Aftermath. CGR President Luciano Maiani (*left*) offered his resignation last week, while a phone conversation between Guido Bertolaso (*center*) and Enzo Boschi (*right*) shed new light on the commission's relation to Bertolaso.

SCIENCE AND THE LAW

Convictions Leave Italy's Civil Protection in Chaos

ROME—Italy's government was left without experts to advise it on natural hazards following the conviction last week of six scientists and a government official for advice they gave ahead of the deadly earthquake in L'Aquila in 2009. The president and several members of the National Commission for the Forecast and Prevention of Major Risks (CGR) have resigned in response to the convictions, while others have threatened to resign. As *Science* went to press this week, the commission remained out of action, its future unclear.

The seven convicted men took part in a CGR meeting on 31 March 2009, 6 days before the magnitude-6.3 earthquake, which killed more than 300 people. Last week, each of the seven were sentenced to 6 years in prison by a judge after having been accused of falsely reassuring L'Aquila's citizens as a result of discussions they held during the meeting (*Science*, 26 October, p. 451). CGR is a consultative body to Italy's Civil Protection Department (DPC); in a note to the press last week, DPC warned that the conviction could lead to "paralysis" of risk forecasting and prevention in Italy.

In an e-mail written on 23 October, the day after the conviction, CGR president, particle physicist Luciano Maiani, told his fellow commission members that he was sending his resignation letter to Prime Minister Mario Monti because he believed CGR could not work "serenely and effectively." The jail terms had highlighted the "fragility" of the commission, Maiani wrote. He also expressed his "most complete solidarity" with the convicted seven.

The commission's president emeritus and vice president also resigned, and about two-thirds of the 60-strong membership have at least announced their intention to do so. In a 26 October Cabinet meeting, however, the Italian government rejected the resignations, leaving the commission's future uncertain for the moment.

CGR members argue that their role as scientific advisers isn't clearly distinguished from that of the decision-makers. The way the CGR works was overhauled last year to avoid the confusion that took place in its now-infamous meeting ahead of the L'Aquila quake, which civil protection officials, local administrators, and others also attended, and which did not result in a summary at the meeting's close. Today, deliberations take place behind closed doors and result in official documents that are sent to DPC. But, says resigning commission member Aldo Zollo of the University of Naples Federico II, the regulations do not explicitly free the scientists of all responsibility for decisions made on the basis of their advice, which may stifle their ability to speak their minds.

A pair of earthquakes earlier this year in the north of Italy provides a case in point, Zollo says. CGR's advice regarding the possibility of a third quake led DPC to take emergency measures; when the quake didn't materialize, the mayor of a town called Finale Emilia threatened to sue the commission because the measures hampered local business.

Not all commission members agree with the resignations, however. Francesco Mulargia, a geophysicist at the University of Bologna, says the judge's decision must be respected: "[I]n a civilized country, justice is administered in courts and not in talk shows, in newspapers, in streets or by 'resigning in protest,' " Mulargia wrote in an e-mail. He maintains that the resigning scientists mistakenly believe science itself to be on trial, whereas, he says, the defendants were actually charged with not correctly conveying that science.

But Mulargia agrees that in the wake of the verdict, new regulations are needed, arguing that "CGR cannot have any responsibility if not the scientific one." Stefano Gresta, president of the National Institute of Geophysics and Volcanology (INGV), says that new rules might be forthcoming as early as this week, either in the form of DPC regulations or new laws. He points out that Maiani and the other heads of CGR were due to meet on 30 October to clarify the commission's role in civil protection.

That a solution is needed was driven home by a magnitude-5 earthquake that struck near the border between the Calabria and Basilicata regions in southern Italy just 3 days after Maiani resigned. The quake was the latest tremor in a more than 2-year-long seismic "swarm," and it represented a significant jump in magnitude—a situation fairly similar to that in L'Aquila a week before the fatal quake. But DPC head Franco Gabrielli could not draw on the expertise of CGR to assess the risks of more significant tremors last week. Fortunately, the commission had analyzed the swarm earlier in the month. "This earthquake is well characterized by that analysis," Gresta says.

In a separate development, the newspaper *La Repubblica* published another recorded phone conversation last week suggesting that scientists serving on CGR were under pressure to bring their public statements in line with the wishes of Guido Bertolaso, then-head of the DPC. (Bertolaso's phone was tapped at the time by prosecutors investigating his possible involvement in corrupt government contracting.) In the call, recorded 3 days after the L'Aquila quake, Bertolaso discusses a CGR meeting scheduled for that day with commission member and then-INGV Director Enzo Boschi. "Today's meeting is aimed at this, so the truth is not to be said," Bertolaso said. At the end of the brief conversation, during which the meeting's aim and "the truth" were not revealed, Boschi reas-

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sures Bertolaso that "ours is a very cooperative attitude. We will do a press release which we will first submit to your attention." In January of this year, *La Repubblica* published the recording of another call in which Bertolaso, talking with a regional official ahead of the 31 March 2009 meeting, says that that meeting was to be "more of a media operation" in which "we want to reassure the public."

Meanwhile, the flood of protests from outside Italy has continued. Michael Halpern of the Union of Concerned Scientists wrote in a blog post last week that the conviction "for failing to accurately predict an earthquake" is "an absurd and dangerous decision," while a *Nature* editorial said: "The verdict is perverse and the sentence ludicrous." But a statement by the American Geophysical Union (AGU) was more reserved, calling the prison sentences "troubling" and pointing out that they "could ultimately be harmful" to combating the threat of natural disasters. Although AGU had called the charges against the seven "unfounded" in 2010, it now merely said that "the facts of the L'Aquila case are complex."

–EDWIN CARTLIDGE

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STEM CELLS

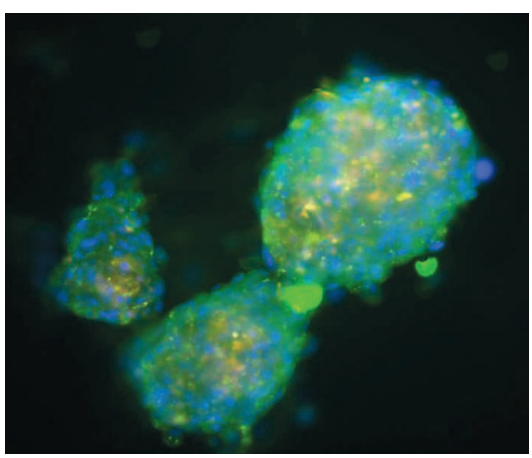
Immune Reactions Help Reprogram Cells

When under threat, it pays to be flexible. That principle may help explain why scientists have been able to use viruses to reprogram differentiated cells into stem cells, an advance that was recognized as part of this year's Nobel Prize in physiology or medicine. In the 26 October issue of *Cell*, a U.S. research team reports that a cell's defensive reaction to viruses seems to make it more open to expressing genes that are usually shut down—whether they be those that trigger inflammation or those that are active in stem cells. The find could help scientists better understand how cellular reprogramming works, and may also help them develop more efficient and safer ways to reprogram cells.

Exactly what happens inside cells during reprogramming remains a mystery. The technique as first described in 2006 by Shinya Yamanaka of Kyoto University in Japan, who shared this year's Nobel Prize, involves giving a cell extra copies of four key genes by infecting it with a retrovirus that inserts the genes into the host cell's genome. In a poorly understood process, the proteins encoded by those genes set off a cascade of signals that turns mature cells into pluripotent cells, which can become any of the body's tissue types. These so-called induced pluripotent stem (iPS) cells have allowed scientists to derive cell lines that are a genetic match with patients, enabling them to study diseases in new ways. They may also someday provide genetically matched tissue for regenerative medicine.

The first techniques used to reprogram cells had a major drawback, however. The virus-inserted genes remained in the iPS cells, raising the possibility that they might cause tumors. Although scientists have found several ways to ferry reprogramming genes into cells without permanently altering the genome, they are still looking for new methods. One especially attractive alternative is protein-only reprogramming, which would avoid the use of foreign genes altogether. By directly inserting the proteins that the reprogramming genes code for, scientists can set off the same signaling cascade, but the process is very inefficient.

John Cooke, a cardiologist at Stanford University School of Medicine in Palo Alto, California, and his colleagues wanted to understand why the proteins worked so poorly. They carefully examined what happened when they treated cells with a single reprogramming factor, either via a gene in a retrovirus or with specially designed versions of the reprogramming proteins that can traverse cell membranes. The cells that received the retrovirus began to express the inserted gene and its downstream counterparts within hours. The proteins took days to have any effect.



Protein makeover. These cells were reprogrammed into stem cells with proteins alone.

Cooke wondered if the virus might be doing more than just ferrying genes. When the researchers added a virus that carried only a marker gene to cells that received copies of a single reprogramming protein, the effect was immediate: Within a few hours, the cells began to react to the protein, expressing the signaling pathway it triggered. Further experiments showed that the virus triggers the cell's innate immune response, primarily through a protein called toll-like receptor 3 (TLR3), and this ends up unwinding chromatin, the complex of DNA and proteins that usually keeps genes that aren't in use tightly bound in compact coils.

"When a cell meets a pathogen, it assumes a more plastic phenotype, which allows it to adapt to survive the pathogenic challenge," says Cooke, who calls this ready-for-anything state "transflammation." For those trying to make stem cells, the looser chromatin apparently allows the reprogramming factors better access to the genes involved in pluripotency.

Cooke's group found that blocking the TLR3 pathway also blocked reprogramming by viral vectors and by another method, the introduction of messenger RNAs that code directly for reprogramming factors. When the researchers added a TRL3-triggering molecule to their protein-only reprogramming recipe, they significantly improved the speed and efficiency of the technique.

"It is intriguing and unexpected that inflammatory pathways play a role in reprogramming," says Konrad Hochedlinger, a stem cell researcher at Harvard University. He notes that TLR3 may affect not only chromatin but also other processes such as a cell's replication rate. The find "adds to the deeper understanding of reprogramming mechanisms," agrees George Daley, a stem cell scientist at Harvard Medical School in Boston.

Cooke says he hopes that the transflammation might also help researchers looking for ways to turn one kind of mature cell directly into another, skipping the pluripotent state altogether. Cooke and his colleagues would ideally like to use it to change skin or other cells into cardiac cells that might help patients suffering from heart disease—turning a cell's perceived threat into a powerful opportunity.

–GRETCHEN VOGEL