second event in the somatic cell, homozygosity or hemizygosity of a recessive mutation is obtained, leading to the formation of a tumor. As shown by the group of Cavenee (9,10) and others, besides mutation or chromosome deletion, this second step may also involve abnormal chromosomal segregation events during mitosis. As both Wilm's tumor and retinoblastoma are embryonic tumors it is tempting to speculate that the genes involved play a part in the development of the target tissues during embryogenesis.

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MOLECULAR GENETICS OF THE IgE RESPONSE IN MAN

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At least two regulators of the IgE response have been distinguished. One is involved in the production of allergen specific IgE antibodies. This regulator segregates in families in linkage to determinants encoded by the major histocompatibility gene complex (HLA). Thus this regulator has been proposed to be encoded by HLA genes. Moreover increased IgE responses have been found to segregate in families. The patterns of inheritance suggest multifactorial expression in spite of more or less clear autosomal dominant or recessive segregation patterns. The hyper IgE syndrome, an immunodeficiency disease accompanied by recurrent infections of the skin in particular, is not associated with allergy. In this syndrome there is evidence that the defect resides in T lymphocytes, involved in the regulation of the IgE level.
We have started investigations on regulatory sequences within the Immunoglobulin heavy chain complex on the long arm of chromosome 14. As a first step we try to characterize the V (= variable) genes involved in the IgE response. For this purpose we have performed experiments to establish human IgE producing B cell lines, the results of which to be discussed.

IMPROVED TOLERANCE TO INHALANT ALLERGENS DURING AN INTENSIVE COURSE OF RUSH-IMMUNOTHERAPY

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Significant reduction in asthmatic symptoms and use of medication was reached by a short term course of allergen immunotherapy. In vivo and in vitro parameters were investigated for their predictive value. Six patients with allergic asthma, 5 sensitized to housedust mite and one with allergy to grasspollen underwent a rush immunotherapy of 8 to 14 days under clinical observation until a maintenance dose was tolerated.
Titrated skin test, conjunctival provocation test (CPT), bronchial provocation test (BPT) and allergen-specific IgE and IgG antibodies were examined before and 8 weeks after the dose build-up period.
A significant improvement was demonstrated clinically by a decrease in reported symptoms and use of medication as well as by increasing the threshhold of tolerance 10 to 100 fold in skin test, CPT and BPT. Specific IgG antibodies increased in all patients.
An intensive short term course of allergen-immunotherapy was shown to be effective in reducing allergic symptoms in patients sensitized to inhalant allergens already within 2 months. Titrated skintest, BPT and specific IgG levels were of predictive value.

Genetics in Allergy: A Model for Studying the Genetics of Human Immune Responsiveness

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Allergy serves a particularly good model for understanding the genetics of human immune response and its relationship to disease, since one can establish a clear causal relationship between specific IgE antibody responses and the expression of specific allergies (1). There is evidence for at least two types of genetic control of IgE responses in man, namely, *HLA*-linked control of specific responses and non-*HLA*-linked control of the overall production of IgE, where high IgE is inherited as a recessive trait.

The primary focus will be on our recent studies of specific IgE and IgG antibody responses to the low mol. wt. *Ambrosia* (ragweed) allergens, *Amb* V (Ra5; refs. 2-5) and *Amb* VI (Ra6; ref. 6). Three species of *Amb* V (mol. wts. 4400-5000 D) have been isolated, *Amb a* V (from *A. artemisiifolia*, short ragweed), *Amb t* V (from *A.trifida*, giant ragweed) and *Amb p* V (from *A. psilostachya*, western ragweed), as well as another allergen species, *Amb a* VI (mol. wt. 11,500 D). Immune responsiveness toward all of the *Amb* V homologues was found to be significantly associated with the Dw2 subspecificity of HLA-DR2 (4,5,7,8), even though these molecules show little, or no, antigenic crossreactivity (6). The association with the *Amb t* V molecule is less striking than with *Amb a* V and *Amb p* V, where 95% or more responder subjects possess DR2/Dw2. In the case of *Amb a* VI, 80% of responders possess HLA-DR5 (9).

We have used a refined version of conventional allergen immunotherapy in a prospective genetic study of immune response to ragweed pollen allergens (10) which, to our knowledge, is the first such study. Twelve matched pairs of DR2+ and DR2– patients were immunized sequentially with giant, western and short ragweed extracts containing known amounts of *Amb t* V, *Amb p* V and *Amb a* V, respectively. Serum was taken before and 12 times after increasing dosages (0.033-11 μg) of each *Amb* V. Eight of 12 DR2+ subjects made IgGAb responses to *Amb t* V (G.M. = 38 ng/ml), whereas 4/12 DR2– subjects made low levels of IgGAb (G.M. = 3.7 ng/ml); $p<0.05$ by t test. Three of the four DR2+ *non*responders have atypical MLR responses toward Dw2 typing cells. Preliminary data show that 8 DR2+ subjects have positive immune responses to *Amb p* V and to *Amb a* V, with the exception of one DR2+/Dw2– subject who failed to respond to *Amb p* V. However, all 8 DR2– subjects who have completed the *Amb p* V regimen, and all 5