episcopalian and divorced. Divorce would have been an issue for Macchiarini as well. However, Alexander said, Macchiarini insisted that he would fix things by visiting his friend and patient in the Vatican.

In October 2014, Alexander recalled, Macchiarini told her that he had met with Pope Francis for four hours and that the Pontiff consented to the couple's marriage and, in yet another sign of his progressive tenure, vowed to officiate. Alexander said Macchiarini referred to himself as Pope Francis's "personal doctor" and maintained that in subsequent meetings his patient offered to host the wedding at his summer residence, the Apostolic Palace of Castel Gandolfo.

A recommendation letter written by Dr. Mark Holterman—who, along with Dr. Pearl, operated on Hannah Warren in Peoria—suggests that Macchiarini's Vatican connections were well known:

> When Pope John Paul II was dying and having trouble breathing from advanced Parkinson's Disease, Professor Macchiarini was called in to provide an urgent consultation

> for the pontiff. The decision to not perform an urgent tracheostomy was jointly made between the doctor and his Holy patient. When Professor Macchiarini renders an opinion on all things involving the diseased airway, people listen. He remains among the world's elite airway surgeons.

Over lunch in New York at the restaurant Print, in Hell's Kitchen, on February 13, 2015, Macchiarini spoke in depth about the wedding plans with Matthew Christopher, a designer who has dressed everyone from Broadway and television star Kristin Chenoweth to World Cup darling Carli Lloyd. He was already hard at work on Benita Alexander's elaborate wedding gown and three additional dresses for the various functions that were planned. Macchiarini "was totally polished. Very much Mr. Big," Christopher recalled, referring to the larger-than-life *Sex and the City* character. According to David Marchi, Christopher's husband and P.R. chief, who was also at the lunch, "He told us the wedding would take place at the Pope's summer residence and because of the enormous security—with the Pope and all these heads of state—that the planning between Matthew and Benita had to be precise. The Pope was going to let Benita use his special carriage. We discussed how to get Benita's dress into this carriage with enough time so that Matthew can get her in, run to the church, and get in the one door before things were locked for security."

Among the V.I.P.'s who Macchiarini said were planning to attend the wedding were Russia's Vladimir Putin, President and Mrs. Obama, Bill and Hillary Clinton, and France's Nicolas Sarkozy. Macchiarini also told people that Andrea Bocelli would sing during the service. As for food, Macchiarini was apparently not sparing any expense: Florence's Enoteca Pinchiorri, with its three Michelin stars, was catering the affair.

Toward the end of their February lunch, Macchiarini asked Alexander to leave the table so he could speak privately with Christopher and Marchi. In a hushed tone, the doctor told them that Pope Francis wanted them to participate more fully in the wedding ceremony. "I almost fell off my chair," recounted Marchi, whose Catholic parents came to the U.S. from Italy. "Growing up, I was always looking for this transformative moment. So when we were told we would take confession and Communion from the Pope as two gay married men, that was it. For me it was almost as if God said, 'You've been waiting for this moment—here it is.' It was very emotional. Matthew and I started crying."

Alexander and Macchiarini returned from the lunch to her apartment in Brooklyn to find that the wedding invitations had arrived. Sheathed in lambskin and engraved with the initials B&P, the invitations were addressed to, among others, the Obamas, the Clintons, the Putins, the Sarkozys, Andrea Bocelli, Kofi Annan, Russell Crowe, Elton John, John Legend, Kenny Rogers, Meredith Vieira, and His Holiness Pope Francis.

By this time, Alexander had met with David Corvo, who as NBC's senior executive producer for prime-time news was ultimately responsible for *A Leap of Faith.* Over lunch at Michael's, Alexander,

by her own account, revealed that she and Macchiarini had been together while the story was in production. Alexander recalled that she gave Corvo details about the wedding, including the Pope's participation. He sent her an e-mail a few weeks later. "Congrats that this is all coming together," he wrote. "With invitations going out, I need to tell [NBC News president] Deborah Turness. Is everything remaining confidential? She'll of course want to discuss coverage soonest. (And exclusivity, as you would expect.) Again, congrats." Alexander says that she and Corvo met again on March 16 and that they discussed how NBC could best cover the wedding. A source close to Corvo confirmed that Alexander told him about the relationship during the lunch at Michael's but, according to the source, had assured Corvo that it had begun only after the reporting and production were finished. The source added that Corvo was always skeptical about the Pope's involvement, made no plans to cover the wedding, and did not tell Deborah Turness about the possibility. By May, when according to Alexander her superiors were aware that she, as the producer of *A Leap of Faith,* had been and continued to be romantically involved with the story's subject, NBC had submitted the program for an Emmy Award. Sources close to NBC say that Vieira and Corvo were not aware of how early the relationship began until approached by *Vanity Fair.* NBC News says that, if any new information reported in this story is relevant to its production of *A Leap of Faith,* it will update it accordingly online, in keeping with its standards practices.

In anticipation of a move to Europe, Alexander on May 13 left her job at NBC and notified her daughter's school that she would not be coming back. She received a glowing video tribute from Vieira:

> I first met Benita nine years ago. We were asked to cover a story—a heartbreaking story—about a beautiful high-school student who had lost her life in Colorado. And you learn a lot about someone when you're in the trenches with them doing that kind of story. I learned that Benita is a fabulous producer. I learned that she is a brilliant writer. But most importantly, I learned that she is an incredibly sensitive and wonderful human being who understands others and wants to connect with them in a very deep and profound way. And ever since that story, every time I was asked, "Is there a particular producer you want?," I would say, "Please, please let me work with Benita." I love her tremendously. Not just as a professional but also as a dear friend. And anybody given the opportunity to work with her would be crazy to say no. Run to Benita. Don't walk. Run to Benita. I wish her the best and I know she that she will do extremely well in her new life in Barcelona.

V. The Reckoning

The very next day, May 14, Alexander received an e-mail from a friend. The subject line read simply: "The Pope." It included a link to an article detailing Vatican plans for Pope Francis to visit South America in July—at the very time when he was supposed to be officiating at her wedding.

In that instant, the bottom fell out. A few weeks later, Alexander would send an e-mail to invited guests in 17 countries, canceling the wedding. Many had already purchased flights, booked hotels, and bought new clothes for what everyone expected to be a wedding for the ages. Alexander recalled that Macchiarini tried to blame the scheduling mix-up on Vatican politics and claimed that he was on his way to Rome to straighten things out. He maintained that her fears were unfounded—that he was acting in good faith and that everything would work out as planned. He said the Pope would be cutting his trip short and returning early. Alexander was unconvinced. She confronted a painful reality. "I just didn't want to put two and two together," she said. "I didn't want Paolo to not be the man I believed him to be. I didn't want the fairy tale to end." After canceling the wedding, she e-mailed Macchiarini: "I believed you were exactly who you presented yourself to be, to me, to my friends and family, to the world. Congratulations. You charmed me, and all of us, into la la land. I will never, ever understand how you could have done this to me, or to Jessie. Who the hell are you and what the hell is wrong with you?"

As Alexander would discover with the help of a private investigator named Frank Murphy, virtually every detail Macchiarini provided about the wedding was false. A review of public records in Italy would also seem to indicate that Macchiarini remains married to Emanuela Pecchia, his wife of nearly 30 years. Murphy, who spent 15 years as a Pennsylvania State Police detective, told me, "I've never in my experience witnessed a fraud like this, with this level of international flair…. The fact that he could keep all the details straight and compartmentalize these different lives and lies is really amazing."

Alexander produced e-mails and WhatsApp chats to support her account of Macchiarini's claims of a relationship with the Pope.In a statement to *Vanity Fair,* Father Federico Lombardi, director of the Holy See's press office, was adamant: "There is no 'personal doctor' of the Pope with [the] name 'Macchiarini.' The Pope has surely never promised to officiate a wedding of 'Macchiarini' and does not know someone with such [a] name. On 11th July the Pope was travelling in Latin America and this was on his agenda long time before July … This is enough." Dr. Mark Holterman, who had written the recommendation letter citing Macchiarini's treatment of Pope John Paul II, acknowledged to *Vanity Fair* that "this was a vignette related to me by Prof. Macchiarini," adding that he had relied "solely on [Macchiarini's] word."

Andrea Bocelli's wife and manager, Veronica Berti, laughed when asked if her husband had agreed to serenade the couple: "He was not booked to sing at a wedding. He doesn't sing at people's weddings. Castel Gandolfo? Absolutely not!" Annie Féolde, Enoteca Pinchiorri's flamboyant co-owner, told me that they were never contacted about, much less contracted for, a wedding on July 11, and that they had never heard of Paolo Macchiarini.

To understand why someone of considerable stature could construct such elaborate tales and how he could seemingly make others believe them, I turned to Dr. Ronald Schouten, a Harvard professor who directs the Law and Psychiatry Service at Massachusetts General Hospital. "We're taught from an early

age that when something is too good to be true, it's not true," he said. "And yet we ignore the signals. People's critical judgment gets suspended. In this case, that happened at both the personal and institutional level." Though he will not diagnose from a distance, Schouten, who is one of the nation's foremost authorities on psychopathy, observed, "Macchiarini is the extreme form of a con man. He's clearly bright and has accomplishments, but he can't contain himself. There's a void in his personality that he seems to want to fill by conning more and more people." When I asked how Macchiarini stacks up to, say, Bernie Madoff, he laughed and said, "Madoff was an ordinary con man with a Ponzi scheme. He never claimed to be the chairman of the Federal Reserve. He didn't suggest he was part of a secret international society of bankers. This guy is *really* good."