

# South Korean policy failure and the Hwang debacle

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**Poor national mechanisms for accountability, competition, transparency and ethical oversight allowed Hwang Woo-Suk's descent into ethical, and ultimately scientific, misconduct.**

With the creation of the World Stem Cell Hub, a project inaugurated officially by South Korean president Roh Moo-hyun in October 2005, embryonic stem (ES) cell pioneer Hwang Woo-Suk had pulled off an astonishing feat. After the publication of a paper in *Science*<sup>1</sup> in the spring of 2005 describing the creation of 11 patient-specific stem cell lines, a clearly stated goal of the World Stem Cell Hub was to ensure South Korean leadership in stem cell research and its medical applications for years to come. Already, negotiations had been under way to found regional subsidiaries of the facility in a number of countries, including the United States, the United Kingdom and Germany. More than 3,500 patients stormed the phone lines and internet servers of the facility on a single day when it opened for patient applications on November 1, 2005.

Today, only a few months later, following confirmation that all of the 11 claimed cell lines were crude fakes and that Hwang committed gross ethical violations in securing egg donations, South Korea's ambitious stem cell research program is in tatters, the cloning king Hwang is dethroned and his paper retracted by the editor of *Science*<sup>2</sup>. South Korea's science minister and the chairman of the country's newly created Bioethics Committee have resigned after being

implicated in the Hwang scandal. Never before has a case of scientific misconduct been more widely reported in the popular press. Hwang's disgrace has sent aftershocks across the world. Commentators are questioning the validity of scientific peer review and floating proposals for its reform. Journal editors are being accused of sacrificing judicious assessment of manuscripts in the quest for the next big story. The pace and competitiveness of biomedical research are portrayed as increasingly out of control, driving scientists toward questionable practices and even fraud.

In short, in the face of mounting global competition, the case of Hwang Woo-Suk is being publicly cast as a double failure: the failure of an individual scientist's moral responsibility and of the peer-review process. But most of these commentators overlook the main reason

for the debacle: the South Korean state's failure to provide an adequate system of science governance. Fueled by overambitious plans to build a national biotech industry and their enthusiasm to turn Hwang Woo-Suk into a celebrity scientist and cheerleader for South Korean science, policy makers violated almost every existing rule for good governance in research. The cost for South Korean biotech will be high, but the lessons apply to any country seeking to rapidly nurture a nascent biotech sector.

## Governance in biotech research

Many commentators tend to attribute the Hwang scandal to the failure of peer review and the ever mounting pressure on scientists to publish and perform at the highest level. But, peer review builds upon trust; its goal is to establish that a finding is new and original

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Revelations about Hwang Woo-Suk's work have left South Korea's dreams of a World Stem Cell Hub in shatters.

and that the interpretation that is given is plausible in the light of what is known. If the goal is to scan a paper for signs of data fabrication or fraud, peer review is simply not the right tool.

The sociologist of science Robert Merton established several decades ago that the results of most research papers are never formally replicated. After all, replicating an experiment is far from trivial, can take considerable time and effort, and often involves the material transfer of research resources or the transfer of special skills. Thus, 'organized skepticism' is, at best, one aspect of the moral economy of science. Although critique is a vital element in scientific research, the same is true for trust. For the most part, scientists 'trust' the experiments done by others. In fact, given the enormous amount of data that are published every day, they have little choice.

Serious cases of misconduct are almost never identified by peer review; rather, it is usually insiders or whistleblowers who first raise concerns and get an investigation started. The Hwang case is no exception. And although peer review is an important instrument of quality control in research, it is certainly not the only one. Even before the Hwang scandal broke, some journals had implemented safeguards to protect themselves against scientific fraud. For example, the *Journal of Cell Biology* hired a full-time person to scan submitted images for signs of improper manipulation. Indeed, new software tools, which can detect whether images have been doctored, are becoming available.

What's more, peer review builds upon a whole range of quality control mechanisms at the institutional or national level. While there is certainly room for improvement, peer review of scientific papers is not an omnipotent tool to ensure good scientific practice; it is part of a larger system of quality management that ensures the good governance of science. Research funding organizations and universities use a broad variety of instruments of control, ranging from hearings to laboratory visits and reporting systems, to determine the quality of research. From the grant application phase to the publication of articles, multiple layers of review tend to reveal irregularities or extra-scientific problems in the research process at the earliest possible time. In well-functioning research environments, scientists are evaluated permanently, from the first day they start to do experiments to their last day. Indeed, if we are to believe Brian Martinson<sup>3</sup>, to manipulate data is not a rare occurrence, but fairly common practice; what keeps the fraudsters at bay is a system of checks and balances and a spirit of continuous debate and scientific critique.

The 'governance of research' is the ensemble of checks and balances that exist to ensure

research quality. As such, it is embedded in a complex web of institutional practices, including governmental regulatory policy. Peer review is only one aspect of this structure. The Hwang scandal is an illustration of the well-known limits of peer review. But responsibility for the Hwang scandal lies not with the peer-review system but with bad science governance.

### Biotech ambitions

The story of Hwang Woo-Suk starts as far back as the early 1990s, when South Korea announced ambitious goals to build, more or less from scratch, an indigenous biotech industry. In 1994, the South Korean government launched an audacious plan, termed Biotech 2000, under which the government and industry pledged to spend US \$18 billion (15.5 trillion won) over a 14-year period on biotech R&D. An offshoot of South Korea's 'Highly Advanced Nation' development agenda, the program aimed to make South Korea into one of the seven leading biotech nations by 2007, a date that was later pushed back to 2010.

Today, with research funding in South Korea at almost 3% of gross domestic product, the number of Korean research publications in leading journals is increasing. Also, there are signs that some of the more ambitious industrial policy efforts are bearing fruit<sup>4</sup>. Still, the biotech enterprise in South Korea remains fragile. In particular, since the launch of the Biotech 2000 program, the South Korean pharmaceutical industry has not been able to increase market share at home, let alone overseas. This is hardly surprising. Less than 10% of South Korea's 600 pharmaceutical firms perform any R&D at all, and even leading firms in the industry typically spend considerably less on R&D than their competitors in the West or in Japan. Market liberalization following the Asian currency crisis has made it easier for foreign firms to access the South Korean market, and imports of pharmaceutical products now surpass exports by nearly a factor of five. By any measure, South Korea's trade and technology balance in the pharmaceutical sector is deep in the red.

In biotech, sizeable investments by some of the large manufacturing groups—such as SK (Seoul) or LG (Seoul)—are starting to pay off, and several biotech products are now on the global market. But most South Korean startups remain small and fragile, and often it is public support that keeps them alive. Although a considerable group of companies was formed just a few years ago, often by professors at national universities, few have survived.

Recent funding growth has resulted in a number of international ventures, such as the Seoul branch of the French Pasteur

Institute, which opened in 2004 with a funding commitment of €100 million (150 billion won) from the South Korean government, to be paid out over a 10-year period, and additional funding from South Korean industry. Still, apart from the Korean Research Institute for Bioscience and Biotechnology (KRIBB), set up in 1984 as the Genetic Research Institute, universities remain the main locus for biomedical research. And, despite spectacular growth in both overall and biotech R&D investments, total spending in biomedicine in the public sector in South Korea is well below the Organization for Economic Cooperation and Development (OECD) average. Whereas biomedical research and biotech now typically account for around half of civilian R&D spending in most countries, in South Korea the numbers are well below 15%. Despite much talk in recent years of increased funding for life science and biotech, the research funding priorities in South Korea remain focused on information technology, electronics and manufacturing.

### A meteoric rise

It was in this climate of often unrealistic ambitions and a relatively narrow base in basic science that the high-flying career of Hwang Woo-Suk was launched. Even before his work on somatic cell nuclear transfer and human ES cells, Hwang was a prominent figure in South Korea. A specialist in theriogenology, he had made headlines with efforts to produce organs for xenotransplantation from cloned pigs. This work was hailed by some as one of the pillars on which South Korean biotech would be built. In 2003, for example, some 200 researchers at a dozen universities were working on xenotransplantation-related efforts funded by the Ministry of Science and Technology and coordinated, in large part, by Hwang. Last summer, the Seoul National University venture MgenBio, set up by Hwang and others, announced that it had succeeded in cloning transgenic pigs that express human leukocyte antigen (HLA)-G, which is thought to improve immune tolerance of humans to transplanted pig tissues.

By 2002, the buildup of South Korean excellence in the field of human ES cell and somatic cell nuclear transfer research had turned into a national project that increasingly was able to secure significant financial resources from various government institutions. But this increase in research funding and output was not accompanied by needed institutional reform. A fully differentiated system of science governance with clearly defined roles, rules, responsibilities and built-in checks and balances is often taken for granted, but it can hardly be assumed to exist worldwide, and it certainly did not exist in South Korea. Although the South Korean sci-

ence system has been thoroughly modernized during the past decades, financial and political accountability, transparency and regulation are still sorely missing, and institutional walls against corruption, cronyism and other forms of misconduct are weak.

South Korean science remains characterized by networks of a few individual scientists with privileged connections and access to politicians, administrators and elites. The distribution of grants and financial support is strongly based on government decisions and strategies rather than on review, competition, hearings and applications. Hwang benefited from these practices, which enabled him to position himself as the key figure not only in his field of research but in South Korean science as a whole. The intrusion of politics into science is evident, for example, in the addition of Park Ky Young, the advisor to the South Korean president for Science and Technology to the list of authors of Hwang's 2004 *Science* paper<sup>1</sup>, a gesture of gratitude from Hwang toward those in political circles responsible for providing him with generous financial support. Meanwhile, scientific review was scarce; a culture of secrecy and of deference left researchers in South Korea, and even in Hwang's own laboratory, in the dark about much of the group's work.

### Hwang's influence

Hwang's publications on human cloning<sup>1,5</sup>, the first cloning of a dog<sup>6</sup> and the production of patient-specific stem cells<sup>1</sup>—all hailed as breakthrough publications by the international press—had an enormous impact upon the South Korean biotech industry. The country's investors were sent into a frenzy for biotech after the publication of Hwang's 2005 *Science* paper<sup>1</sup>, with Korean biotech stocks rising threefold. During May 2005, the daily trading volume of Macrogen, Korea's genomics pioneer and an investor in MgenBio, was above 80 billion won (\$81 million) per day on average, around half of the volume for Korea's largest company, Samsung Electronics (Seoul), a company with a market value almost 500 times larger than Macrogen's.

But Hwang's sphere of influence extended beyond science and the stock market to the people who were making decisions about human ES cell research ethics in South Korea. When on January 4, Yang Sam-sung, the head of South Korea's National Bioethics Committee tendered his resignation, it was revealed that Yang had participated in several panel meetings while he was still Hwang's lawyer (that is, before the November 24 press conference when Hwang apologized for lying about egg donations by junior researchers). This was particularly worrisome not only because of

Yang's clear conflict of interest as head of South Korea's chief bioethics advisory panel and as Hwang's lawyer, but also because the South Korean government and Yang's bioethics panel allowed Hwang's research to proceed with lax ethical oversight compared with researchers in other countries.

The key countries involved in human ES cell research and cloning, such as the United Kingdom, discussed the creation of appropriate regulatory structures before research in the field could go ahead. In contrast, South Korea allowed its scientists to forge ahead while the ethics of this research was discussed, regardless of the outcome of this debate. The shaping of ES cell regulations in South Korea was delayed until 2005, when the Bioethics and Biosafety Act came into effect. With hindsight, it seems that this delay gave Hwang's group a competitive advantage to operate completely unobstructed by regulatory demands.

The conflicts of interest of both Park Ky Young, the advisor to the President for Science and Technology, and Yang Sam-sung as head of the National Bioethics Committee reflect alarming faults in the South Korean system of science oversight. Hwang Woo-Suk used South Korean decision making structures for his purposes; in turn, he was used by the political elites to project the image of South Korea as an emerging player in international biomedical research.

### What lessons?

For biotech in South Korea, the implications of the Hwang affair are significant. At least for some time, investors are likely to stay away from biotech stocks. Although investors had quickly forgotten the technology bubble of 2000, it is perhaps safe to assume that the fallout of the Hwang affair is likely to affect the Korean biotech industry for several years to come and small companies with unproven technologies will likely find it difficult to access capital for the foreseeable future. Also, at least for a certain period of time, it is possible that South Korean stem cell researchers will find their papers under increased scrutiny at top journals. Scientists from industrializing or developing countries will find that, to avoid similar mistakes, editors will look even more carefully into their publications than had previously been the case.

The Hwang affair could also have a cathartic function. Seoul National University certainly deserves credit for its quick decision to launch an investigation, and perhaps this episode will catalyze a major reform of science governance throughout South Korea. So far, the signs are not encouraging.

For other emerging countries aspiring to world leadership in biotech, the Hwang case

provides several take-home messages. First, it illustrates that local institutions must be up to the task of ensuring that the science carried out within their walls is of requisite quality and veracity. Especially in an area like biomedicine, where experimental results are often messy and difficult to replicate, good governance is crucial for research.

Second, it highlights the dangers of using a single laboratory's progress in a basic biomedical research area—in this case Hwang's research on somatic cell nuclear transfer in human ES cells—as the sole foundation to drive a country's technology-based economy, particularly when development cycles for basic research and biotech are so long and a return on investment is so far in the future. Too much rides on a country's biotech sector for its success to be placed in the hands of a single group or even single individual.

Third, although the absence of regulation might allow research to progress unimpeded, this is not always beneficial for research. Regulatory oversight of research adds yet another layer to the web of quality control in research. To provide scientists with exceptions from accepted rules is hardly an approach to gaining public trust in science. And although the tacit acceptance by regulators of violations of ethical principles by researchers may not necessarily lead to scientific fraud, a *laissez-faire* atmosphere of oversight is unlikely to discourage those intent on scientific fabrication or falsification.

In the end, there is no perfect approach to prevent scientific misconduct or fraud. Neither is 'good governance' a guarantee of 'good science.' But governments must do everything to reduce the likelihood of scientific misconduct. In the case of Hwang Woo-Suk, misguided industrial policy ambitions, together with a neglect of the basic principles of good governance, achieved exactly the opposite and paved the way for one of the largest scientific fraud scandals to date. South Korean biotech entrepreneurs are likely to be dealing with the fallout for years to come.

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