Short Communication

Clearance of infection in cats naturally infected with feline coronaviruses is associated with an anti-S glycoprotein antibody response

V. Gonon,1 V. Duquesne,2 B. Klonjkowski,2 M. Monteil,1 A. Aubert2 and M. Eloit1

1URA INRA de Génétique Moléculaire et Cellulaire, Génétique Virale, Ecole Nationale Vétérinaire d’Alfort, 94704 Maisons Alfort, France
2Virbac, BP 27, 06516 Carros, France

We have investigated by Western blotting the antibody responses against the three major structural proteins in cats naturally infected with feline coronaviruses that cleared virus infection (group I), established chronic asymptomatic infection (group II) or were sick (group III). The cats of group I developed an anti-S glycoprotein response that was, relative to the anti-M glycoprotein response, at least 30-fold higher than that of chronically infected cats from groups II and III. These results suggest that the anti-S glycoprotein response against antigenic domains revealed by Western blot is associated with clearance of the virus after natural infection, and is not a risk factor for the establishment of a chronic infection.

Feline infectious peritonitis (FIP) is a fatal immune-mediated coronavirus infection of cats which is caused by some strains of feline coronaviruses (FCoVs). FCoVs can be divided into two serotypes (I and II) according to neutralization assays, epitope specificity of the spike glycoprotein S, and proximity to canine coronavirus (Fiscus & Teramoto, 1987; Hohdatsu et al., 1991b; Motokawa et al., 1995; Herrewegh et al., 1995b; Motokawa et al., 1996). Vaccination by the parenteral route with live vaccines has been unsuccessful. In fact, in most cases, vaccinated cats developed a faster and more severe disease after challenge than control cats (reviewed by Olsen, 1993). This ‘facilitation’ was linked to the antibody response against the S glycoprotein of the virus, as demonstrated with recombinant vaccines expressing this glycoprotein, but not the M glycoprotein or N protein (Vennema et al., 1990, 1991; Gorin et al., 1995). It is believed that this antibody-dependent enhancement of infection is due to the facilitation of macrophage infection by virus–antibody complexes through internalization after interaction with the Fc receptor (Hohdatsu et al., 1991a). Nevertheless, this facilitation of infection has only been described in experimental conditions of challenge. Epidemiological data suggest that, in field conditions, sero-positive cats develop a protective immunity against natural infection rather than an increased sensitivity (Addie et al., 1995).

Preliminary observations showed that naturally sero-positive cats, following isolation to avoid successive reinfections, follow two types of behaviour. Some of them maintain an antibody response for several months, suggesting a chronic infection. In others, a decrease in antibody titres is observed until a negative response is recorded, which may be a sign of elimination of the virus (V. Gonon, unpublished data). To analyse if such differences between virus–host interactions could be associated with immune recognition targeted to specific virus proteins, we planned to investigate the antibody response against the major structural proteins of the virus.

To this aim, 13 catteries from different areas of France that comprised 150 seropositive cats, with previous (eight catteries) or no (five catteries) recorded cases of FIP, were included in the protocol. All the cats were isolated from each other by their owners at the beginning of the protocol, so as to minimize superinfection events. The antibody responses were regularly screened (every 2 months) for 1 to 2 years by an immunofluorescence assay. Because, in certain cases, the owners did not maintain strict conditions of isolation, we discarded some samples and conserved only those of 90 strictly isolated cats, which were processed for further analysis. At the end of the observation period, we ranked the cats into two groups (I and II), depending on their antibody titres. Group I included the 42 cats that became antibody-negative. RT–PCR identification of virus sequences as described in Herrewegh et al. (1995a) was conducted using samples of blood and faeces from each cat at the end of the observation period, and gave negative results (data not shown). Group II included the 48 cats that did not show any evidence of decrease in antibody titres. RT–PCR analysis was conducted on samples from 36 cats at the end of the observation period and gave positive results in all cases. A sample of serum corresponding to the isolation date, or close to it, was used for Western blot analysis. The cats were ranked

Author for correspondence: M. Eloit.
Fax +33 1 43 96 71 31, e-mail eloit@vet-alfort.fr
V. Gonon and others

Fig. 1. Specific antibody response of cats. Reactivity of serum antibodies from cats of group I \((n = 42)\), II \((n = 48)\) and III \((n = 43)\) against structural proteins of 79-1146 type II FCoV was tested by Western blot. The mean ratio of the intensity of each protein spot to the sum of the intensity of all the spots is depicted \((\pm SEM, P = 0.05)\).

We have analysed the antibody responses of cats naturally infected with FCov. We demonstrated here that cats that cleared a natural FCov infection developed an antibody response against one or several domain(s) of the S glycoprotein, relative to the M glycoprotein, that was on average 30 times higher than that of cats either chronically infected or sick. Because our study was designed to investigate antibody responses following natural infection, we could not control all the variables that differed between groups. In particular, infecting strains and their virulence, doses of infection,
variation between cat breeds or lineages could not be matched between groups. Another limitation was that each serum was tested at a unique dilution which was chosen after preliminary calibration. Because it is likely that the intensity of the spots was not proportional to antibody concentration in all ranges of concentrations, this could under or overestimate the value of the S/M ratio. Nevertheless, a clear difference was seen between antibody responses from groups I and II/III. Because cats that cleared FCoV infection (group I) came from catteries that either experienced FIP cases or did not record any case of FIP, it is unlikely that the difference between groups I and II/III is linked solely to the virulence of the FCoV strain. We postulate that this difference reflects a more complex interaction between the virus and the host. This interaction could be different, for a given strain, from cat to cat for several reasons, including the genetic background of the host and the virus infecting dose (which might also explain the observed differences regarding the natural or experimental conditions of challenges).

At this time, it is not clear whether the anti-S antibody response is a mechanism or only a marker of virus clearance. To address this question, we plan to identify the domains of the S glycoprotein preferentially recognized by the antibodies from cats of group I and to test them in vaccination experiments. In fact, as this antibody response was identified by Western blot in denaturing conditions, it is likely that the antigenicity of corresponding domain(s) is not highly dependent upon the glycoprotein conformation. The antibody response against conformational epitopes was not investigated in this study. The results presented here show that, in natural conditions, the anti-S response does not seem to be a risk factor in the development of FIP disease, which should challenge the widely accepted idea of the detrimental effect of the S glycoprotein in FIP recombinant vaccines.

References


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