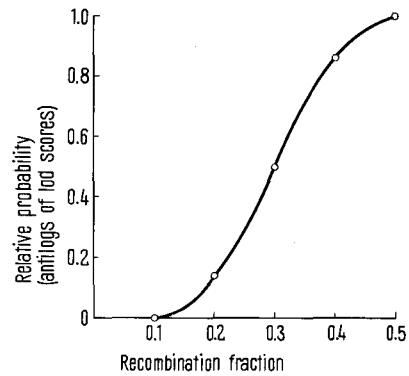
Lack of Linkage Between the Lp and Ld Serum Systems

The inherited serum system Lp was demonstrated by means of rabbit immune sera[1]. Absorbed sera from immunized rabbits demonstrated an antigenic β-lipoprotein factor, the Lp(a) factor, present in some but not all human sera. The presence of the factor was governed by a simple, autosomal, dominant mode of inheritance[1,2]. The Lp system was found to be completely independent of the Ag system, which also refers to the β-lipoprotein of human serum[3]. No linkage or association was demonstrable between the Lp system and the systems ABO, MNS, Rh, Le, Lu, P, Fy, K, Jk, Hp, Gc, Gm, Inv and Ag[4-6].

In 1963, during a study of sera from patients who had received several blood transfusions, a serum was found which formed a precipitate with some, but not all, human sera in agar gel double diffusion experiments[7,8]. In subsequent experiments, the serum antigen demonstrated by the patient's serum was shown to belong to the low density β-lipoproteins[9]. Investigation of serum samples from members of 81 families with a total of 363 children revealed that the antigen was inherited as a dominant, autosomal trait[9]. No obvious relation between this antigen and the Lp or Ag systems was found, and it was tentatively concluded that the demonstrated antigen was part of a new serum system[9]. This system was called the Ld system, where Ld stands for 'low-density' lipoprotein. According to this notation, people who possess the Ld antigen in their serum are of phenotype Ld(a^+) and possess the autosomal gene Ld^a in single or double dose.

Both the Lp and Ld factors have phenotype frequencies that make them very useful genetic markers (about 35% Lp(a^+) and about 42% Ld(a^+) in the Norwegian population). Since both antigens are found in the β-lipoproteins of human serum, it was thought desirable to investigate whether the gene loci controlling the 2 systems were linked. Thus, 81 families which had been tested for the Ld(a) factor, were scored for the Lp(a) factor[10]. Of this number, 9 families provided linkage information for the Lp and Ld systems. For each family, linkage scores at several different values of the recombination fraction were estimated, employing the 'lod' scores of MORTON[11], with proper corrections. The score from each family was then added up, giving the 'lod' scores of the total material, at different values of the recombination fraction. These data are shown in the Table.

The data presented, which are shown graphically in the Figure, are sufficient to exclude definitely close linkage, and even looser linkage is unlikely. The most likely recombination fraction is 0.5, or free recombination. It is concluded that the Lp and Ld loci are not linked[12].



The Lp and Ld serum systems: the relative probabilities of various recombination fractions.

The Lp and Ld serum systems: lod scores

Family No.	Scoring		Recombination fraction θ 0.00	0.05	0.10	0.20	0.30	0.40	0.50
1	Z_1 (1:3)	e_1 (2:2)	$-\infty$	− 0.491	− 0.253	− 0.077	− 0.019	− 0.003	0
2	Z_2 (0:1:2:0)	d_2 (1:2)	0.240	0.184	0.153	0.095	0.045	0.012	0
3	Z_2 (3:0:1:1)	e_2 (4:1)	0.188	0.162	0.136	0.085	0.041	0.011	0
4	Z_2 (1:0:1:1)	d_2 (1:2)	− 0.085	− 0.069	− 0.054	− 0.030	− 0.014	− 0.003	0
5	Z_3 (4:2:0)	e_3 (5:1)	− 0.120	− 0.103	− 0.081	− 0.045	− 0.018	− 0.005	0
6	Z_3 (2:1:1)	e_3 (3:1)	$-\infty$	− 0.568	− 0.315	− 0.113	− 0.037	− 0.007	0
7	Z_1 (3:4)	e_1 (3:4)	$-\infty$	− 2.167	− 1.334	− 0.585	− 0.228	− 0.053	0
8	Z_2 (2:2:1:0)	e_2 (3:2)	0.068	0.058	0.048	0.028	0.014	0.004	0
9	Z_2 (1:1:1:1)	d_2 (2:2)	$-\infty$	− 0.795	− 0.503	− 0.227	− 0.091	− 0.022	0
Sum of lod scores			$-\infty$	− 3.789	− 2.203	− 0.869	− 0.307	− 0.066	0
Antilog = relative probabilities of θ					0.006	0.135	0.493	0.859	1.0

Zusammenfassung. Mehrere genetisch determinierte Antigenspezifitäten am menschlichen Serum β-Lipoprotein, darunter Lp- und Ld-Antigen, sind beschrieben; 9 Familien, in denen beide Antigene segregieren, sind untersucht worden. Es wird gezeigt, dass beide Antigene unabhängig voneinander segregieren, so, dass die Lp- und Ld-Loci nicht eng gekoppelt sein können und demonstriert, dass Loci, die Antigenspezifitäten am selben Serumprotein bestimmen, nicht unbedingt gekoppelt sein müssen.

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