



Augusta GA, USA



NONDELESYONEL ALFA TALASEMİLER



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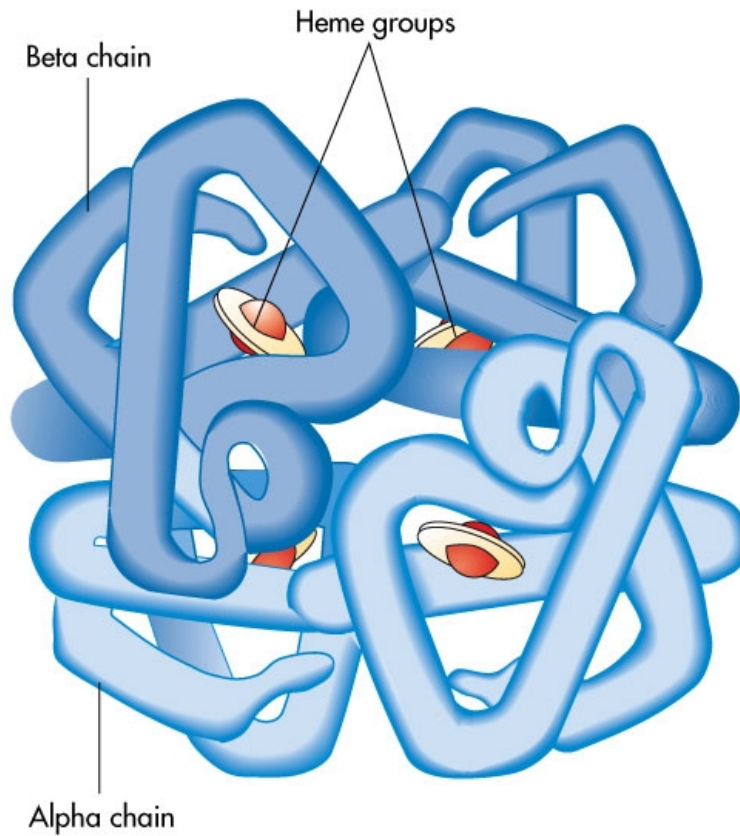




Kırmızı kan hücreleri



Hemoglobin Molekülü

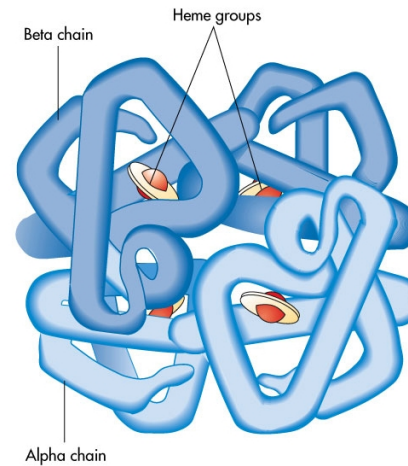


Beta talasemi taşıyıcılığı



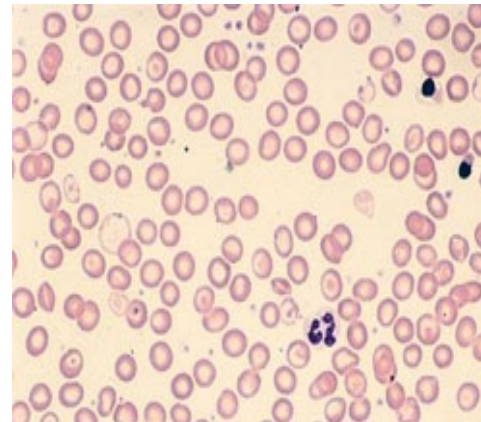
HbA (2 α 2 β) ↓

HbA₂ (2 α 2 δ) ↑



HbA₂ >%3.7

MCV < 78



Alfa talasemi taşıyıcılığı

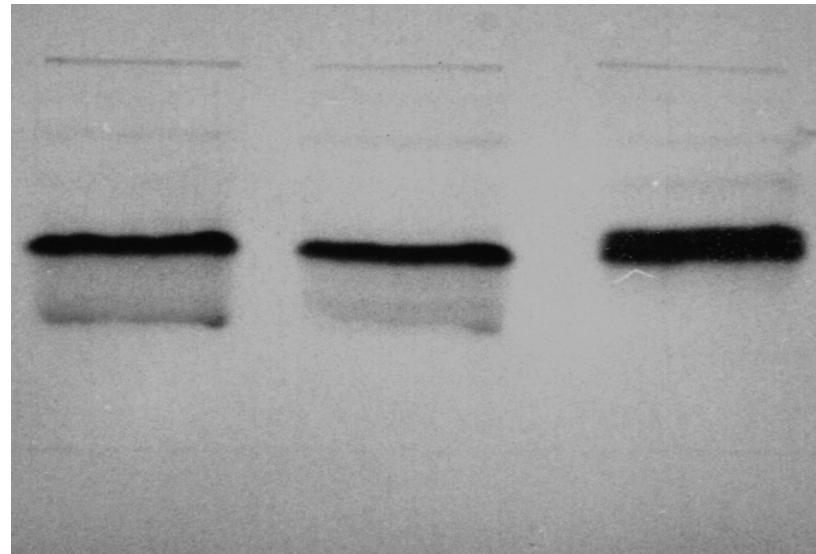


HbA ($2\alpha 2\beta$)

HbA₂ ($2\alpha 2\delta$) ↓

HbA₂ < %3

HbH (β_4) ↑



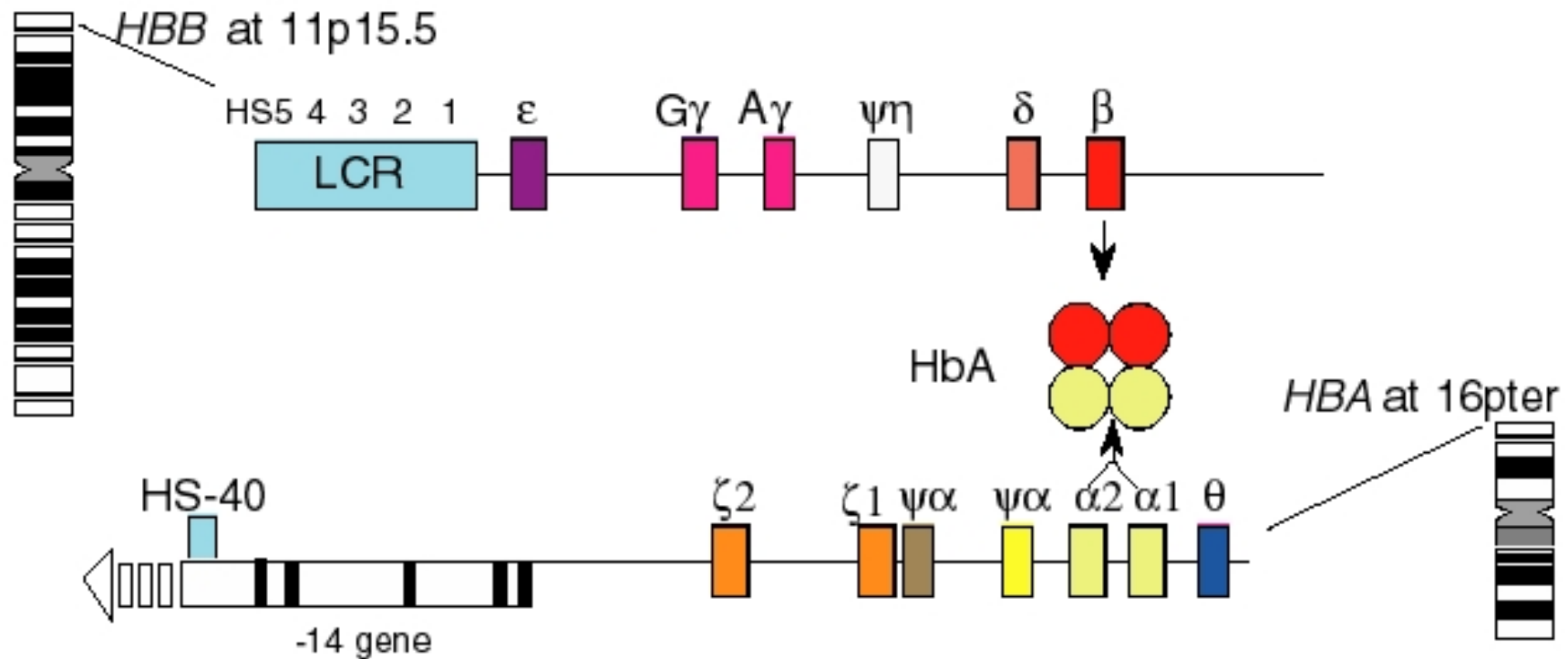
HEMOGLOBİNOPATİLERİN YAPISAL ÇEŞİTLİLİĞİ

<u>Hemoglobinopatiler</u>	<u>Türkiye</u>	<u>Dünya</u>
Alfa Talasemiler	20	100
Beta Talasemiler	42	200
Anormal Hemoglobinler	52	1000

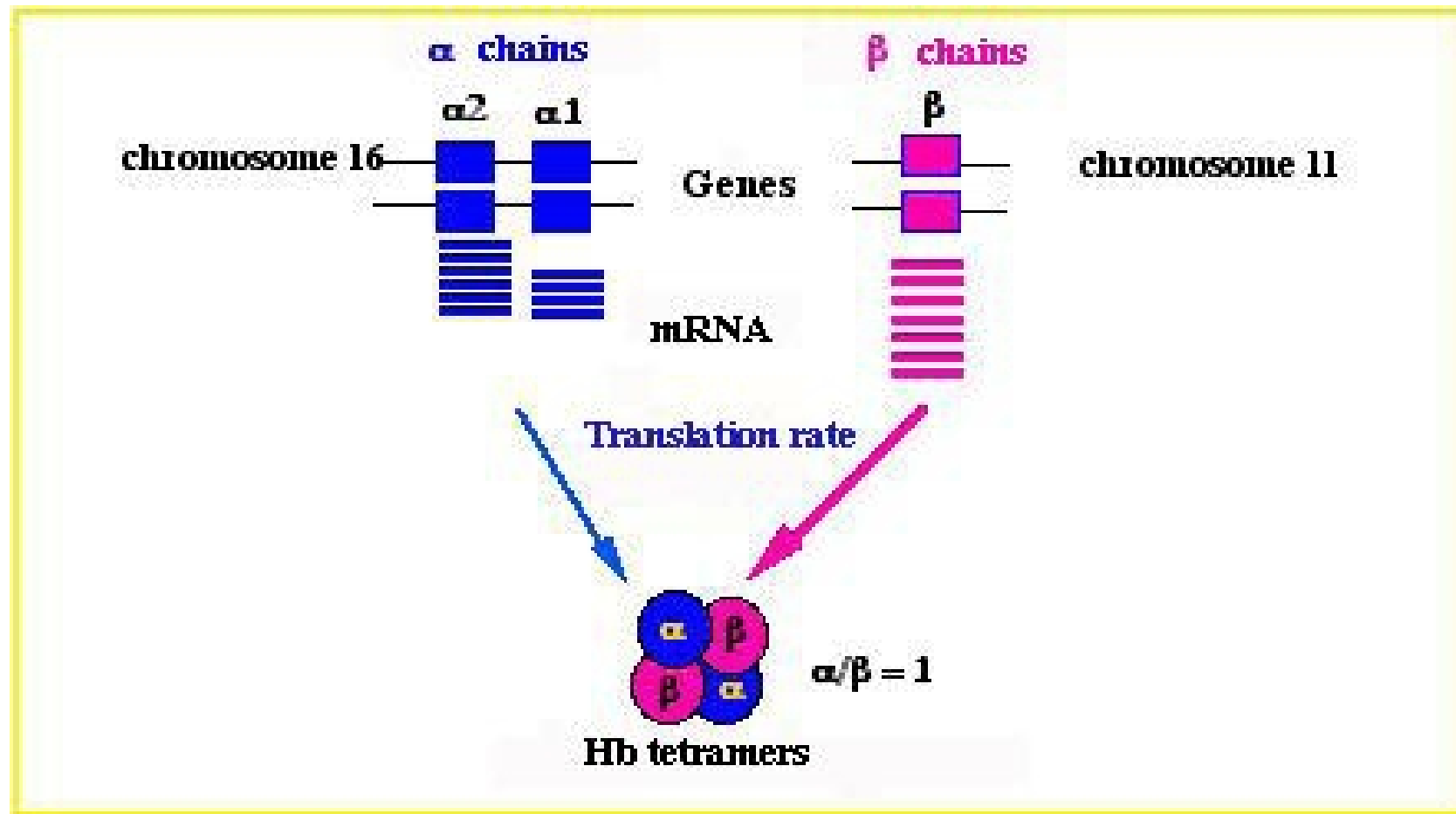
Normal insan hemoglobinleri

Embriyonik Hemoglobinler	Fetal Hemoglobin	Erişkin Hemoglobinleri
Hb Gower 1 ($\zeta_2\epsilon_2$)	Hb F ($\alpha_2\gamma_2$)	Hb A ($\alpha_2\beta_2$)
Hb Gower 2 ($\alpha_2\epsilon_2$)		Hb A ₂ ($\alpha_2\delta_2$)
Hb Portland ($\zeta_2\gamma_2$)		

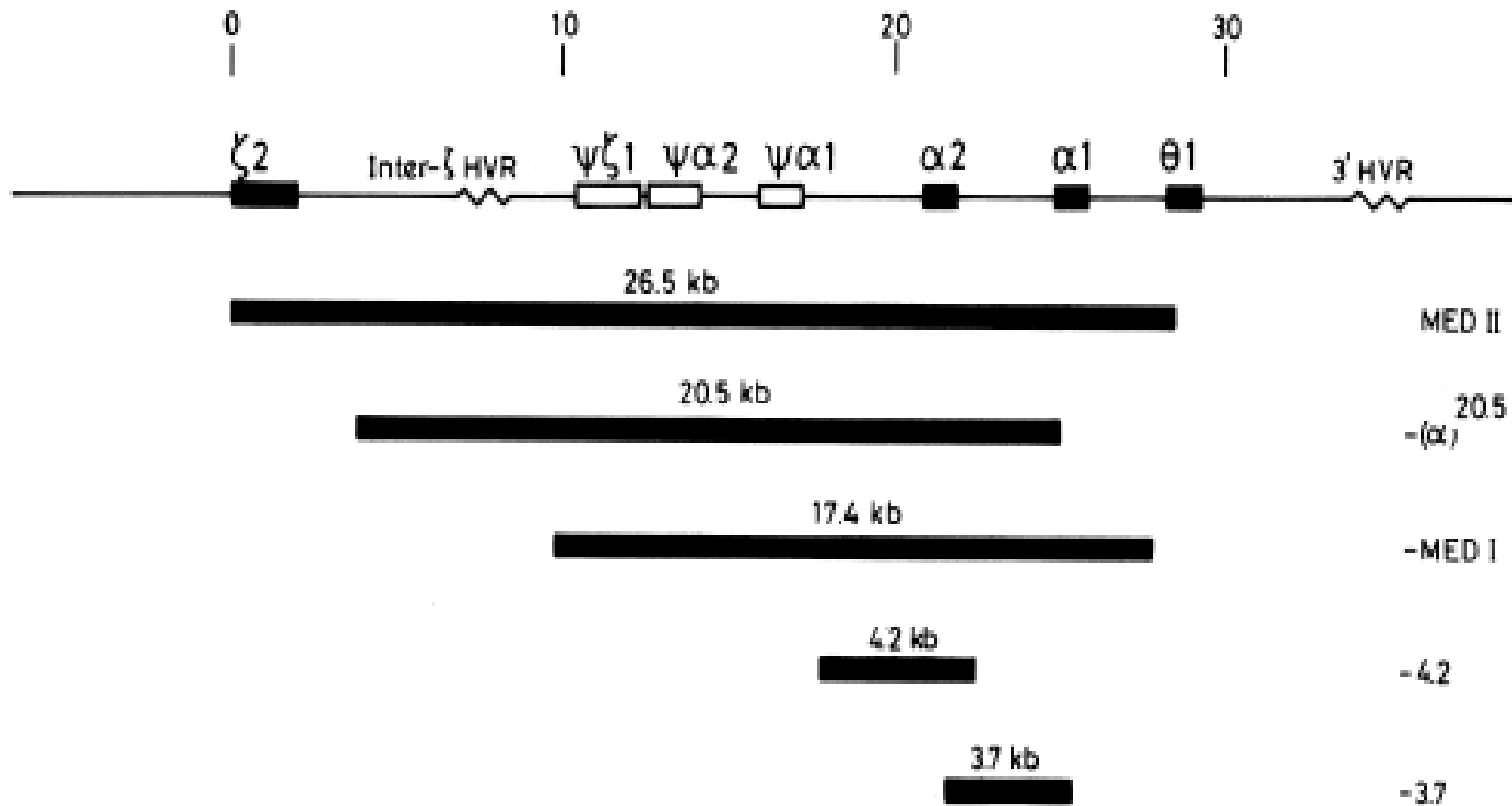
Alfa ve beta globin gen kümeleri



Hb molekülünde alfa ve beta globin zincir oranı



Alfa globin gen delesyonları



$\alpha 1$ CGCGCACGTGGACGACATGCCCAACCCGCTGTCCCCCTGAGCGACCTGCACGCGCACAAGCTTCGGGTGGACCC

$\alpha 2$ -----

$\alpha 1$ CGTCAACTTCAAGgt gageggcgggcgggagcgat ct gggt cgaggggcgagat ggcgcct t cct cgcagggca

$\alpha 2$ -----t-----

$\alpha 1$ gaggat cacgcgggt t gcgggaggt gt agcgcaggcggcggct gcgggcct gggccct cggccccact gaccct c

$\alpha 2$ -----*****---g-----

$\alpha 1$ t t ct ct gcacagCTCCTAAGCCACTGCCTGCTGGTGACCTGCCCCGCCACCTCCCCGCCGAGTTCACCCCTCCG

$\alpha 2$ -----

$\alpha 1$ GTGCA CGCCTCCCTGGACAAGTTCCTGGCTTCTGTGACCACCGTGCTGACCTCCAAATACCGTTAAgct ggagcc

$\alpha 2$ -----

$\alpha 1$ t cggg ggccat gct t ct t gccct t gggcct cccccagccct cct cccct t cct gcacccgt accccgt ggt

$\alpha 2$ -----a---g-t-c--c---ga-----aa-g-a-----*c--tt-c----

$\alpha 1$ ct t t gaat aa gt ct gagt gggcggcagcct gt gt gt gcct gagt t t t t ccct c*agaaacgt gccage*at gg

$\alpha 2$ -----g--c-c--tg--cc-g--t-----a-a----

Ülkemizde tespit edilmiş alfa zincir varyantaları (n:14)

Hb Adı	Rezidü/Değişim	Mutasyon
O-Padova	30Glu→Lys	<u>G</u> AG→ <u>A</u> AG
Hasharon	47Asp→His	<u>G</u> AC→ <u>C</u> AC
Montgomery	48Leu→Arg	<u>C</u> TG→ <u>C</u> GG
Adana*	59Gly→Asp	<u>G</u> GC→ <u>G</u> AC
J-Anatolia	61Lys→Thr	<u>A</u> AG→ <u>A</u> CG
Ube-2	68Asn→Asp	<u>A</u> AC→ <u>G</u> AC
Q-Iran	75Asp→His	<u>G</u> AC→ <u>C</u> AC
Moabit	86Leu→Arg	<u>C</u> TG→ <u>C</u> GG
M-Iwate	87His→Tyr	<u>C</u> AC→ <u>T</u> AC
Çapa*	94Asp→Gly	<u>G</u> AC→ <u>G</u> GC
G-Georgia	95Pro→Leu	<u>C</u> CG→ <u>C</u> TG
Strumica	112His→Arg	<u>C</u> AC→ <u>C</u> GC
J-Meerut (J-Birmingham)	120Ala→Glu	<u>G</u> CG→ <u>G</u> AG
Costant Spring	142+31 Amino asit	

ALFA TALASEMİ GENOTİPLERİ

Normal Genotip	$\alpha\alpha/\alpha\alpha$	
Sessiz taşıyıcı	- $\alpha/\alpha\alpha$	α -Thal-2
Homozigot	- $\alpha/-\alpha$	
Ağır Taşıyıcı	- $-/\alpha\alpha$	α -Thal-1
Hb Bart's	- $-/-$	
Nondelesyonel α -thal.	$\alpha^*\alpha/\alpha\alpha$	
HbH	- $-/- \alpha$	α -thal-1/ α -thal-2
HbH	- $-/ \alpha^*\alpha$	
HbH	- $-/ \alpha \alpha^*$	
HbH	$\alpha^*\alpha / \alpha^*\alpha$	

* Nokta mutasyonu

Poly A mutasyonu taşıyan bir çiftin hematolojik değerleri

Yaş	Hb g/dL	RBC 10 ¹² /L	MCV fL	MCH pg	MCHC g/dL	HbA ₂ %	HbF %
Anne 28	13.4	5.2	80.9	25.8	31.8	1.9	0.8
Baba 32	14.6	5.6	78.0	26.0	33.3	2.4	0.6

GTGCA CGCCTCCCTGGACAAGTT CCTGGC
TTCTGTAG ACACCGTGCTGACCT CCAAATA
CCGTTAAgctggagcctcgg tggccatgcttcttgcccctt
gggcctccccccagcccctcctccccttcc tgcacccgtaccccc

PolyA

gtggtctttaataagtctgagtgggcggcagccgttgtgtg

↓ ↓

g g

cctgagttttt ctgtcccggaatgtgccaacaatgg

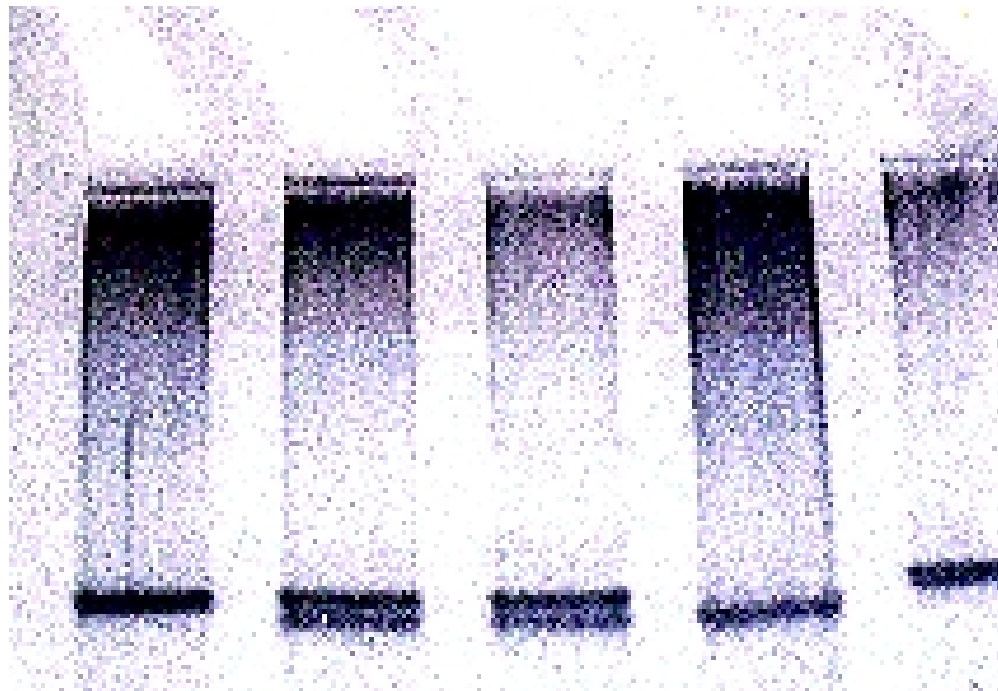
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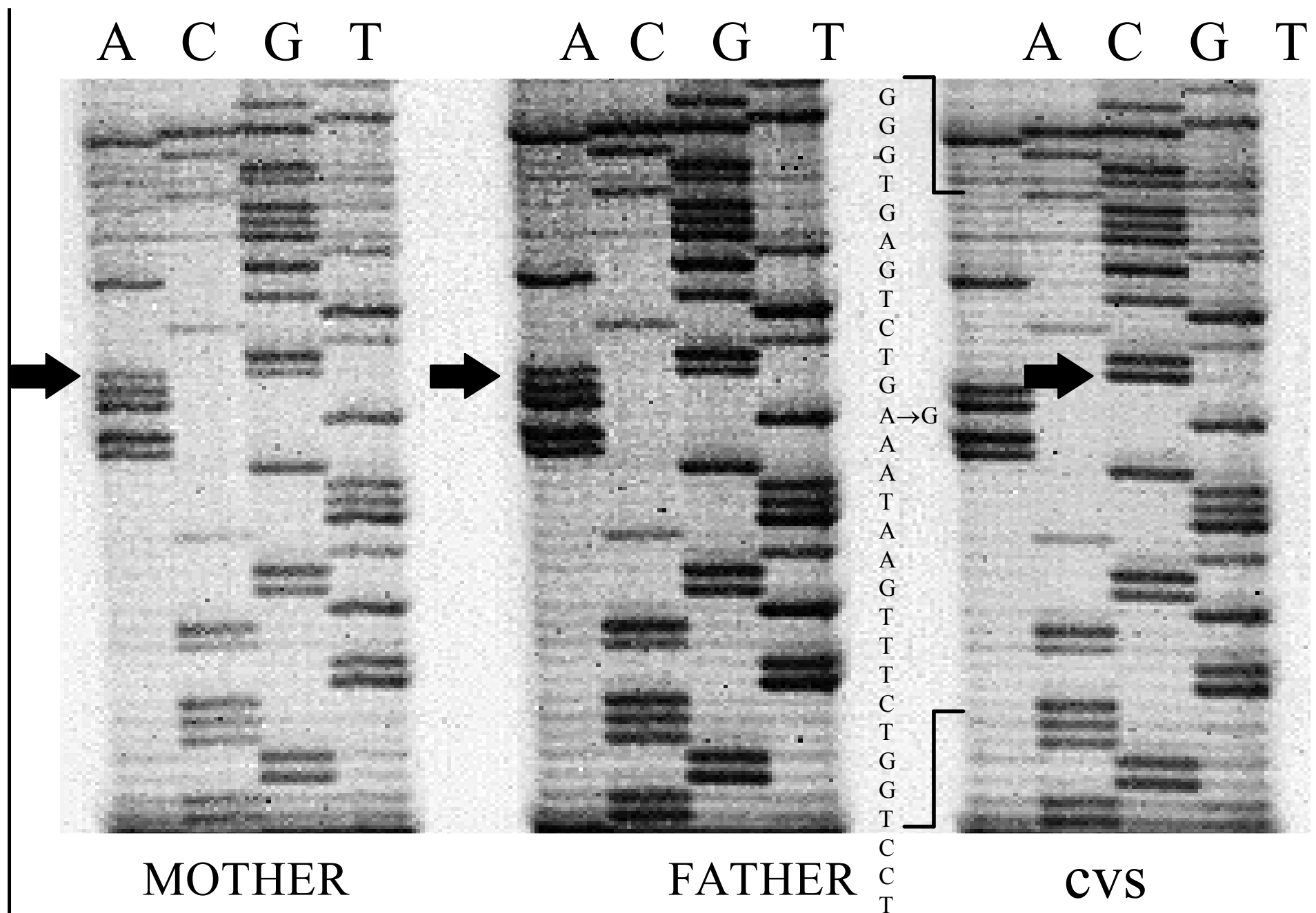
M

F

CVS

C





Türkiyede görülen alfa, beta, gama ve delta globin zincir varyantları

No	Mutasyon Adı	Mutasyon Türü	No	Mutasyon Adı	Mutasyon Türü
1	Adana	$\alpha 59 \text{ Gly} > \text{Asp}$	27	J-Antakya	$\beta 65 \text{ Lys} > \text{Met}$
2	Ankara	$\beta 10 \text{ Ala} > \text{Asp}$	28	J-İran	$\beta 77 \text{ His} > \text{Asp}$
3	A ₂ Yialousa	$\delta 82 \text{ Ala} > \text{Ser}$	29	J-Meerut	$\alpha 120 \text{ Ala} > \text{Glu}$
4	Antalya	Delesyon ve İnsersiyon	30	Knosos	$\beta 27 \text{ Ala} > \text{Ser}$
5	Başkent	$\gamma 128 \text{ Ala} > \text{Thr}$	31	Köln	$\beta 98 \text{ Val} > \text{Met}$
6	Beograd	$\beta 121 \text{ Glu} > \text{Val}$	32	Lepore-Boston	Hibrit
7	Brocton	$\beta 138 \text{ Ala} > \text{Pro}$	33	M-Iwata	$\alpha 87 \text{ His} > \text{Tyr}$
8	Bronova	$\alpha 103 \text{ His} > \text{Leu}$	34	Moabit	$\alpha 86 \text{ Leu} > \text{Arg}$
9	C	$\beta 6 \text{ Glu} > \text{Lys}$	35	Monthgomery	$\alpha 48 \text{ Leu} > \text{Arg}$
10	City of Hope	$\beta 69 \text{ Gly} > \text{Ser}$	36	N-Baltimore	$\beta 95 \text{ Lys} > \text{Glu}$
11	Costant Spring	Uzamış α zinciri	37	O-Arab	$\beta 121 \text{ Glu} > \text{Lys}$
12	Çapa	$\alpha 94 \text{ Asp} > \text{Gly}$	38	O-Podova	$\alpha 30 \text{ Glu} > \text{Lys}$
13	D-Iran	$\beta 22 \text{ Glu} > \text{Gln}$	39	O-Nilotic	Hibrit
14	D-Punjab	$\beta 121 \text{ Glu} > \text{Gln}$	40	Pyrgos	$\beta 83 \text{ Gly} > \text{Asp}$
15	D-Ouled Rabah	$\beta 19 \text{ Asn} > \text{Lys}$	41	Q-İran	$\alpha 75 \text{ Asp} > \text{His}$
16	E	$\beta 26 \text{ Glu} > \text{Lys}$	42	S	$\beta 6 \text{ Glu} > \text{Val}$
17	E-Saskatoon	$\beta 22 \text{ Glu} > \text{Lys}$	43	Sarrebürg	$\beta 131 \text{ Gln} > \text{Arg}$
18	G-Copenhagen	$\beta 47 \text{ Asp} > \text{Asn}$	44	Setif	$\alpha 94 \text{ Asp} > \text{Tyr}$
19	G-Copenhagen	$\beta 47 \text{ Asp} > \text{Asn}$	45	Siirt	$\beta 27 \text{ Ala} > \text{Gly}$
20	G-Georgia	$\alpha 95 \text{ Pro} > \text{Leu}$	46	Strumica	$\alpha 112 \text{ His} > \text{Arg}$
21	G-Szuhu	$\beta 80 \text{ Asn} > \text{Lys}$	47	Summer Hill	$\beta 52 \text{ Asp} > \text{His}$
22	Hakkari	$\beta 31 \text{ Leu} > \text{Arg}$	48	Tunis	$\beta 124 \text{ Pro} > \text{Ser}$
23	Hamadan	$\beta 56 \text{ Gly} > \text{Arg}$	49	Tyne	$\beta 5 \text{ Pro} > \text{Ser}$
24	Hasharon	$\alpha 47 \text{ Aspu} > \text{His}$	50	Ube-2	$\alpha 68 \text{ Asn} > \text{Asp}$
25	Istanbul	$\beta 92 \text{ His} > \text{Gln}$	51	Volga	$\beta 27 \text{ Ala} > \text{Asp}$
26	J-Anatolia	$\alpha 61 \text{ Lys} > \text{Thr}$	52	Yauzi	$\beta 79 \text{ Asp} > \text{Asn}$

Farklı alfa talasemi taşıyıcılarının hematolojik değerleri

Yaş Cins	RBC 10 ¹² /L	Hb g/L	Hct %	MCV fL	MCH pg	MCHC g/dL	Hb Tipi	HA ₂ %	β-globin Genotipi
Erkek (n:5)	4.82	13.9	44	92.3	28.8	31.2	AA	2.5	αα/αα
Kadın (n:7)	4.69	13.6	43	93.2	29.0	31.1	AA	2.5	αα/αα
E-12	5.26	12.5	41	77.9	23.8	30.5	AA	2.1	- α(3.7)/αα
K-22	4.57	11.9	36	80.0	26.0	32.6	AA	3.0	- α(4.2)/αα
K-25	5.25	10.8	35	70.2	21.4	30.4	AA	2.0	--(17.4)/αα
E-14	6.64	12.7	42	63.7	19.1	30.0	AA	1.9	--(20.5)/ αα
K-43	5.57	10.9	37	67.9	19.6	28.8	AA	2.4	--(26.5)/ αα
E-15	4.47	12.8	38	85.6	28.5	33.3	AA	1.4	αα/α ^{5nt} α
E-28	5.22	13.3	46	89.1	25.5	28.6	AA	2.5	αα/ α ^{PA1} α
K-29	5.20	13.4	42	80.9	25.8	31.8	AA	1.9	αα/α ^{PA2} α

HbAS ve α -talasemili kiřilerin hematolojik deęerleri									
Yař Cins	RBC 10 ¹² /L	Hb g/L	Hct %	MCV fL	MCH pg	MCHC g/dL	Hb Tipi	HA ₂ %	β -globin Genotipi
K-30	4.79	14.0	44	92.3	29.2	31.7	AS	3.1	$\alpha\alpha/\alpha\alpha$
E-33	4.48	13.0	40	90.6	29.0	32.0	AS	3.5	$\alpha\alpha/\alpha\alpha$
K-7	5.01	13.4	44	88.8	26.7	30.1	AS	3.5	$-\alpha(3.7)/\alpha\alpha$
K-27	4.63	12.3	40	86.4	26.6	30.7	AS	3.3	$-\alpha(4.2)/\alpha\alpha$
E-32	6.22	13.7	43	70.2	22.0	31.3	AS	4.0	$--(17.4)/\alpha\alpha$
K-29	5.20	10.4	33	63.9	20.0	31.3	AS	3.3	$--(20.5)/\alpha\alpha$
E-14	5.16	11.3	35	69.6	21.9	31.5	AS	3.7	$--(26.5)/\alpha\alpha$
E-52	5.95	11.8	36	90.9	29.9	32.9	AS	3.3	$\alpha\alpha/\alpha^{PA2}\alpha$
K-20	5.70	9.2	31	55.5	16.1	29.0	AS	1.2	$--(17.4)/-\alpha(3.7)$
E-30	6.09	10.8	36	60.4	17.7	29.3	AS	1.4	$--(26.5)/\alpha^{PA2}\alpha$

HbH; Farklı α -talasemi genotipleri ve hematolojik deęerleri

Yaş Cins	RBC 10 ¹² /L	Hb g/L	Hct %	MCV fL	MCH pg	MCHC g/dL	Hb Tipi	HA ₂ %	β -globin Genotipi
E-16	4.72	8.8	30	64.0	18.7	29.2	AH	1.7	- -(MED I)/- α (3.7)
K-45	4.67	9.1	35	75.0	20.0	26.0	AH	0.5	- -(20.5)/- α (3.7)
K-41	4.71	9.5	34	71.8	20.1	28.0	AH	0.5	- - (20.5)/- α (4.2)
E-29	5.38	10.3	37	69.4	19.2	22.5	AH	1.4	--(MED II)/- α (3.7)
E-18	4.06	6.4	24	59.0	16.0	27.0	AH	1.5	- -(MED I)/ $\alpha^{5nt}\alpha$
K-23	3.81	7.8	26	67.0	20.0	30.0	AH	0.8	- -(MED I)/ $\alpha^{PA1}\alpha$
E-22	3.28	7.4	31	96.0	22.0	23.0	AH	1.3	- -(20.5)/ $\alpha\alpha^{CD59}$
K-11	4.87	8.6	30	62.0	18.0	29.0	AH	0.4	- -(MED II)/ $\alpha^{5nt}\alpha$
E-29	4.42	7.8	33	78.0	18.0	24.0	AH	0.8	$\alpha^{PA1}\alpha/\alpha^{PA1}\alpha$

Çukurova Bölgesinde Görülen HbH Genotipleri

Cins/Yaş	RBC 10 ¹² /L	Hb g/dL	Hct %	MCV fL	MCH pg	MCH C g/dL	Hb Tipi	Hb A ₂ %	Hb H Genotipi
E-16	4.72	8.8	30	64.0	18.7	29.2	AH	1.7	-- (MED I)/-α(3.7)
K-45	4.67	9.1	35	75.0	20.0	26.0	AH	0.5	-- (20.5)/-α(3.7)
K-41	4.71	9.5	34	71.8	20.1	28.0	AH	0.5	-- (20.5)/-α(4.2)
E-29	5.38	10.3	37	69.4	19.2	22.5	AH	1.4	(MED II)/α(3.7)
E-18	4.06	6.4	24	59.0	16.0	27.0	AH	1.5	-- (MED I)/α ^{5nt} α
K-23	3.81	7.8	26	67.0	20.0	30.0	AH	0.8	-- (MED I)/α ^{PA1} α
E-22	3.28	7.4	31	96.0	22.0	23.0	AH	1.3	-- (20.5)/αα ^{CD59}
K-11	4.87	8.6	30	62.0	18.0	29.0	AH	0.4	-- (MED II)/α ^{5nt} α
E-29	4.42	7.8	33	78.0	18.0	24.0	AH	0.8	α ^{PA1} α/α ^{PA1} α

Alfa ve beta talaseminin birlikte olduğu Aile bireylerinin hematolojik değerleri



Family	RBC 10 ¹² /L	Hb g/dL	Hct %	MCV fL	MCH Pg	Hb Elect	HbA ₂ %	Genotype
Anne Z.K.26	4.5	10.1	31.7	67.2	21.3	AA	4.8	IVS1-110 /N
Baba M.K.28	6.2	12.3	40.4	64.3	19.6	AA	1.7	- -/αα 20.5 kb
Boy K.K.6	4.5	9.4	29.0	63.4	20.6	AA	4.2	IVS1-110/ 20.5 kb
Kız D.K.2	5.35	9.5	29.5	55.0	17.8	AA	4.3	IVS1-110 /N

Anne β-Thal (IVS1-110) ve Baba α-Thal-1 (20.5kb del)



Katıldığınız için teşekkür ederim

Alfa-1, alfa-2 ve beta geninde yeni Mutasyon

Mutasyon Türü ve yeri Yayınlanan Dergi ve yılı

- Hb Adana $\alpha 1$ geni Am J Hematol 1993
- IVS1-117 $\alpha 1$ geni Br J Hematol 1993
- Poly A $\alpha 2$ geni Br J Hematol 1992