

HAPTEN-SPECIFIC T CELL RESPONSES TO 4-HYDROXY-3-NITROPHENYL ACETYL

VI. Evidence for Different T Cell Receptors in Cells That Mediate H-2I- restricted and H-2D-restricted Cutaneous Sensitivity Responses*

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Imanishi and Makela (1, 2) first reported that the primary anti-4-hydroxy-3-nitrophenyl acetyl (NP)¹ antibody has a heteroclitic fine specificity in most strains of mice expressing the Igh-1^b allotype, with anti-NP antibodies binding chemical analogues such as 4-hydroxy-5-iodo-3-nitrophenyl acetyl (NIP) with greater affinity than NP itself; the idiotype, termed NP^b, was found predominantly expressed along with lambda light chains. Cramer et al. (3) furthered these observations, describing the occurrence of the NP^b idiotype on both primary anti-NP antibodies and on NP-specific receptors isolated from immune T cells of mice with the Igh-1^b allotype. Weinberger et al. (4-6) noted a similar fine specificity pattern on functional subpopulations of T cells, namely NP-specific delayed-type hypersensitivity (DTH) effector and NP-specific suppressor inducer T cells, showing the sharing of idiotypic structures between receptors on functional subpopulations of NP-specific T cells and anti-NP antibodies.

In a previous report, we described the expression of cross-reactive cutaneous sensitivity (CS) responses induced by NP-*O*-succinimide (NP-*O*-Su) and elicited by NIP-*O*-succinimide (NIP-*O*-Su) in strains of mice possessing the Igh-1^b allotype, but not in strains bearing allotypes Igh-1^c or Igh-1^j (7). The present report extends these observations by analyzing the cross-reactivity of NP-*O*-Su-induced CS responses in additional inbred strains of mice. Some strains of mice that failed to demonstrate cross-reactive NP-induced DTH responses were able to mount cross-reactive CS responses after NP-*O*-Su priming, despite the absence of NP^b idiotype in these strains.

The present report also presents evidence for the existence of at least two T cell subsets within the NP-specific CS effector cell population, at least in the AKR strain: one H-2I-restricted, the other H-2K/D-restricted; each associated with a distinct fine specificity pattern, presumably the manifestation of different receptors on these T cell subpopulations.

Materials and Methods

Mice. All mice were either purchased from The Jackson Laboratory, Bar Harbor, Maine, or were bred in the animal facilities at Harvard Medical School, Boston, Mass. Mice were used

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¹ *Abbreviations used in this paper:* BGG, bovine gamma globulin; CS, cutaneous sensitivity; DMSO, dimethyl sulfoxide; DTH, delayed-type hypersensitivity; NIP, 4-hydroxy-5-iodo-3-nitrophenyl acetyl; NIP-*O*-Su, NIP-*O*-succinimide; NP, 4-hydroxy-3-nitrophenyl acetyl; NP-*O*-Su, NP-*O*-succinimide.

at 2–12 mo of age, and were maintained on laboratory chow and acidified, chlorinated water *ad libitum*.

Antigens. NP-O-Su and NIP-O-Su were purchased from Biosearch Co., San Rafael, Calif. Dimethylsulfoxide (DMSO) was purchased from Fisher Scientific Co., Pittsburgh, Pa.

Immunization for CS Responses. Animals were shaved and primed subcutaneously with saturated solutions of NP-O-Su (7 g/100 ml) or NIP-O-Su (7 g/100 ml) in DMSO. A total of 0.1 ml of antigen was divided equally between two sites on either ventral flank, followed by 0.1 ml of borate-buffered saline at pH 8.6.

Elicitation of CS Responses. 6 d after immunization or 1–2 h after adoptive transfer, mice were challenged for the CS response. Antigen solutions were prepared 1 min before challenge, as follows: 15 μ l of NP-O-Su (2 g/100 ml DMSO) or NIP-O-Su (1 g/100 ml DMSO) was added to 300 μ l of phosphate-buffered saline, pH 7.2, in a glass tube. These experimental conditions were chosen to minimize the nonspecific inflammatory response. 25 μ l of the antigen solution was injected into the left footpad. Footpad swelling was measured 24 h after challenge, using an engineer's micrometer (Schlesingers for Tools Ltd., Brooklyn, N. Y.). Swelling was determined as the difference, in units of 10^{-3} cm, between the left and right footpad thickness.

Adoptive Transfer of CS Responses. Mice were immunized as described above. 6 d after priming, the animals were sacrificed, inguinal lymph nodes removed, and a single cell suspension prepared (using a fine mesh screen). The cells were washed twice in Eagle's minimal essential medium. Viable cells were counted using trypan blue. 4.0×10^7 viable cells were injected intravenously into untreated recipients. Control mice received lymphocytes from normal donors. The recipients and control mice were challenged with NP-O-Su or NIP-O-Su 1–2 h after transfer, as described above.

Data Analysis. Two-tailed Student's *t* tests were used to perform statistical analyses. Data are expressed as the mean incremental footpad swelling \pm SE in units of 10^{-3} cm.

Results

Genetic Control of the Fine Specificity of NP-O-Su-induced CS Responses. To extend our knowledge of the strain distribution of the fine specificity pattern of CS responses induced by NP-O-Su, fine specificity analyses were conducted in 10 inbred strains of mice. Using the reactive compounds NP-O-Su or NIP-O-Su as 7% solutions in DMSO, mice were primed subcutaneously on either ventral flank. Subsequently, mice were challenged with a 0.1% solution of NP-O-Su or a 0.05% solution of NIP-O-Su in the left hind footpad on the sixth day after sensitization because this induction period has been shown to result in peak responses (7). The results of these experiments are summarized in Table I. All strains of mice tested responded to homologous challenges, that is, to NP-O-Su challenge after NP-O-Su priming, and to NIP-O-Su challenge after NIP-O-Su priming. Further, all except the DBA/2 and C3H strains showed significant levels of cross-reactivity to NIP-O-Su challenge after NP-O-Su priming. Our previous studies demonstrated that genes in the Igh region controlled the ability to mount such cross-reactive CS responses (7). The present results imply that, in addition to mice with the Igh-1^b allotype, strains bearing allotypes Igh-1^a, -1^d, -1^e, and -1^f may also be able to generate NIP-cross-reactivity in NP-induced CS responses. This is in contrast to DTH responses induced by NP-bovine gamma globulin (BGG), in which NIP cross-reactive responses were only elicited in strains bearing the Igh-1^b allotype, but not in strains possessing the Igh-1^a, Igh-1^c, Igh-1^d, Igh-1^e, or Igh-1^f allotypes (4, 8).

Genetic Restrictions and Fine Specificity of the Ability to Adoptively Transfer NP-O-Su-induced CS Responses. In contrast to NP-specific DTH responses, where donor-recipient homology at I-A is required for successful transfer of reactivity (7), it has already been reported (7) that homology at either the H-2K, I, or D regions is sufficient for transfer

TABLE I
Genetics of Cross-Reactivity in NP-O-Su-induced CS Responses*

Strain	H-2	Igh-1	Immunogen	Footpad swelling responses‡	
	Haplo-type	Allo-type		NP-O-Su	NIP-O-Su
BALB/c	d	a	NP-O-Su	28.3 ± 3.8 (3)	22.3 ± 2.7 (4)
			NIP-O-Su	NT	27.2 ± 1.8 (5)
C57L	b	a	NP-O-Su	32.8 ± 3.7 (4)	33.8 ± 1.1 (4)
			NIP-O-Su	NT	22.0 ± 2.6 (4)
C57BL/6	b	b	NP-O-Su	17.5 ± 1.5 (6)	22.2 ± 3.5 (5)
			NIP-O-Su	NT	16.2 ± 3.7 (5)
DBA/2	d	c	NP-O-Su	28.8 ± 2.8 (5)	0.7 ± 0.7 (6)
			NIP-O-Su	NT	19.8 ± 2.3 (6)
AKR	k	d	NP-O-Su	16.5 ± 1.3 (4)	23.8 ± 2.2 (4)
			NIP-O-Su	NT	37.5 ± 2.5 (4)
A/J	a	e	NP-O-Su	24.0 ± 2.2 (4)	16.3 ± 1.3 (4)
			NIP-O-Su	NT	16.0 ± 3.1 (3)
A.CA	f	e	NP-O-Su	26.8 ± 4.6 (5)	13.8 ± 3.3 (6)
			NIP-O-Su	NT	24.9 ± 2.7 (5)
A.SW	s	e	NP-O-Su	32.0 ± 4.0 (3)	29.0 ± 2.7 (5)
CE/J	k	f	NP-O-Su	29.5 ± 2.4 (4)	43.6 ± 1.1 (5)
			NIP-O-Su	NT	39.7 ± 0.3 (3)
C3H	k	j	NP-O-Su	32.0 ± 3.1 (5)	6.8 ± 1.9 (5)
			NIP-O-Su	NT	19.8 ± 0.5 (5)

* See text for experimental protocols.

‡ Responses expressed as mean increment ± 1 SEM in units of 10^{-3} cm. The number of mice/group is in parentheses. NT, not tested. $P < 0.005$ compared with unprimed mice challenged with the same agent. Background swellings for mice receiving challenges alone were: 8.8 ± 0.8 (18) for NP-O-Su; 8.0 ± 1.0 (15) for NIP-O-Su.

of NP-specific CS responses. Those earlier experiments used donors that carried the Igh-1^b allotype, and in all cases both NP- and NIP-reactivity were transferred concomitantly by NP-O-Su immune lymph node cells. To confirm and extend our earlier work, in the present study we first transferred NP-O-Su-primed lymph node cells from B10.BR, a strain which bears the H-2^k haplotype, Igh-1^b allotype, Igh-Np^b gene for NP^b idiotype, and exhibits cross-reactive CS responses. As is evident in Table II, these cells were able to concomitantly transfer both NP- and NIP-reactivity into naive recipients compatible at either H-2I (i.e., TBR-3, which is homologous with the H-2^k haplotype at the I-A and, possibly, the I-B and I-J subregions) or H-2D (i.e., C3H.OH) regions, but not into those without H-2 homology (B10.RIII). Nonimmune B10.BR cells were unable to transfer NP-specific CS reactivity into any of the recipient strains.

To complement these findings, a similar experiment was conducted using donor C3H mice, which carry the H-2^k haplotype, Igh-1^j allotype, and are unable to mount NIP-cross-reactive CS responses after NP priming. NP-O-Su-primed C3H lymph node cells could successfully transfer NP-reactivity into both TBR-3 and C3H.OH naive recipients, but not into B10.RIII. NIP-cross-reactivity was not tested in these transfer experiments because C3H had already been shown to lack this property (Table I).

Prompted by both the distinct genetics of transferability and the different allotype-

TABLE II
*Fine Specificity Analyses of Genetic Restrictions in the Ability to Adoptively Transfer NP-O-Su-induced CS Responses in B10.BR and C3H**

Experiment	Donor cells	Recipient	Regions of H-2 compatibility	Footpad swelling responses [‡]		
				NP-O-Su	NIP-O-Su	
I	B10.BR NP-O-Su Primed	TBR-3	I	28.3 ± 2.3 [§] (4)	25.2 ± 2.0 [§] (5)	
		C3H.OH	D	27.3 ± 2.4 [§] (4)	27.0 ± 1.1 [§] (4)	
		B10.RIII	None	15.5 ± 0.5 (2)	13.7 ± 2.6 (3)	
	B10.BR Nonimmune	TBR-3	I	13.2 ± 0.5 (2)	NT	
		C3H.OH	D	14.6 ± 1.8 (5)	NT	
		B10.RIII	None	13.8 ± 1.2 (5)	NT	
	No transfer	B10.RIII		14.4 ± 1.4 (5)	16.0 ± 0.9 (5)	
	II	C3H NP-O-Su Primed	TBR-3	I	23.4 ± 1.0 [§] (5)	NT
			C3H.OH	D	25.8 ± 1.5 [§] (5)	NT
B10.RIII			None	9.3 ± 3.4 (4)	NT	
C3H Nonimmune		TBR-3	I	12.0 ± 1.9 (5)	NT	
		C3H.OH	D	12.0 ± 1.1 (5)	NT	
		B10.RIII	None	13.2 ± 1.6 (6)	NT	
No transfer		B10.RIII		15.0 ± 1.1 (6)	NT	

* See text for experimental protocols.

[‡] Responses expressed as mean increment ± 1 SEM in units of 10⁻³ cm. The number of mice/group is in parentheses. NT, not tested.

[§] *P* < 0.005 compared with unprimed mice challenged with same agent.

linkage patterns observed between CS and DTH responses, we then transferred NP-O-Su-sensitized AKR lymph node cells into various recipient strains. The AKR strain also carries the H-2^k haplotype and bears the Igh-1^d allotype; it lacks the Igh-1^b allotype and NP^b idio type, yet is able to give cross-reactive CS responses to NIP-O-Su challenge after NP-O-Su priming. Our observations are summarized in Table III. It is apparent that when there was complete H-2 homology between donor and recipient, 4.0 × 10⁷ NP-O-Su immune AKR lymph node cells effectively transferred CS responsiveness to challenge with either NP-O-Su or NIP-O-Su. Further, when there was H-2 compatibility at H-2D or at H-2K + I-A, both NP-O-Su and NIP-O-Su could elicit CS responses after transfer of NP-immune cells. In contrast, when these same cells were transferred into mice which were incompatible at the K, I, and D regions of the H-2 complex, no immunity was transferred. However, when there was homology at the H-2I region alone (i.e., TBR-3 as the recipient) we were unable to elicit cross-reactive CS responses to NIP-O-Su challenges, although homologous NP-specific CS responses were clearly observed. Therefore, in the AKR strain, the specificity of cells that recognize NP in association with H-2D differs from that of cells that recognize NP in association with I region products.

Discussion

It was long believed that the T cell-dependent phenomena of DTH and contact sensitivity were effectively the same process induced and elicited by protein antigens

TABLE III
*Fine Specificity Analyses of Genetic Restrictions in the Ability to Adoptively Transfer NP-O-Su-induced CS Responses in AKR**

Donor cells	Recipient	Regions of H-2 compatibility	Footpad swelling responses [‡]	
			NP-O-Su	NIP-O-Su
AKR	AKR	K,I,S,D	20.6 ± 1.7§ (5)	23.8 ± 2.2§ (5)
NP-O-Su	C3H.OL	S,D	20.2 ± 1.0§ (10)	20.8 ± 1.7§ (9)
Primed	C3H.OH	D	20.4 ± 2.2§ (5)	20.6 ± 0.7§ (5)
	4R	K,I-A	22.8 ± 1.0§ (5)	20.0 ± 2.5§ (4)
	TBR-3	I	23.1 ± 1.4§ (11)	5.6 ± 1.5 (8)
	B10.S	None	9.5 ± 1.1 (6)	7.4 ± 2.3 (5)
	B10.GD	None	6.6 ± 1.5 (5)	6.4 ± 1.8 (5)
AKR	C3H.OL	S,D	6.0 ± 1.7 (6)	NT
Nonimmune	C3H.OH	D	NT	10.4 ± 1.8 (5)
	4R	K,I-A	5.0 ± 2.4 (5)	NT
	TBR-3	I	8.4 ± 2.2 (5)	7.3 ± 3.2 (4)
	B10.S	None	5.5 ± 1.9 (6)	NT
	B10.GD	None	NT	9.3 ± 1.1 (4)

* See text for experimental protocols.

[‡] Responses expressed as mean increment ± 1 SEM in units of 10⁻³ cm. The number of mice/group is in parentheses. NT, not tested.

[§] *P* < 0.005 compared with unprimed mice challenged with same agent. Background swellings for mice receiving challenges alone are given in the legend to Table I.

or by reactive haptens, respectively (9, 10). That is, both reactions exhibit a delayed-type kinetics of elicitation, are transferable by appropriately sensitized T cells, and are characterized histologically by a similar mononuclear cell infiltrate (11). It was subsequently demonstrated that a genetic difference also existed between the two reactions, namely, in that contact sensitivity to epicutaneously applied 2,4-dinitrofluorobenzene (12) or to NP-O-Su (7) could be transferred between strains of mice sharing either H-2K, I, or D regions of the murine major histocompatibility complex in contrast to DTH responses to protein antigens, where only I region homology is sufficient for adoptive transfer of reactivity (4, 12, 13). However, there are reports of DTH responses that do not follow similar genetics: Zinkernagel (14) found that transfer of DTH responsiveness to lymphocytic choriomeningitis virus was H-2K/D restricted; more recently, Weiner et al. (15) noted that DTH responses to reovirus were restricted by H-2D and by H-2K or I-A/B. Thus, it appears that genetic restrictions are not distinguishing characteristics that separate CS and DTH responses. The cellular mechanisms directing these T cell-dependent responses may be better understood if we consider the genetic criteria of the effector population rather than the method of sensitization. Thus, the H-2K/D-restricted reactivity may reflect a CTL-like effector cell population with antigen recognized in association with K/D region products on the surface of the target cell, whereas I-region-restricted responses involve macrophage presentation of antigen in company with I-region products. Support for this contention has been obtained from preliminary experiments demonstrating that NP-specific footpad swelling could be elicited with NP conjugated to a heterologous protein carrier only if the NP-O-Su-primed donor cells were compatible

with the recipient at H-2I, whereas NP coupled directly to syngeneic cells could only elicit responses in H-2K/D-restricted combinations (16). We now extend the list of the differences between I region- and K/D-restricted T cell subpopulations by further genetic approaches: that is, by a demonstration of distinct fine specificity patterns of H-2D- vs. I region-restricted clones.

It was originally found by Imanishi and Makela (1) that the primary anti-NP antibody has a heteroclitic fine specificity in most strains of mice carrying the Igh-1^b allotype, with anti-NP antibodies binding chemical analogues, such as NIP, with higher avidity than NP itself. The idiotype, called NP^b, was expressed predominantly along with lambda light chain. These experiments were extended by Cramer et al. (3) who described the presence of the NP^b idiotype on both primary anti-NP antibodies and on NP-specific receptors isolated from immune T cells from strains of mice expressing the Igh-1^b allotype. More recently, Weinberger et al. (4-6) have discovered a similar fine specificity pattern on functional subpopulations of T cells, namely NP-specific DTH effectors and NP-specific afferent suppressor T cells, thus illustrating idiotypic sharing between receptors on NP-specific T cells and anti-NP antibodies. Only strains of mice bearing the Igh-1^b allotype demonstrated NIP-cross-reactive DTH responses to NIP-bovine serum albumin challenge after NP-BGG priming.

The strain distribution patterns of NIP-cross-reactive responses after NP-specific induction differ between DTH and CS responses. In addition to the strains of mice carrying the Igh-1^b allotype, strains expressing the heavy chain linkage groups associated with the Igh-1^a, -1^d, -1^e, and -1^f allotypes are also able to respond to NIP-O-Su challenge after NP-O-Su priming. Although this pattern of association is distinct from that for DTH or antibody responses, CS reactivity is nonetheless apparently linked to the Igh complex, based on the previously reported finding that C3H.SW (Igh-1^b) does not mount an observable NIP-cross-reactive response, whereas its Igh congenic strain CWB (Igh-1^b) does (7). Further, the inability of NP-O-Su-primed C3H (Igh-1^b) to demonstrate NIP-cross-reactive responses (Table I) does not appear to be due to the failure of mice carrying the C3H background genes to recognize NP in association with H-2K/D region products. As is evident in Table II, C3H NP-O-Su primed cells can indeed manifest significant CS reactions to NP-O-Su challenge in recipients homologous at either H-2I or H-2D.

It is possible that the broader strain distribution pattern of NIP-cross-reactivity in CS responses may be related to the triggering of lower affinity clones in non-Igh-1^b strains by a high concentration of antigen on the presenting cell surface. Consistent with this postulate are the reports of Stashenko (17) and Karjalainen (18) who observed predominantly heteroclitic antibodies in the early (up to day seven) anti-NP antibody response of strains with non-Igh-1^b allotypes, including BALB/c, A/J, and AKR, during this time-period of maximal tissue antigen concentrations. However, this would not explain the absence of NIP-cross-reactive NP-induced CS responses in DBA/2 mice, nor would it easily account for the observed fine specificity of K/D- vs. I-restricted clones.

The possibility that the lack of NIP-cross-reactivity in non-Igh-1^b, I region-restricted clones was the result of a specific suppressor cell is less likely in view of the observation that cyclophosphamide pretreatment of AKR mice before NP-O-Su priming did not

significantly alter the fine specificity of responsiveness (M. Sunday, Unpublished data.).

With these strain distribution patterns in mind, we can now analyze the differing fine specificities of H-2D-restricted vs. I region-restricted clones in NP-induced CS responses. It has already been demonstrated that when the donor strain of NP-immune lymph node cells bears the Igh-1^b and NP^b idio type and, therefore, manifests NIP-cross-reactive NP-induced DTH responses, both K, D-restricted, and I-restricted clones give NIP-O-Su-elicited cross-reactions (7). This was confirmed in the present study using B10.BR (H-2^k, Igh-1^b) as the donor of NP-O-Su immune cells (Table II). It should be noted that this does not necessarily imply that the I-restricted and D-restricted clones from NP-O-Su primed B10.BR bear identical idiotypic receptors, but only that both clones manifest a similar fine specificity pattern under the conditions employed. Further experiments are required to determine if the H-2I and H-2D restricted CS cells from the B10.BR strain share similar receptors.

However, as can be seen in Table III, when cells from the AKR strain, which carries the Igh-1^d allotype and lacks the NP^b idio type, are transferred into I-A region compatible recipients, an NIP-cross-reactive NP-induced CS response cannot be elicited. In contrast, the AKR H-2D-restricted clone manifests NIP-cross-reactive NP-induced CS responsiveness. In the case of transfer of AKR NP-immune cells into 4R, a donor-recipient combination with H-2 homology at H-2K + I-A, the observed NIP-cross-reactivity may be attributed to the K-restricted cells because, as noted above, I-A region homology is not sufficient to transfer cross-reactive CS responses. The differing fine specificities of I- vs. K- or D-restricted combinations in AKR NP-induced CS responses supports the existence of two separate effector cell populations, or clones, in CS reactions. Further, these results are consistent with the concept originally suggested by Miller (12) and elaborated by others (7, 19, 20, 21) that at least two distinct sets of T cells may be capable of mediating the inflammatory reaction in the contact sensitivity response. These two cell populations may bear distinct surface receptors, leading to their functional divergence: the first being DTH-like, I-restricted, and unable to give NIP-cross-reactive NP-induced responses in non-Igh-1^b strains of mice; the second being CTL-like, K/D-restricted, and having a different pattern or NIP-cross-reactivity, consistent with the observation that NP-specific CTL lack the NP^b idio type (22-24). Binz et al. (25) have reported the observation that different spectra of idiotypes exist on two subgroups of T cells generated in the same mixed leukocyte culture, namely, allo-Ia-binding Ly 1 + 2⁻ blasts and H-2K/D-binding Ly 2⁺ killer cells. The evidence in the present study suggests that such a dichotomy in idiotypic receptors between T cell subpopulations may be a generalized finding.

The process by which the cell regulates which Igh-V region genes are selected to recognize the same antigen in association with distinct H-2 region products is not understood. However, at least two major possibilities could be considered: (a) different Igh-V region genes are selected to bind NP-modified H-2D and H-2I molecules. (b) The same Igh-V region gene is selected but it can be modified by different self-H-2-recognition products to account for the differential specificity of immune cells from AKR mice.

Summary

We have previously shown that cross-reactive cutaneous sensitivity (CS) responses induced by 4-hydroxy-3-nitrophenyl acetyl-O-succinimide (NP-O-Su) and elicited by

its 5-iodo analogue, 4-hydroxy-5-iodo-3-nitrophenyl acetyl-*O*-succinimide were observed in strains of mice possessing the Igh-1^b allotype, but not in strains bearing allotypes Igh-1^c or Igh-1ⁱ. These CS responses are mediated by T cells and can be transferred to naive recipients that are homologous at either the H-2K, H-2I, or H-2D regions of the major histocompatibility complex. We now extend our analysis of cross-reactive 4-hydroxy-3-nitrophenyl-acetyl (NP)-induced CS responses to inbred strains of mice expressing additional Igh-1 allotypes. In contrast to NP-induced delayed-type hypersensitivity responses, which only display 4-hydroxy-5-iodo-3-nitrophenyl acetyl (NIP) cross-reactivity in Igh-1^b-bearing mice, cross-reactive CS responses can also be elicited in NP-primed mice carrying the Igh-1^d, Igh-1^e, or Igh-1^f allotypes. Moreover, cross-reactive NP-induced CS responses could be transferred by NP-O-Su-primed lymph node cells from the AKR (Igh-1^d) strain, into naive recipients homologous at the H-2D region, but only non-cross-reactive NP responses could be transferred into strains homologous at the H-2I region. Furthermore, the lack of cross-reactivity in the Igh-1ⁱ-bearing C3H strain was not the result of an inability of these mice to recognize NP in association with H-2K/D products, because NP-O-Su-primed cells from C3H donors transferred NP-specific CS responses into both H-2D and H-2I homologous recipients. The results are discussed with respect to the nature of the T cell receptors that control NP responses.

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