The necessity of molecular diagnostics for avian flu

To the editor:

Since late last year, avian flu has spread to ten Asian countries and killed around 50 million chickens either directly as a result of the disease or indirectly due to culls designed to halt disease spread. If the epidemic worsens, an avian pandemic may occur, and countries with big poultry industries, such as Mexico and Brazil, could potentially be encumbered with culls of equal of even greater magnitude.

The World Health Organization (WHO; Geneva) and health departments in many countries appear to have underestimated the virulence of the current strain of influenza, H5N1, despite last year's experience with severe acquired respiratory syndrome (SARS). We believe that the use of molecular diagnostics as a first step in screening potential bird flu virus carriers would have enabled international efforts to better coordinate public health responses to the outbreak.

The deployment of PCR-based tests to monitor the current viral load of influenza strains in wild birds and farmed poultry would allow us to act before the next potential epidemic can strike. It would also avoid the necessity for 'hysterical' attempts to slaughter massive numbers of uninfected animals as a last ditch effort to halt an outbreak. These animals, whether chickens, ducks or pigs, have lives too, and almost no religion on earth would condone such massacres of living organisms on such a scale, especially with the availability of preventative measures. Besides, culling all suspected animals may not be a good approach for preventing avian flu, as evident from the resurgence of the disease in early January after a cull of 1.8 million chickens and ducks in South Korea.

To ensure that a tragedy on the scale of the SARS outbreak does not repeat itself, the use and wide adoption of sensitive and reliable diagnostic tests for detecting the avian flu viruses should become a priority (similar to SARS[1]). In contrast to time-consuming conventional means of pathogen detection, such as microbial culture or antibody testing, molecular diagnostics enable mass screening at high speed. Indeed, success of viral culture depends on the presence of infectious viral particles in the samples, and antibody-based detection methods often lack sensitivity and specificity. Therefore, we should be using new-generation detection methods based on nucleic acid sequence based amplification (NASBA) or PCR to deal with disease outbreaks in this new century. To this end, our laboratories are working to develop expeditious molecular diagnostic methods for detecting avian flu of H1 to H15, H5, H7 subtypes[2–4]. Our bird flu virus detection systems are all validated by actual field tests, using samples collected from infected birds found in Hong Kong and other parts of the world.

Winning the war against infectious disease will require not only sufficient supplies of protective gear and drugs for attenuating and eliminating pathogens, but also systems of sensitive and fast detection methods as the first line of alarm. An experienced military brigade with the most advanced weapon arsenal cannot win the battle without a good radar system to detect the enemy. To avoid tragedies similar to the SARS outbreak, we cannot overemphasize the necessity of a sensitive and effective avian flu virus detection system.

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RNA interference detected 20 years ago?

To the editor:

As your review in the December issue attests (*Nat. Biotechnol.* **21**, 1457–1466, 2003), RNA interference has recently emerged as one of the hottest new research topics in science, an important research tool and potentially a new type of experimental therapy. I would like to bring to your readers' attention work carried out some 20 years ago by myself, Paul Lemke and Karl Esser—published in *Bio/technology*[1] and *Applied Microbiology and Biotechnology*[2]—that demonstrated the gene-silencing effect of double-stranded (ds)RNA and the employment of viruses as transmission vehicles.

When investigating extrachromosomal influences on the formation of aflatoxin—a naturally occurring, highly carcinogenic mycotoxin produced by two *Aspergillus* spp. that can contaminate crops, such as rice and corn—we came across a nontoxigenic strain of *Aspergillus flavus* that displayed unusual properties: it harbored very low concentrations of minor dsRNA components close to the limit of detection as well as proteinaceous capsids of heterogeneous sizes, most of them void of nucleic acids. Upon treatment with dsRNA antimetabolites, this originally nontoxigenic strain started to produce aflatoxins and continued to do so in the absence of these inhibitors while having lost its dsRNA components and capsids[1]. As these dsRNA traits showed similarities in structure and size to the genome of a dsRNA virus (PcV) from *Penicillium chrysogenum*, we conducted