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Gm, Km and ISf Allotypes in the Lebanese Population

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Gm, Km, ISf systems.

Summary

The results of a population genetic investigation on Lebanese are given and compared with the results obtained on other populations from near and Middle-East. 2005 unrelated male and female individuals of different ages were tested for the allotypes G1m(1, 2 et 3) and G3m(5,10,11,13,14 and 21); a smaller number of them was also tested for G1m(17), G2m(23) and G3m(6). The allotype ISf(1) on 380.

The Lebanese population presents with a great frequency the four Gm haplotypes most commonly found in a Caucasoid population, $Gm^{3,23,5\ 10\ 11\ 13\ 14}$ (.5568), $Gm^{1,17;...;21}$ (.1726), $Gm^{3;...;5\ 10,11,13,14}$ (.1661) and $Gm^{1,2,17;...;21}$ (.0224), which can explain 85,64% of the observed phenotypes.

The $Km^{1,2}$ allele frequency (.072) as well as the variations of the frequency of ISf(1) phenotype according to the age, are also characteristic of

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a Caucasoid population. Our values show the transition between the ones observed in Europe and those, previously described, of several populations from Near and Middle East.

A few haplotypes $Gm^{1,17,...,5,10,11,13,14}$ (.0365), $Gm^{1,17,...,10,11,13}$ (.0336) and $Gm^{1,2,17,...,5,10,11,13,14}$ (.005) may indicate a low mongoloid and negroid admixture, or represent rare haplotypes, without a race admixture, in this very ancient population.

Résumé

Les allotypes G1m(1,2 et 3) et G3m(5,10,11,13,14 et 21) ont été étudiés sur un échantillon de 2005 Libanais, non apparentés. Les marqueurs G1m(17), G2m(23) et G3m(6) ont été également étudiés sur un effectif plus faible. Les allotypes Km(1 et 2) ont été recherchés sur 3038 Libanais et l'allotypes ISf(1) sur 380.

La population libanaise présente, avec une grande fréquence, les quatre haplotypes Gm habituellement rencontrés dans une population caucasoïde: $Gm^{3,23,5,10,11,13,14}$ (.5568), $Gm^{1,17,...,21}$ (.1726), $Gm^{3,...,5,10,11,13,14}$ (.1661) et $Gm^{1,2,17,...,21}$ (.0224), qui peuvent expliquer 85,64% des phénotypes observés.

La fréquence de l'allèle $Km^{1,2}$ (.072), ainsi que les variations de fréquence du phénotype ISf(1), selon l'âge, sont aussi caractéristiques d'une population caucasoïde. Les valeurs trouvées pour les divers gènes marquent la transition entre celles observées en Europe et celles précédemment décrites pour des populations du Proche et du Moyen Orient.

Quelques haplotypes: $Gm^{1,17,...,5,10,11,13,14}$ (.0365), $Gm^{1,17,...,10,11,13}$ (.0336) et $Gm^{1,2,17,...,5,10,11,13,14}$ (.005) indiquent peut-être un très faible métissage mongoloïde et négroïde ou représentent des haplotypes rares, sans apport extérieur, dans cette très ancienne population.

Introduction

It seems interesting to study the genetic structure of the Lebanese population for many reasons. Lebanon is a crossroad between Mesopotamia, Egypt, the Arabic Peninsula and the Mediterranean sea. Besides, its mountains always helped it to be a refuge for persecuted religious minorities, among which matings and genetic exchanges are rare.

We started such a study with exploring different genetic makers of human blood (LALOUEL et al., 1975) and we present the results of our investigation on the immunoglobulin allotypes Gm, Km and ISf in the Lebanese population.

Material and Methods

Different medical laboratories from Beirut and "la Faculté Française de Médecine et de Pharmacie" provided us with 90 per cent of the sera. The rest comes from villages of the "Mont-Liban". The samples were issued from unrelated male and female individuals of different ages.

2005 sera were tested for the G1m(1,2 and 3) and G3m(5,10,11,13,14 and 21) allotypes, 876 for G2m(23), 160 for G1m(17), 149 for G3m(6), 3038 for Km (formerly Inv) (1 and 2) and 380 for ISf(1) by the hemagglutination inhition technique on slides (ROPARTZ and RIVAT, 1967) using red blood cells coated with either incomplete Rh antisera or myeloma proteins coupled using chromic chloride (GOLD and FUDENBERG, 1967).

The reagents and nomenclature used are presented in Table I.

Table I

List of reagents using to determine the allotypes

Subclasses	Nomenclature		Anti-allotypes	Coating
	Alphameric	Numeric		
Heavy Chains				
IgG1	G1m(a)	G1m(1)	LAR	276
			CUI	
	(x)	(2)	LEM	276
	(f)	(3)	GIR	99
	(z)	(17)	L92	276
IgG2	G2m(n)	G2m(23)	L704	IgG2G2m(23)
IgG3	G3m(b0)	G3m(11)	CAZ	275
	(b1)	(5)	ALL	275
			BEN	
	(b3)	(13)	GRA	275
	(b4)	(14)	BON*	275
			BUR*	626
			MAL	275
	(b5)	(10)	LET	275
	(c3)	(6)	3200*	561
	(g)	(21)	L224A	287
Light Chains				
K chains	Km(1)	Km(1)	COL	3
			LEC	
	Km(a)	Km(2)	VIR	3
IgG1	ISf(1)	ISf(1)	C227	102
			CRO	535

The nomenclature is that suggested by the WHO (Workshop, Rouen, July 1974).Only the numeric notation of the two suggested will be used in this work.

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Results

The 14 phenotypes Gm, as well as their frequencies, observed among 2005 Lebanese during our study at random are presented in Table II. (The allotypic markers tested are written in the numerical order of the subclasses, with semicolons separating the subclasses and commas separating the allotypic markers).

Table II

Gm phenotypes		
Phenotypes	N	%
Gm (3;5,10,11,13,14)	1055	52.62
Gm (1,3;5,10,11,13,14,21)	513	25.59
Gm (1,3;5,10,11,13,14)	207	10.32
Gm (1;21)	65	3.24
Gm (1,2,3;5,10,11,13,14,21)	61	3.04
Gm (1;10,11,13,21)	24	1.20
Gm (1,2;21)	23	1.15
Gm (1;5,10,11,13,14,21)	21	1.05
Gm (1,2,3;5,10,11,13,14)	16	0.80
Gm (1;5,10,11,13,14)	11	0.55
Gm (1,2;5,10,11,13,14,21)	5	0.25
Gm (1,2;10,11,13,21)	2	0.10
Gm (1,2;5,10,11,13,14)	1	0.05
Gm (1;10,11,13)	1	0.05
Total	2005	100.00

All sera were tested for G1m(1,2,3) and G3m(5,10,11,13,14 and 21). Only the present allotypes are noted.

The determination of the G2m(23) allotypes on 876 of these Lebanese, including particularly people with a rare phenotype, subdivided 9 phenotypes into 18 according to the serum samples, either positive or negative for the G2m(23); [G2m(23) is the only allotype presently defined on the IgG2 heavy chain, two dots are used to indicate that a specimen was tested and found to be negative for G2m (23)].

The 5 other phenotypes did not possess this allotype. The 23 phenotypes and probable genotypes obtained are listed in Table III.

Eight uncommon phenotypes, the starting point of family investigations, were excluded from the present study (LEFRANC et al., 1975, LEFRANC et al., to be published).

6 Gm haplotypes were enough to explain the 14 phenotypes, when the

G2m(23) was not tested. Their frequencies, determined by the maximum likelihood method through an adaptation by LALOUEL of Yasuda's ALL TYPE programme (MIKI et al., 1969), are listed in Table IV.

Table III
Phenotypes and probable Gm genotypes

N	Gm Phenotypes	Probable Gm genotypes**
398	Gm(3;23;5,10,11,13,14)*	$Gm^{3,23,5}/Gm^{3,23,5}$ or $Gm^{3,...,5}$
27	Gm(3; . .; 5,10,11,13,14)	$Gm^{3,...,5}/Gm^{3,...,5}$
151	Gm(1,3;23; 5,10,11,13,14,21)	$Gm^{3,23,5}/Gm^{1,...,21}$
51	Gm(1,3; . . ; 5,10,11,13,14,21)*	$Gm^{3,...,5}/Gm^{1,...,21}$
79	Gm(1,3;23; 5,10,11,13,14)*	$Gm^{3,23,5}/Gm^{1,...,5}$
19	Gm(1,3; . .; 5,10,11,13,14)*	$Gm^{3,...,5}/Gm^{1,...,5}$
58	Gm(1, . .;21)	$Gm^{1,...,21}/Gm^{1,...,21}$
2	Gm(1; 23;21)	$Gm^{1,..,21}/Gm^{1,23,21}$
17	Gm(1,2,3;23; 5,10,11,13,14,21)	$Gm^{3,23,5}/Gm^{1,2,...,21}$
1	Gm(1,2,3; . .; 5,10,11,13,14,21)	$Gm^{3,...,5}/Gm^{1,2,...,21}$
18	Gm(1,2; . .;21)	$Gm^{1,2,...,21}/Gm^{1,2,...,21}$ or $Gm^{1,...,21}$
2	Gm(1,2;23;21)	$Gm^{1,2,...,21}/Gm^{1,23,21}$ or $Gm^{1,2,23,21}/Gm^{1,...,21}$
9	Gm(1,2,3;23; 5,10,11,13,14)	$Gm^{3,23,5}/Gm^{1,2,...,5}$
1	Gm(1,2,3; . .; 5,10,11,13,14)	$Gm^{3,..,5}/Gm^{1,2,...,5}$
9	Gm(1; . .;5,10,11,13,14,21)	$Gm^{1,...,21}/Gm^{1,...,5}$
2	Gm(1;23; 5,10,11,13,14,21)	$Gm^{1,...,21}/Gm^{-,23,5}$***
1	Gm(1,2; . .; 5,10,11,13,14,21)	$Gm^{1,2,...,21}/Gm^{1,...,5}$ or $Gm^{1,...,21}/Gm^{1,2,...,5}$
1	Gm(1,2;23;5;10,11,13,14,21)	$Gm^{1,2,...,21}/Gm^{-,23,5}$***
20	Gm(1; . .;10,11,13,21)	$Gm^{1,...,21}/Gm^{1,...,10,11,13}$
6	Gm(1; . .;5,10,11,13,14)	$Gm^{1,...,5}/Gm^{1,...,5}$ or $Gm^{1,...,10,11,13}$
2	Gm(1,2; . .;10,11,13,21)	$Gm^{1,2,...,21}/Gm^{1,...,10,11,13}$
1	Gm(1,2; . .;5,10,11,13,14)	$Gm^{1,2,...,5}/Gm^{1,2,...,5}$ or $Gm^{1,...,5}$ or $Gm^{1,...,10,11,13}$
1	Gm(1; . .;10,11,13)	$Gm^{1,...,10,11,13}/Gm^{1,...,10,11,13}$
876		

All sera were tested for G1m(1,2,3), G2m(23) and G3m(5,10,11,13,14 and 21).
*Among each of these phenotypes one serum was positive for G3m(6).
**N.B.: For the Gm haplotypes, we note: 5 for 5,10,11,13,14 when all these G3m allotypes are present.
***The G1m(3) allotype is absent. The existence of the $^{-,23,5}$; haplotype was demonstrated by the study of the two families.

Table IV
Gm haplotype frequencies

Samples not tested for the G2m(23) allotype		Samples tested for the G2m(23) allotype	
Haplotypes	Frequencies	Haplotypes	Frequencies
$Gm^{3,5\ 10\ 11\ 13\ 14}_{,,\ ,\ ,\ ,}$	.7249	$Gm^{3,23,5\ 10\ 11\ 13\ 14}_{,,,,,\ ,\ ,}$	.5568
$Gm^{1,21}_{,}$	.1776	$Gm^{1\ 17...21}_{,\ ,\ ,}$	.1726
$Gm^{1,5\ 10\ 11\ 13\ 14}_{,,\ ,\ ,\ ,}$	.0365	$Gm^{3,...,5\ 10\ 11\ 13\ 14}_{,,,,,,,,,}$	.1661
$Gm^{1,10\ 11\ 13}_{,\ ,\ ,}$	.0336	$Gm^{1\ 17...,5\ 10\ 11\ 13\ 14}_{,,,,,,\ ,\ ,}$	.0365
$Gm^{1\ 2,21}_{,,\ ,}$	.0224	$Gm^{1\ 17...,10\ 11\ 13}_{,,,,\ ,\ ,}$	.0336
$Gm^{1\ 2,5\ 10\ 11\ 13\ 14}_{,,,\ ,\ ,\ ,}$	.0050	$Gm^{1\ 2\ 17...,21}_{,,,,\ ,}$	.0224
χ^2=7.08		$Gm^{1\ 2\ 17...,5\ 10\ 11\ 13\ 14}_{,,,,,,\ ,\ ,\ ,}$	.0050
8 D.F.		$Gm^{1\ 17,23,21}_{,\ ,\ ,\ ,}$	.0050
P# $^{.50}$		$Gm^{-,23,5\ 10\ 11\ 13\ 14}_{,,,\ ,\ ,\ ,}$	.0020

G1m(17): only 160 serum samples were tested for this allotypes; it was present everytime G1m(1) was present too; we suppose the G1m(1) and G1m(17) allotypes are present together.

9 Gm haplotypes were required for the 23 phenotypes when the G2m(23) was tested too. Although the G1m(17) was only determined on a smaller effective, we mentioned it in the haplotypes where its presence seemed certain.

The frequencies of Km phenotypes and alleles are presented in Table V, and ISf(1) phenotypes according to age groups are given in Table VI.

Table V
Km phenotypes and gene frequencies

Phenotypes	N	%	Alleles	Frequencies
Km(-1,-2)	2584	85.05		
Km(1,2)	421	13.86	$Km^{1,2}$	.0720
Km(1,-2)	33	1.09	Km^{1}	.0058
Total	3038	100.00		

Table VI
ISf(1) phenotype frequencies according to age groups

Age	1 to 20		21 to 60		61 to 90	
Phenotype	N	Frequencies	N	Frequencies	N	Frequencies
ISf(1)	16	.302	148	.542	34	.630
ISf(-1)	37	.698	125	.458	20	.370

Discussion

The three haplotypes $Gm^{3;5,10,11,13,14}$, $Gm^{1;21}$ and $Gm^{1,2;21}$ can explain the phenotypes of 1717 individuals (Table II). We always found the G1m(17) allotype associated with the G1m(1) in the 160 samples tested for that allotype. So, it seems that we are dealing with the 3 common Caucasoid haplotypes: $Gm^{3;5,10,11,13,14}$, $Gm^{1,17;21}$ and $Gm^{1,2,17;21}$ (Table IV).

In order to compare the results of our study with the gene frequencies found in other populations living in Near and Middle East and already found in Lebanon, the frequencies of Gm^{1}, $Gm^{1,2}$, Gm^{5} and $Gm^{1;5}$ genes were calculated by considering only the measure of the G1m(1 and 2) and G3m(5) allotypes. The results comparing those gene frequencies with references, are given in Table VII. The frequency of the Gm^{1} (.2112), $Gm^{1,2}$ (.0273), Gm^{5} (.7249) and $Gm^{1;5}$ (.0365) found in the present study is comparable to the one obtained by other workers in the same population and shows the transition between the values observed in Europe and those, previously described of Near-East, Middle-East and South Asia (Table VII).

The increase of Gm^{1} and the decrease of Gm^{5} frequencies from the West towards the East, already noted in Europe (ROPARTZ et al., 1963; FRASER et al., 1969a; FRASER et al., 1969b) continues in Near and Middle East.

After the determination of G2m(23) allotype, the haplotypes mentioned above are converted into five: $Gm^{3,23;5}$, the most frequent, $Gm^{3;5}$, $Gm^{1,17,21}$, $Gm^{1,2,17;21}$ and very rarely $Gm^{1,17,23,21}$ (.005) (Table IV). The frequency of this gene complex is very low in caucasoid populations (.005) (NATVIG and KUNKEL, 1968) and might proceed from a crossing-over between the Cγ2 and Cγ3 cistrons (VAN LOGHEM et al., 1970).

In 236 other phenotypes (Table II), the G3m(21) allotype is absent when the G1m(1) is present. Among these, 17 have the allotype G1m(2). 11 samples Gm(1;..;5,10,11,13,14) and another Gm(1,2;..;5,10,11,13,14) can be explained by the presence of the $Gm^{1,17,5,10,11,13,14}$ and $Gm^{1,2,17,5,10,11,13,14}$ haplotypes which is confirmed by family studies. The $Gm^{1,17,5,10,11,13,14}$ haplotype is the one most often met among the Negroids, but it is not absent from the Caucasoid populations (RUFFIE et al., 1964; LOGHEM Van and NATVIG, 1970; ROPARTZ et. al., 1972). It was also found in circum-Mediterranean populations which have varying amounts of African admixture. The frequency of this haplotype in the present study (.0365) probably reveals a negroid admixture made possible by the geographical location of Lebanon. The determination of the G3m(6), a typical negroid allotype, on 149 individuals demonstrated the presence of this antigenetic determinant in 4 of them. These sera presented

Table VII. Gm and Km gene frequencies among several populations in Europe and Near-and Middle-East

Populations	References	Gene frequencies					
		Gm^1	$Gm^{1,2}$	Gm^5	$Gm^{1,5}$	$Km^{1,2}$	Km^1
Yugoslavian: four villages	Ropartz et al., 1972	.159	.047	.794		.039	.001
Lebanese	Present study*	.201	.027	.725	.037	.072	.006
	Ruffié and Taleb, 1965	.255	.033	.687	.025		
Jordan:	Taleb and Ruffié, 1968						
Transjord. Sedentary		.196	.032	.616	.156		
Cisjord. Sedentary		.111	.057	.641	.191		
Bedouins		.214	.047	.639	.100		
Kurdish Jews: from	Steinberg et al., 1970*						
Northern Iraq		.099		.811	.090		.041
Eastern Turkey		.240		.710	.050		
Kurdish: from	Blanc et al., 1972*	.212	.041	.716	.031	.071	
Syria and Lebanon	Taleb et al., 1973						
Iranian							
Soldiers	Ropartz et al., 1962	.304	.039	.657		.059	
Teheran	Bajatzadeh and	.152	.047	.683	.118		.164
North Iran	Walter, 1963	.222	.061	.717			.164
North West Iran		.206	.061	.733			.148
West Iran		.237	.068	.695			.122
Central and South		.163	.063	.774			.076
East Iran		.178	.075	.747			.134
Blood donors	Podliachouk et al., 1962	.271	.050	.679			
From India	Steinberg et al., 1973*						
First sample		.307	.047	.646			.008
Second sample		.293	.077	.610	.020		
Pakistanese	Vos et al., 1963						
Punjabis		.369	.081	.550			
Pathans		.326	.091	.583			
India	Vos et al., 1963						
Oraons		.182	.018	.297	.503		
Todas		.204	.041	.755			
Kurumbas		.392	.070	.538			
Irulas		.358	.115	.527			
Parsis	Steinberg et al., 1973						
a		.368	.024	.538	.071		.034
b		.353	.024	.518	.105		

*Gm^1 haplotype frequency is the sum of the:
$Gm^{1,\ldots,21}$ and $Gm^{1,\ldots,10\ ,11\ ,13}$ haplotype frequencies (present study)
$Gm^{1,\ldots,21}$, $Gm^{1,\ldots,13}$, $Gm^{1,3,\ldots,21}$ haplotype frequencies (STEINBERG et al., 1970, 1973; BLANC al., 1972).

the following phenotypes: Gm(3;23;5,6,10,11,13,14), Gm(1,3,17;..;5,6,10,11, 13,14,21), Gm(1,3,17;23;5,6,10,11,13,14) and Gm(1,3,17;..;5,6,10,11,13,14). It is obvious that in the first phenotype, the G3m(6) allotype can be carried only by the haplotypes $Gm^{3;23;5\ 6\ 10\ 11\ 13\ 14}$ or $Gm^{3;...;5\ 6\ 10\ 11\ 13\ 14}$. In the second case the probable genotype is $Gm^{1,17;...;21}/Gm^{3;...;5\ 6\ 10\ 11\ 13\ 14}$. The family study of the third revealed the presence of two haplotypes carrying G3m(6): $Gm^{3;...;5\ 6\ 10\ 11\ 13\ 14}$ and probably $Gm^{1,17;...;5\ 6\ 11}$. The existence and transmission of the gene so called $Gm^{3;...;5\ 6\ 10\ 11\ 13\ 14}$ had already been demonstrated among the Caucasoid population (STEINBERG et al., 1963; RUFFIE et al., 1964; LOGHEM Van and STEINBERG, 1966; LOGHEM Van and NATVIG, 1970) and also in some populations of the Near and Middle East (PODLIACHOUK et al., 1962; RUFFIE and TALEB, 1965; STEINBERG et al., 1970; BLANC et al., 1972).

The family study of the fourth case showed transmission of the $Gm^{1,17;..;5\ 6\ 11}$ negroid haplotype. The haplotype $Gm^{1,2\ 17;...;5\ 10\ 11\ 13\ 14}$ (.005) which is very rare in the Lebanese population was found among Kurdish people from Syria and Lebanon (BLANC et al., 1972) with a comparable frequency to ours.

The 21 Gm(1;5,10,11,13,14,21) individuals probably are heterozygous $Gm^{1;1;...;21}/Gm^{1\ 17;...;5\ 10\ 11\ 13\ 14}$ and the five Gm(1,2;5,10,11,13,14,21) probably are $Gm^{1\ 2\ 17;..;21}/Gm^{1\ 17;...;5\ 10\ 11\ 13\ 14}$ or $Gm^{1\ 17;...;21}/Gm^{1\ 2\ 17;..;5\ 10\ 11\ 13\ 14}$.

The Gm(1;..;10,11,13,21), Gm(1,2;..;10,11,13,21) and Gm(1;..;10,11,13) phenotypes found among 23 individuals (Table III), could be explained by the presence of the $Gm^{1,17;..;10\ 11\ 13}$ common mongoloid haplotype. The frequency of this haplotype in Lebanon (.0336) is lower than the frequencies observed among Kurdish people from Syria and Lebanon (BLANC et al., 1974), and Kurdish Jews from Northern Iraq and Eastern Turkey (STEINBERG et al., 1970). Its presence in Lebanon might reveal a Mongoloid admixture, which might also be confirmed by the low frequency (.258) of gene Hp^1 from the haptoglobin system, one among the other genetic markers studied on the same samples (LALOUEL et al., 1975).

The Gm(1;23;5,10,11,13,14,21) and Gm(1,2;23;5,10,11,13,14,21) phenotypes characterized by the absence of the G1m(3) allotype are explained by the uncommon haplotype $Gm^{-;23;5\ 10\ 11\ 13\ 14}$ whose transmission was demonstrated by the study of the two families. The presence of such a haplotype was already observed in Caucasoid families (LOGHEM Van and NATVIG, 1970) and its formation was explained by an unequal crossing-over resulting in the loss of a γl cistron.

The model of the six haplotypes, allowing to explain the 14 phenotypes described among the 2005 people, provides suitable agreements between the number of observed and expected phenotypes ($\chi^2 = 7.08$ for D.F. = 8).

As for the Km system, the determination of Km(1 and 2) allotypes only allowed us to demonstrate the existence of the 2 alleles $Km^{1,2}$, Km^1. The frequency of the $Km^{1,2}$ allele is .072 whereas the Km^1 gene is extremely rare (.0058). The $Km^{1,2}$ frequency is comparable to the ones obtained among the Iranians (ROPARTZ et al., 1962), Kurdish individuals from Syria and Lebanon (TALEB et al. 1974) and Kurdish Jews from Northern Iraq (STEINBERG et al., 1970). Another study concerning the population in different areas from Iran (BAJATZADEH and WALTER, 1968) in which only Km(1) was tested, shows variations in the regional distribution of Km(1) and Km(-1) phenotypes (Table VII). The frequencies obtained in Lebanon are comparable to those observed in Central and South Iran. They are close to the frequencies found among the European Caucasoid populations (ROPARTZ et al., 1963; RITTER H. et al., 1966), but quite different from those observed among the Negroids and Mongoloids which are very much higher; this statement might be argument against important negroid and mongoloid admixtures.

As for the ISf system, the frequency of the ISf(1) phenotype is nearly 52%. It presents the variations according to the age (Table VI) as already described (ROPARTZ et al., 1968) for the Caucasoid populations; its value is 30% among the young individuals, 54% among the adults and 63% among the people older than sixty.

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