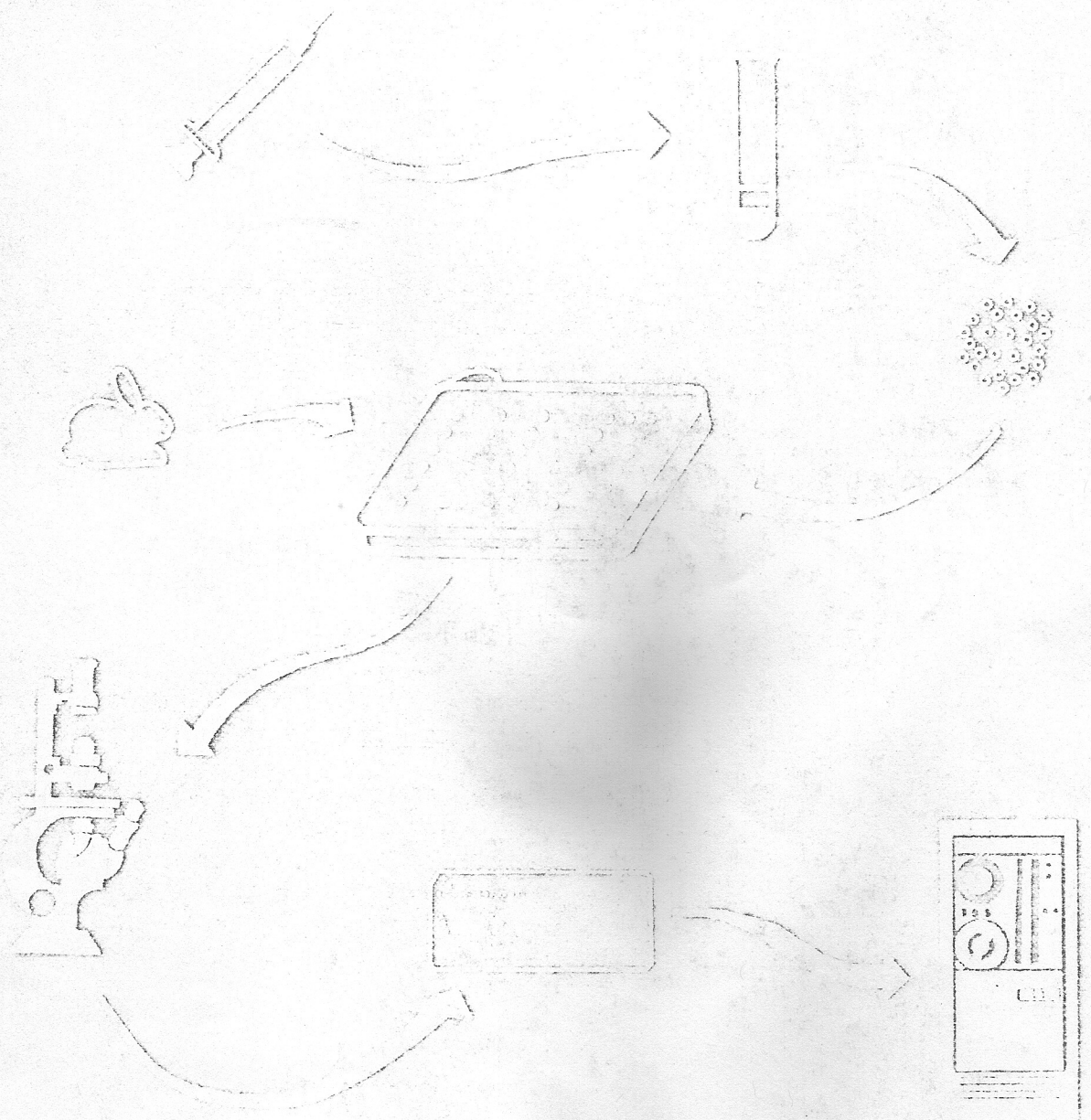


# Histocompatibility Testing 1980



# HLA-DRW4 ANTIGEN AND B40-CW3-DRW4 HAPLOTYPE IN RHEUMATOID ARTHRITIS

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The first evidence of an association between rheumatoid arthritis (RA) and HLA was reported by Stastny (1,2) and corresponded to HLA-DW4. In 1977, as a result of the 7th International Workshop, a striking association with HLA-DRW4 was found (3). Stastny reported DRW4 to be present in 70% of 53 patients with RA and in 28% of 68 controls; the relative risk for the disease in relation to DRW4 was 6 (4).

During the 8th International Workshop, we studied 23 RA patients, fulfilling ARA criteria for RA and 30 controls, testing for HLA-A,B,C, and DR antigens. Table 1 shows a highly significant increase of DRW4 antigen frequency in RA patients (69.5%) as compared to controls (23.3%), with a relative risk of 7.5. HLA-CW3 was also found increased, and the relative risk for the disease in relation to CW3 is also high (6.1). Disease associations with HLA-C locus antigens are rare and it is probably secondary to DRW4 association, since CW3 and DRW4 are in linkage disequilibrium with a delta value of 16 in our controls (Table 2). Nevertheless, the observed frequency of the CW3-DRW4 haplotype is actually 140 compared to the expected frequency of 74.5, giving a delta value of 77. It was also striking to find delta values of 77 and 93 for B40-DRW4

and B40-CW3 haplotypes, respectively, in our patients, when compared to controls (Table 2).

B40, CW3, and DRW4 antigens are in linkage disequilibrium, and we tried to assume that the real association of RA is with DRW4, and CW3 and B40 could represent a result of such disequilibrium. In Table 3 we show that the relative risk for the B40-CW3-DRW4 haplotype is about the same as that for the combinations of 2 of the 3 antigens; comparing the frequency of the haplotype in AR patients (21.7%) with that in controls (3.3%) by a 2x2 contingency table, a p value between 0.1 and 0.05 is obtained. It will be necessary to expand the sample in order to conclude whether there is a true association of a disease gene to the haplotype B40-CW3-DRW4 in RA patients, or whether the gene is exclusively linked to the DRW4 antigen.

## REFERENCES

1. Stastny P. Mixed lymphocyte culture typing cells from patient with rheumatoid arthritis. *Tissue Antigens* 1974, 4:571.
2. Stastny P. Mixed lymphocyte cultures in rheumatoid arthritis. *J Clin Invest* 1976, 57:114.
3. Batchelor JR, et al. HLA and disease. In *Histocompatibility Testing 1977*, Bodmer WF, et al, eds, Munksgaard, Copenhagen, 1978, 218.
4. Stastny P. Association of the B-cell alloantigen DRW4 with rheumatoid arthritis. *N Engl J Med* 1978, 298:869.

Table 1. Antigen frequency and relative risk in R.A.

HLA	Controls n=30		Patients n=23		R.R.
	AF%	G.F.	AF%	G.F.	
B40	6.6	0.034	26	0.141	4.94
CW3	6.6	0.034	30.4*	0.166	6.1
DRW4	23.3	0.125	69.5**	0.449	7.5

AF : Antigen frequency

GF : Gene frequency ( $1 - \sqrt{1-F}$ )

RR : Relative risk

$\chi^2$  with Yate's correction for discontinuity

\*  $\chi^2 = 3.66$  0.1 p 0.05

\*\*  $\chi^2 = 9.52$  p 0.005

Table 3. Haplotype frequencies and relative risk.

Haplotype	Patients n=23	
	H.F.	R.R.
B40-Cw3	21.7	8
B40-DRW4	26	10.2
Cw3-DRW4	26	10.2
B40-Cw3-DRW4	21.7	8

Table 2. Haplotype frequencies and delta values.

Haplotype	Controls n=30				A.R. Patients n=23			
	HF%	Exp.	Obs.	$\Delta$	HF%	Exp.	Obs.	$\Delta$
B40-CW3	3.3	1.1	17	16	21.7	23.4	116	93
B40-DRW4	6.6	4.2	14	30	26	63.3	140	77
CW3-DRW4	3.3	1.1	17	16	26	74.5	140	77

HF : Haplotype frequency

GF : Gene frequency (x 1.000)

$\Delta$  : Delta value (x 1.000)

Exp: Expected

Obs: Observed