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Interferon induction in swine lymphocyte antigen-defined miniature pigs

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SUMMARY

Interferon was induced in two groups of swine lymphocyte antigen (SLA)-defined miniature pigs with polynosinic:polycytidylic acid complexed with poly-L-lysine and carboxymethylcellulose. The group 1 pigs were low antibody-response phenotypes (SLA^d/d, SLA^a/c, SLA^c/c), and the group 2 pigs were high antibody-response phenotypes (SLA^d/d, SLA^a/a, SLA^c/c). Six hours after induction the antiviral titres were not influenced by the SLA group, but higher titres were observed in females. Higher antiviral titres were found in group 2 pigs before treatment and 24 hours after treatment, and higher titres were found in female pigs. The antiviral titres before and after treatment were also influenced by the sire. Group 2 pigs had lower total leukocyte counts before treatment, and there was a significant reduction in leucocyte numbers in both groups six hours after induction, due mainly to a large reduction in lymphocyte counts.

There are no data on the effect of a pig's SLA genotype on interferon (IFN) induction, although antibodies to porcine MHC class II antigens block the induction of IFN-α by transmissible gastroenteritis virus (Charley and Lavenant 1990). The objective of the present study was to compare the levels of induced IFN in pigs of high and low antibody-response phenotypes.

The miniature pigs used were divided into two groups on the basis of their SLA class II genotypes (Mallard 1987). Group 1 consisted of 15 pigs from four litters of the SLA^d/d, SLA^a/a, SLA^a/c, SLA^c/c, and SLA^g/g genotypes, which are considered to be low antibody-response phenotypes (Mallard et al 1989a). The high-responder pigs also produce antibodies of higher avidity (Appleyard et al 1992) and have higher serum IgG concentrations (Mallard et al 1989b).

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The statistical tests were based on normally distributed log-transformed data, and confidence intervals of 90 per cent or greater were considered significant.

The serum antiviral titres are shown in Table 1. The treatment with poly-ICLC resulted in a significant rise in titre (P<0.001) six hours after inoculation, and the antiviral activity in selected samples was characterised as type I IFN by standard criteria (Loewen and Derbyshire 1988). These pigs were similar to those observed

| Measurement | SLA group* | Treatment† | 0 | 6 | 24 |
|-------------|------------|------------|---|---|---|
| Antiviral activity | 1 | PICLC | 2 (4) | 167 (80) | 9 (13) |
|             | 2 | Control | 17 (7) | 7 (6) | 13 (6) |
|             | 2 | PICLC | 7 (6) | 160 (83) | 14 (7) |
|             | 2 | Control | 20 (0) | 10 (0) | 15 (7) |
| Leucocytes | 1 | PICLC | 22.3 (4.7) | 7.9 (3.0) | 12.7 (2.6) |
| (10^9 litre^-1) | 2 | Control | 23.4 (3.2) | 27.2 (4.0) | 23.9 (4.0) |
|             | 2 | PICLC | 17.9 (3.7) | 9.8 (2.9) | 15.1 (2.0) |
|             | 2 | Control | 11.7 (1.5) | 14.8 (0.5) | 11.6 (0.6) |
| Neutrophils | 1 | PICLC | 8.6 (2.4) | 4.6 (2.9) | 3.2 (1.3) |
| (10^9 litre^-1) | 2 | Control | 9.0 (3.4) | 11.9 (2.6) | 8.4 (2.0) |
|             | 2 | PICLC | 5.7 (1.8) | 4.4 (1.7) | 3.0 (1.3) |
|             | 2 | Control | 4.7 (1.2) | 7.3 (3.3) | 3.7 (0.7) |
| Lymphocytes | 1 | PICLC | 12.5 (3.7) | 0.7 (0.5) | 8.4 (2.1) |
| (10^6 litre^-1) | 2 | Control | 12.7 (1.7) | 15.9 (2.1) | 14.3 (0.7) |
|             | 2 | PICLC | 11.3 (3.8) | 1.0 (1.0) | 9.2 (2.0) |
|             | 2 | Control | 6.4 (0.1) | 6.7 (2.6) | 7.4 (1.3) |

See text for significant differences between treatments.
higher titres in the female pigs, which could have resulted from sex-related differences in the kinetics of IFN production, correspond with similar findings in mice (Zawatzky et al 1982), but contrast with the finding that men had higher IFN-alpha levels than women (Bever et al 1985), although Abb et al (1984) found no difference in the production of IFN-α between men and women.

The antiviral titres before treatment and 24 hours after treatment (Table 1) were influenced by the SLA group, the sex and the sire (P<0.05) of the pigs. However, the low levels of IFN activity prevented it from being characterised as IFN-γ and it may have been associated with other cytokines, although Bocci (1988) postulated that low levels of IFN may represent a physiological response to the animal’s microbial environment. The group 2 pigs had significantly higher titres (P<0.01) than the group 1 pigs, and the titres in the females were again higher than in the males (P<0.01). The higher levels of antiviral activity in the group 2 pigs were of particular interest because these pigs belonged to the high immune response phenotypes.

The group 2 pigs (Table 1) also had fewer circulating leukocytes before the poly-ICLC treatment (P<0.0015), and if the circulating antiviral activity at this time was IFN, it may have contributed to these lower counts by sequestering cells in lymphoid tissue (Gresser et al 1981) or by bone marrow suppression (Greenberg and Mosny 1977). The treatment of both groups of pigs with poly-ICLC significantly reduced the numbers of leukocytes, probably as a result of leucocyte sequestration (Gresser et al 1981), by six hours after induction (P<0.001), and the numbers were still low after 24 hours (P<0.005), in accordance with earlier findings (Loewen and Derbyshire 1988). The numbers of segmented neutrophils were significantly reduced six and 24 hours after induction (P<0.05) but the severe lymphopenia six hours after induction (P<0.005) was the main cause of the lower total leukocyte counts. By 24 hours, the lymphocyte counts in the treated pigs were within the normal range, but still significantly lower than in the control pigs (P<0.05).

This study provided no evidence of an effect of SLA genotype on the response of miniature pigs to IFN induction with poly-ICLC, but there was evidence of non-MHC related genetic effects on their response to poly-ICLC, and on the low levels of circulating antiviral activity before induction, which were also influenced by the SLA genotype.

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