59) Lack of Genetic Linkage Between Susceptibility to Hypertension and the Major Histocompatibility Complex in Spontaneously Hypertensive Rats.
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The SHR strain spontaneously develops hypertension which is genetically determined to a certain degree. Current information by Tanase (Exp. Anim., 28: 519, 1979) indicates that the development of hypertension in SHR is regulated by a single major gene and several other genes with minor effects.

In this report, we confirm that the hypertension trait of SHR is controlled by a single gene or gene cluster. In addition, we have determined if susceptibility to hypertension in this rat strain is linked to the major histocompatibility complex (MHC) of the rat.

(Materials and Methods)

Inbred strains of SHR and ACI rats were used for genetic analysis; they were fed with rat chow (CE2, Nippon Krea) and sterilized tap water, and were kept under semi barrier conditions. Blood pressure was measured by the tail pulse pickup method without anesthesia. The expression of class I MHC antigens was determined by a Ficoll hemagglutination technique. Rat antibodies reacting with RT1k(SHR) and RT1^a(ACI) were prepared by hyperimmunization of appropriate rat strains with three skin grafts.

(Results)

1. Genetic control of blood pressure. The average blood pressure of 25 female SHR and 20 ACI rats measured 168 ± 5 mmHg and 110 ± 2 mmHg respectively. The mean blood pressure level of F₁, F₂ and two kinds of backcross generations measured 136 ± 10 , 139 ± 32 , 144 ± 24 and 120 ± 20 mmHg respectively, and did not differ significantly from the mid-parent value. If a single locus determines the blood pressure level, there will be a 1:1 segregation in the backcross and a 1:2:1 in the F₂ generation. Therefore, individuals in the F₂ and backcross generations were divided into three phenotypes according to the blood pressure level: types, that is, of ACI rats with normotension (≤ 130 mmHg), of F₁ hybrids with intermediate blood pressure ($130 \leq \leq 150$ mmHg) and of SHR with hypertension (≥ 150 mmHg). The phenotypic segregation ratio at each generation was the expected ratio of 1:1 in the backcross generations and 1:2:1 in the F₂ generation. This result indicates that the susceptibility to hypertension of SHR is controlled by a single gene.

2. Genetic linkage between susceptibility to hypertension and RT1 locus. The SHR and ACI rats are of k/k and a/a genotypes at the A region of RT1. In 20 of the F₂ progeny, 3 out of 5 rats who serotyped k/k had hypertension of the SHR type while the remaining 2 rats showed the ACI type with normotension. Of the 10 rats with the k/a genotype, 2 were the SHR type, 4 were the F₁ type and the remaining 4 were the ACI type. In 28 (F₁ x SHR) backcross progeny, 7 out of 13 rats with the k/k genotype were the F₁ type and the remaining 6 were the SHR type. Of the 15 rats with the k/a genotype, 8 were the F₁ type and 7 were the SHR type. These results indicate that the development of hypertension is not associated with the RT1 complex of the rat.

(Conclusion)

The results from genetic crosses between SHR and ACI rats showed that the hypertensive disposition of SHR is regulated by a single gene but is not linked to the rat MHC.