Italy’s Influenza Diva

She set in motion a worldwide movement to share information on avian influenza. Italian bird flu scientist Ilaria Capua says what she thinks—and often gets what she wants

LEGNAPO, ITALY—When she traveled from Italy to Paris in mid-March, Ilaria Capua had a plan. She was going to attend a meeting of the scientific committee of OFFLU, an international network of bird flu experts, and she wanted participants to commit to getting more genetic data about the H5N1 bird flu strain in the public domain—a cause she had championed since January of this year. With scientists sitting on their samples, Capua believes, it’s impossible to track the virus’ movements and understand the tricks it may play on humankind.

But persuading her 13 colleagues, gathered in the graceful Parisian mansion of the World Animal Health Organization (OIE), wasn’t easy, and the debate dragged on. Some were opposed, whereas others were sympathetic to Capua’s cause but saw clear drawbacks as well. For instance, if every sequence became public information, how could they prevent others from scooping them with a scientific paper? But Capua insisted, and in the end, the group committed to sharing. As a first step, all participants identified at least 20 bird flu strains in their collections to be fully sequenced by the U.S. National Institutes of Health, which has a flu genome sequencing project, and then released.

It was quintessential Capua, says Christianne Bruschke, an OIE officer charged with bird flu who was at the meeting. “She’s somebody with strong opinions,” says Bruschke. “She’s very dominant; she knows how to convince people.” Adds Juan Lubroth of the Food and Agriculture Organization (FAO) of the United Nations: “She is very charismatic, and she has a big persona. When Ilaria says something, it carries weight.”

Capua’s in-your-face opinions do occasionally rub people the wrong way. “There are people who don’t like her because of that,” says virologist Albert Osterhaus of Erasmus University Medical Center in Rotterdam, the Netherlands. Still, her campaign for openness around H5N1 data has been unexpectedly successful and has won her wide admiration. Colleagues, newspaper editorialists, and even Web loggers have heaped praise on her.

Within the world of avian influenza, however, Capua already had a “very good reputation,” says Michael Perdue, an avian influenza expert at the World Health Organization (WHO) headquarters in Geneva, Switzerland. In 8 years, she has put the world on notice with the beauty queen.

Not so crazy

Born in Rome, Capua obtained a degree in veterinary science at the University of Perugia in 1989, then worked at a few other labs before she became head of the virology department at the institute here in 1998, in a calm period when bird flu wasn’t considered much of a problem. That changed, at least in Italy, in 2000, when a major outbreak of a highly pathogenic (HP) influenza strain named H7N1—which, unlike H5N1, is not dangerous to humans—struck poultry farms in a belt stretching roughly from Milan to Venice.

Although the Italian government managed to quash the outbreak by culling more than 13 million poultry, a so-called low-pathogenic (LP) version of H7N1 kept circulating, and researchers feared it might revert without warning to the HP version and kick off a new disaster. A massive poultry vaccination campaign in the area might help root out the LP strain. But widespread use of an H7N1 vaccine would pose an economic problem: Like any vaccine, this one would trigger the same antibodies as the disease, so that a standard test wouldn’t be able to tell vaccinated from infected chickens. That, in turn, would prevent the country from showing that it was disease-free, endangering its trading status.

Capua’s team argued that the so-called DIVA strategy might circumvent that classic problem. Instead of baseing a vaccine on the H7N1 strain already infecting poultry, they
suggested using a closely related strain, H7N3, which differs in a viral coat protein called neuraminidase. Vaccinated animals could be distinguished from infected ones because they would carry antibodies against the N3 variety of the neuraminidase protein instead of N1, the team argued.

Convincing European Union authorities that this approach would wipe out the disease was tough. “Some people thought I was crazy, that we would make the disease endemic,” says Capua. But the team persisted, developing a new, fast test for antibodies against N1 and showing that it was reliable. And 4 months after the vaccination campaign went live in November 2000, the LP strain of H7N1 was eliminated. A year later, when an H7N3 outbreak swept the area, the same trick was put in reverse, using an H7N1 vaccine.

“Many people were talking and thinking about DIVA strategies, but she was the first to actually take it to the field and implement it,” says Perdue. In theory, the same tactic, called heterologous vaccination, could also be used against H5N1, but it hasn’t so far. Many at-risk countries don’t have a good network of veterinary labs to screen poultry for infection.

After the Italian outbreaks died down, bird flu surfaced in other locations: There was an outbreak of H7N2 in Virginia in 2002, a massive H7N7 outbreak in the Netherlands in 2003, and the worldwide spread of H5N1, now in its third year. The increasing prominence of the disease helped Capua build up her lab. Staff tripled to almost 50 in 6 years. More than 70% of them are women—not necessarily because Capua wanted it that way, but because most graduates in veterinary science these days are women. It does have an advantage, however, she observes: “Men are incapable of multitasking, as I’m sure you’re aware.”

After Capua took over, IZSVe became Italy’s reference lab for bird flu, testing samples from all over the country. In 2002, OIE asked Capua if IZSVe could serve as one of its global reference labs as well; FAO asked in 2004. As a result, the institute has received a steady stream of samples from H5N1-affected countries, primarily in the Middle East and Africa.

It was because she was at the hub of this research that Capua became aware of the lapse in data sharing. Her discomfort began in February, when WHO asked her to deposit the sequence of a sample from Nigeria, the first African country affected, in a closed-off compartment of a flu database at Los Alamos National Laboratory in New Mexico, to which fewer than 20 labs have access. If she shared her sequence, WHO scientists said, she would have access to the rest of the hidden Los Alamos data.

Capua refused and instead deposited her sequences in GenBank for the entire world to see. At the same time, in a message on ProMED, an e-mail list for emerging infectious diseases, she asked her colleagues to follow suit (her posting won ProMED’s annual award in August); she also asked Science to investigate (3 March, p. 1224).

WHO defended the closed database on the grounds that H5N1-affected countries often don’t want reference labs in the developed world to publish information about the strains circulating within their borders. But Giovanni Cattoli, the director of research and development in Capua’s lab, says that “is simply not our experience,” noting that of the 15 countries the Capua team has dealt with, 14 said sharing data was “fine.” As to scientists’ worries that they might be scooped if they post their sequences in real time, Capua says: “What is more important? Another paper for Ilaria Capua’s team or addressing a major health threat? Let’s get our priorities straight.”

Sexist world
Eventually, Capua’s call resulted in a new organization uniting dozens of researchers, called the Global Initiative on Sharing Avian Influenza Data (GISAID), that plans to set up a system for sharing (Science, 25 August, p. 1026). GISAID’s charter is still being hashed out with specialists in intellectual property and bioinformatics, and it’s unclear exactly how it will work.

But no matter what comes of the deal, says Capua, momentum for sharing is clearly building. Although some at WHO were irked by the sudden announcement of GISAID—most people weren’t aware of what was going on, Perdue says—WHO does support the idea. The Indonesian government and the U.S. Centers for Disease Control and Prevention in Atlanta, Georgia, both recently released a series of sequences. And on a visit to the United States this week, Capua was set to discussing the sequencing of a large number of strains from OFFLU labs at The Institute for Genomic Research in Rockville, Maryland.

Meanwhile, Capua’s lab seems set to grow. She’d like to lure back Italian talent now working overseas. “Italians are very creative,” she says. “Look at the food, the fashion.” It pains her that Italian science has such a bad image; in a recent issue of Nature, for instance, one editorial praised Capua’s sharing initiative whereas another one on the same page slammed the Italian government for its research management.

Capua says she’s driven in part by the desire to show that it’s possible to do outstanding research in Italy. Doing so, however, requires a hefty dose of determination—especially if you’re a woman, she says. “My husband tells me I come of yore if you’re a woman, she says. “My husband tells me I come from a dragon, like Condoleezza Rice,” she says, slamming her hand on her desk as if to illustrate what she’s talking about. “But I have to defend my ideas and make sure I get heard. We live in a sexist world, especially here in Italy.”

Then she adds: “But I’m not very concerned about how other people perceive me. I just tend to do my thing and get on with it.”

“I’m very brave. I’m often ahead of others in thinking about important issues.”

—Ilaria Capua

Help wanted. Capua, here with colleagues Giovanni Cattoli and Paola De Benedictis, says she’d like to lure Italian talent working abroad back home.