Severe acute respiratory syndrome coronavirus and viral mimicry

Sir—Viruses have evolved various strategies to counteract host-cell processes, notably our immune responses toward their invasion. Oleszak and colleagues reported that the spike proteins of coronaviruses, particularly the mouse hepatitis virus, bovine coronavirus, and transmissible gastroenteritis virus, display Fc gamma receptor activity. Such molecular mimicry of components of our own immune system might even have a role in viral pathogenicity. This phenomenon, if shown to be true with the severe acute respiratory syndrome (SARS) virus, could help to explain why seemingly healthy individuals with active immune responses make up a large proportion of the patients who die from SARS. This mimicking of the Fc receptor might result in binding of non-specific IgG to the mimic receptor, expressed on virus or virus-infected cells, which would then inhibit neutralisation by virus-specific IgG because of steric hindrance. Such mimicry might also protect infected cells from antibody-dependent cell-mediated cytotoxicity and complement neutralisation.

Antibody-dependent enhancement of infection has been described for certain viruses, including the feline infectious peritonitis virus (FIPV), which is a coronavirus. Such enhancement involves the binding of virus-antibody complexes to Fc or complement receptors on the surface of monocytes or macrophages, resulting in virus uptake via receptor-mediated endocytosis, instead of neutralising the infection. With FIPV, antibody-dependent enhancement is mediated by specific sites on the spike protein. Whether the SARS virus exhibits such properties needs to be investigated.

Viruses affect the occurrence or course of certain autoimmune diseases. Talbot and colleagues have suggested that molecular mimicry between part of the human coronavirus (HCV) 229E and myelin basic protein of the central nervous system might contribute to the pathogenesis of multiple sclerosis. Autoreactive T cells specific to myelin components are cross-reactive with HCV 229E, and coronavirus-like particles have been isolated from patients with multiple sclerosis. We need to be vigilant as to whether the SARS virus (and vaccine) would also have such mimicry.

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Diagnosis of tuberculosis

Sir—Katie Ewer and colleagues (April 5, p 1168) confirm what colleagues in veterinary science have previously shown, although none of their reports were referenced. In 1991, Wood and colleagues wrote that interferon-γ production can be used as an indicator for exposure to tuberculosis in cattle and hence provide an alternative diagnostic assay for tuberculosis. Several groups have also reported, as long ago as 1997, that the use of highly specific antigens, such as the 6 kDa early secretory antigen target (ESAT-6), further improves the specificity of the assay and discriminates between infected animals and those vaccinated with BCG.

The particular assay for interferon-γ production (enzyme-linked immuno-spot, ELISPOT) used by Ewer and colleagues, although elegant, might not be practical as a routine diagnostic test. The labour-intensive need to isolate lymphocytes and the need to have access to sophisticated equipment greatly limits ELISPOT’s usefulness and undoubtedly makes it an expensive procedure for routine use. To avoid these constraints and to create a viable diagnostic alternative to the tuberculin skin test, the preference has been to use simple whole-blood cultures and well-established ELISA technology to measure interferon-γ production. Such an assay system has been extensively validated and is routinely used as a diagnostic test in cattle and primates, and has also gained approval from the US Food and Drug Administration for use in human beings.

The use of tuberculosis-specific antigens in both the whole blood interferon-γ test and the ELISPOT method has obvious benefits for improved specificity. In cattle, commensurate sensitivity between the two test methods was observed when cocktails of ESAT-6 and peptides from a 10 kDa culture filtrate protein (CFP-10) were compared as antigens. However, it is noteworthy that the amount of ESAT-6-specific interferon γ measured by ELISA, but not the frequency of responding cells (ELISPOT), correlated positively with the degree of pathology after infection with Mycobacterium bovis.

The effect of skin testing on boosting subsequent interferon-γ responses has also been shown by several groups, although this issue was not discussed by Ewer and colleagues. The finding that a previous tuberculin test will boost a subsequent interferon-γ response is now being used in New Zealand, with the interferon-γ assay replacing the comparative skin test in cattle. The fact that the children in Ewer and colleagues’ study had a Heaf test 1–2 months before being tested with ELISPOT would have had an effect on the results of this study, even allowing for the fact that tuberculin-specific antigens were used. Therefore, whether the ELISPOT assay will have a similar sensitivity for the diagnosis of latent tuberculosis in individuals who have not had a recent skin test is yet to be established.

CSL manufactures diagnostic products based on interferon-γ technology.

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