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*Gene-Antigen Register*

# The *H-2* Haplotype of the PN (Palmerston North) Inbred Strain

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Inbred Palmerston North (PN) mice have been established as an animal model of the multisystem autoimmune disease, systemic lupus erythematosus. Disease in these animals is characterized by the presence of antibodies to nuclear antigens and immune complex glomerulonephritis (Walker et al. 1978). Because of the usefulness of this animal model for further studies of autoimmune disease, and because of the well-known relationship between the major histocompatibility complex (MHC) and autoimmune disease development, it is of considerable interest to determine the *H-2* haplotype carried by this strain. To accomplish this identification, antigens in the *K*, *D*, and *I* regions of the MHC were determined by microcytotoxic assay (Frelinger et al. 1974) in the laboratory of one of us (C. S. David).

PN mice are descendents of albino mice purchased in a New Zealand pet shop in 1948. The offspring of these albinos were raised at Palmerston North Hospital in Palmerston North, New Zealand, and were then taken to Massey University and subsequently sent to the Glaxo Laboratories of New Zealand. Breeding pairs were returned to Dr. Richard D. Wigley at the medical research department of Palmerston North Hospital. In 1964 a brother-sister mating program was begun with selection for positivity for anti-nuclear antibody (ANA). The resulting strain was called PN/nA. At the F9 generation a subline (PN/nB) was begun from a first cousin mating and was continued with brother-sister matings. In March 1975, when the A subline was in the F28 generation and the B subline in the F23 generation, breeders of both sublines were shipped to the United States. Animals currently in use are from the B subline.

Initially, three PN mice were killed and their spleen cells tested by the microcytotoxicity test with a battery of anti-H-2 and anti-Ia sera. We noticed that whenever an H-$2^q$ strain was one of the recipients used for the antiserum production, the PN mice failed to react. This suggested that strain PN could possibly carry the *H-*$2^q$ haplotype. Next, antisera directed against most of the private antigens of the *H-2*, *K*, *D*, and *I* regions were tested against cells of three more PN mice. The results with two of these mouse cells are shown in Table 1.

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**Table 1.** Reciprocal of cytotoxic titers of antisera with B10.Q, PN-1, and PN-2 cells

| Antiserum | Specificity | B10.Q | PN-1 | PN-2 |
|---|---|---|---|---|
| (B10.A × A)$F_1$ anti-B10.AQR | H-2.K17 | 1280 | 1280 | 1280 |
| A.TL anti-A.AL | H-2.K11, 23 | 80 | 160 | 160 |
| (B10 × A)$F_1$ anti-B10.AKM | H-2.K30 | 40 | 80 | 80 |
| (CBA × B10)$F_1$ anti-B10.S(21R) | H-2.D4, 13 | 80 | 80 | 80 |
| (A.TL × BZ.H)$F_1$ anti-A.AL | H-2.K23 | 0 | 0 | 0 |
| (B10.AKM × A)$F_1$ anti-B10.MBR | H-2.K33 | 0 | 0 | 0 |
| (B10.A × BZ.H)$F_1$ anti-B10.D2 | H-2.K31 | 0 | 0 | 0 |
| (B10.AQR × A)$F_1$ anti-B10.T(6R) | Ia.10 | 80 | 80 | 80 |
| (B10.MBR × D2.GD)$F_1$ anti-B10 | Ia.9 | 160 | 40 | 40 |
| [B10.F(14R) × A]$F_1$ anti-B10.F | Ia.13 (H-2.16) | 320 | 160 | 160 |
| (B10 × A)$F_1$ anti-B10.D2 | Ia.16 (H-2.31) | 40 | 20 | 20 |
| (C3H.Q × B10.D2)$F_1$ × anti-B10.AQR | Ia.22 (17, 18, 19) | 0 | 0 | 0 |
| [B10.A(5R) × DBA/1]$F_1$ anti-B10.MBR | Ia.8 | 0 | 0 | 0 |

An antiserum directed against H-2.17, the private specificity of $K^q$, was strongly reactive with PN cells as well as with cells of the control B10.Q strain. An antiserum detecting H-2.11, 23 was reactive with three target strains while a specific antiserum detecting H-2.23 failed to react. H-2.11 is expressed by the $-2^q$ haplotype, but H-2.23 is not. For the *H-2D* locus, both anti-H-2.30 and anti-H-2.13, which are markers for $D^q$, reacted with PN cells and B10.Q control strain cells. Antisera directed against other private H-2 specificities did not react with PN or B10.Q targets. A battery of anti-Ia sera was tested against the PN cells and the control B10.Q cells. As can be seen in the table, antibodies directed against Ia.10, Ia.9, Ia.13, and Ia.16, markers for $I^q$, reacted with the three targets, whereas most of the other anti-Ia sera that were not expected to react with cells of the $H\text{-}2^q$ haplotype did not react. These studies provide positive evidence that PN strain mice are of the $H\text{-}2^q$ haplotype. Further confirmation of the presence of the $H\text{-}2^q$ haplotype in PN mice is obtained from the finding that PN mice are C4 high, Slp negative, and G7 (C4d) negative. All of these serological findings are consistent with the hypothesis that the PN strain carries the $H\text{-}2^q$ haplotype.

To provide further confirmation that the $H\text{-}2^q$ haplotype is indeed the haplotype of the PN strain, skin grafts were performed. The grafting method employed has been previously described by Billingham and Silvers (1961). Graft recipients were male or female (PN × B10)$F_1$ animals between the ages of 3 and 6 months. Donors were B10.Q mice of the same sex as the recipients. In all, 10 males and 11 females received grafts. Four male to male and three female-to-female grafts resulted in technical failures. The remaining grafts survived to greater than 75 days. In situations in which skin graft donor and recipient differ in *H-2*, grafts are rejected in less than 18 days. Since B10.Q grafts survive in the $F_1$ recipient, the recipient must carry the $H\text{-}2^q$ haplotype as well as the B10 background genome. The B10 parental strain is $H\text{-}2^b$. Therefore, the $H\text{-}2^q$ haplotype must be present in the PN parental strain. Serological typing has thus been confirmed by skin graft data.

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