NZBNZW1F (NZB x NZW)F1

Origin
NZBNZW1F/OlaHsd
This F1 hybrid is a cross between NZB/OlaHsd females and NZW/OlaHsd males.

Characteristics
The F1 hybrid of two inbred strains can be a useful animal for many purposes. It is genetically uniform and heterozygous for all the genes for which the two parental strains differ. F1 animals are easy to produce (hybrid vigor) and are less susceptible to environmental influences than the parent inbred strain.

Animal model
The NZBNZW1F is a mouse model for systemic lupus erythematosus.

Anatomy
The comparative study of the thymus in autoimmune and normal strains, revealed that important changes of the large medullary epithelial cells, involved in the formation of Hassall’s corpuscles, occur in NZB, NZW and (NZB x NZW)F1 mice (De Vries and Hijmans, 1967).

Behavior
Autoimmunity is associated with increased anxiety and less exploratory behavior (Schrott and Crnic, 1996).

Genetics
Coat color genes  - a/A, b/B, c/C, p/P : agouti.
Histocompatibility  - H-2^k
The NZBNZW1F will be heterozygous for all the loci where the NZB and NZW differ and homozygous for all the loci where both parental strains are the same.
NZBNZW1F hybrids develop a systemic lupus erythematosus (SLE)-like syndrome. It has been proposed that the NZB parent contributes the dominant Ads-1 and Ads-2 genes controlling anti-dsDNA production, and the NZW parent contributes the dominant Ads-3 and Ads-4 genes, which are modifier genes. Similarly, the NZW parent contributes two dominant genes Ass-3 and Ass-4, which enhance the effect of Ass-1 and Ass-2 in the production of anti-ssDNA antibodies. The Agp-3 gene of NZW intensifies the effect of NZB Agp-1 gene controlling anti-gp70 circulating immune complexes. However, the NZW Aem-1 gene suppresses the activity of the NZB Aia-1 gene responsible for anti-erythrocyte antibody production. Finally, a dominant trait for lupus nephritis, Lpn-1, is modified by two additional genes, Lpn-2 and Lpn-3, both of which are donated by the NZW partner. The genes Ass-3, Ads-3, Agp-3 and Lpn-2 are linked to the H-2^k haplotype of NZW (Shirai et al, 1984; 1987; Bearer et al, 1986). The net result is that NZBNZW1F hybrids have an intensified production of anti-dsDNA antibodies, anti-ssDNA antibodies, and circulating immune complexes; an increased susceptibility to lupus nephritis; and a decreased production of anti-erythrocyte antibody when compared with NZB.

Although evidence exists for each of the proposed loci listed above, there is still disagreement concerning the precise assignment of genetic loci to autoimmune phenotype (Kotzin and Palmer, 1987).
Kotzin et al (1985) demonstrated a large deletion (8.8-kilobase segment) in the DNA containing Cß1, Dß2, and Jß2 cluster encoding the T-cell ß chain; this has been confirmed by Theofilopoulos (1986). The functional significance of this deletion in the NZBNZW1F hybrid is unknown.

Husbandry
While certain infectious agents have been shown to induce autoantibodies and immune complex disease in normal mice (Schulman et al, 1964; Barnes and Tuffrey, 1967; Dixon et al, 1969), other infectious agents have been shown to inhibit and ameliorate disease in NZB and NZBNZW1F hybrid mice (Oldstone and Dixon, 1972). Engleman et al (1981) proposed that virus-induced type 1 interferon is responsible for the accelerated autoimmune
glomerulonephritis. This is associated with decreased life span and diminishes histological evidence of glomerulonephritis. This is associated with decreased expression of platelet-derived growth factor-A (Troyer et al., 1997).

NZBNZF1 mice develop a disease characterized by high levels of antibodies directed toward nucleic acid antigens, progressive immune complex glomerulonephritis, and a marked enhancement of the disease in females. As early as two months of age, Anti-Nuclear Antibodies (ANA) can be detected in some NZBNZF1 mice. By 12 months of age all NZBNZF1 hybrids have detectable levels of ANA (Andrews et al., 1978; Quimby and Schwartz, 1982). The anti-dsDNA antibodies have nephritogenic properties and appear to be principally responsible for the immune complexes deposited in the glomerulus (Lambert and Dixon, 1968).

Histopathology of renal lesions has been described by Hicks and Burnet (1966). Unique subsets of T- and B-lymphocytes are found in NZBNZF1 mice that are responsible for the production of pathogenic (caticionic) IgG anti-DNA (Datta et al., 1987).

Rabin (1985) reported a significant difference in the survival of NZBNZF1 hybrids associated with the cage type. Mice held in wire mesh cages lived considerably longer than F1 hybrids housed in solid-bottom cages.

**Miscellaneous**

Characteristics of the NZBNZF1 hybrid have been described by Festing (1997) and ILAR (1989).

### References


15. Oldstone MBB, Dixon FJ (1972) Inhibition of antibodies to nuclear antigen and to DNA in New Meze mice infected with Lactate dehydrogenase virus. Science 176, 764-786.