TAG 2007 335

6th Genodermatoses in Mediterranean working session
1st TAG meeting

May 22 - May 25, 2009, Greece

B.Bouadjar
Dpt of dermatology , CHU Bab El Oued, Algiers

Genodermatosis: frequency

Increased recrutment of patients

- Thesis on psoriasis and metabolic syndrome
- Reactivation of sentinel medical network
- Paediatricians more implicated

Genodermatosis in Algeria 2008-2009

- Xeroderma pigmentosum : 380 cases , 100 families
- Recessive ichthyosis : 220 cases , 120 families
- Mal de Meleda : 65 cases, 40 families

- Hereditary epidermolysis bullosa : 110 cases, 70 families
- Familial psoriasis : 100 cases, 90 families
- Familial vitiligo : 40 cases, 20 families
- Sclérose tubéreuse of Bourneville : 28 cases ,10 families
- Epidermodysplasia verruciformis : 26 cases, 22 families
- Others : Kindler syndrome, Papillon-Lefèvre syndrome, Chanarin Dorfman syndrome

Ichthyosis

220 cases

Uptaded genetic analysis in algerian families

J.Fischer , Evry

N°	classé	Lot	Medecin	Famille	Nom	att.	non-att	consang	2	3	14	17	19p	X	5	19pq
5	ICH	1	BOU	6717	Deriouche	1	8	oui	**M**							
11	ICH	1	BOU	6581	Bouhamidi	2	8	oui	X							
14	ICH	2c	BOU	11959	Tchambaz	1	2	oui		**M**						
16	ICH	4	BOU	15046	Lamara	2	3	oui		**M**						
17	ICH	4	BOU	15252	Zerouali	1	6	oui		**M**						
28	ICH	2c	BOU	6582	Rezik	1	2	oui			**M**					
31	ICH	4	BOU	15204	Ezzouaoui	1	4	oui			**M**					
55	ICH	8	BOU	17667	Benammrane	1	2	oui				**ex**				
56	ICH	8	BOU	16965	Kefti	1	3	oui				**M**				
57	ICH	8	BOU	17637	Hadri	2	3	oui				**M**				
139	ICH	2c	BOU	6583	Escid	1	8	oui				1Mhet				
69	ICH	4	BOU	15198	Lamri	1	6	oui					M			
70	ICH	8	BOU	17149	Boghaf	2	6	non-ind					M			
71	ICH	8	BOU	17666	Kahouadji	1	2	oui					M			
72	ICH	8	BOU	17796	Boudefoua	3	7	oui					M			
74	ICH	10	BOU	22064	Bouchafa	2	7	oui					M			
75	ICH	10	BOU	22084	Belabbas	2	2(no par)	oui					M			
76	ICH	10	BOU	22103	Lotmano	2	3	oui					M			
196	ICH	4	BOU	15162	Bekkis	1	7	oui					M			
205	ICH	5	BOU	ICH_15873	Serai	1	7	oui					1M(del)			

J.Fischer

80	ICH	2c	BOU	12761	Lamri	1	3	non							M	
81	ICH	4	BOU	13926	Tikerdoudar	1	10	oui							M	
85	ICH	5	BOU	**ICH_15786**	Kendil	**4**	3	oui							M	
88	ICH	8	BOU	17707	Diab Djeffal	1	2	oui							M	
90	ICH	2c	BOU	12116	Bouyella	1	4	oui		?	X				M	
145	ICH	2c	BOU	6715	Rahal	2	2	oui						del		
153	ICH	1	BOU	6986	Bakhsis	2	5	oui						del		
202	ICH	5	BOU	ICH_15428	Douidi	1	4	?						del		
204	ICH	5	BOU	ICH_15866	Berrami	2	4	?			?			del		
210	ICH	6	BOU	ICH_15947	Makhlouf	1	4	oui						del		
211	ICH	6	BOU	ICH_16551	Saïdami	4	5	?						del		
			BOU	17740	Bouzerki	3*	5	?	ex	ex	ex	ex	ex	del	ex	ex
			BOU	19022	Aissa	2	1	oui				?		del		
			BOU	19205	Slimani	1	2	?						del		
234	ICH	9	BOU	19558	Elouzri	1	5	?						del		
137	ICH	2c	BOU	6437	Aichaoui	1	6	oui								
144	ICH	2c	BOU	6714	Arab	1	5	oui			exclus					
146	ICH	2c	BOU	6716	Hioul	2	4	oui								
147	ICH	2c	BOU	6777	Hamrat	2	7	oui								
150	ICH	2c	BOU	6900	Benserradj	1	6	oui			exclus					
152	ICH	2c	BOU	6984	Sellam	2	3	oui								
175	CBB	2a	BOU	10809	Farah	2	6	oui								
179	ICH	2c	BOU	10949	Bouzerki	1	3	non								
191	ECIS	8	BOU	13627	Rezaoui	1	7	oui								
203	ICH	5	BOU	ICH_15528	Benadji	1	5	oui			exclus					
206	ICH	5	BOU	ICH_15911	Khaldi	1	4	?								
207	ICH	5	BOU	ICH_15912	Boumrah**	3	3	non								
212	ICH	6	BOU	ICH_16813	Mechid	2	4	oui								
213	ICH	6	BOU	**ICH_16814**	Saayoud	**4**	1	oui								
218	ICH	8	BOU	17116	Lekhal	1	5	non-ind								
219	ICH	8	BOU	17141	Messaoudi	1	5	?								
220	ICH	8	BOU	17146	Madani	1	1	oui								
221	ICH	8	BOU	17517	Ghedabna	1	8	oui								
222	ICH	8	BOU	17638	Tahir	1	3	?								
229	ICH	9	BOU	19156	Berrabeh	1	4	oui								
231	ICH	9	BOU	19286	Aichatene	2	2	?							X	
232	ICH	9	BOU	19325	Benamrane		4				X				X	
233	ECIS	9	BOU	19502	Hammadouche	1	2	oui								
235	*KLS*		BOU	19659	Khalafat	1	6	?								
236	ECIS	9	BOU	19948	Fellah	2	7	oui	X							
238	ICH	9	BOU	20894	Achit	1	4	oui	ex	ex	ex	X	ex		ex	X
240	ICH	10	BOU	21984	Cheab	1	6	oui								
241	ICH	10	BOU	22101	Haif Si Haif	1	5 (*)	oui								
242	ICH	10	BOU	22104	Soltani	1	2	oui								
243	ICH	10	BOU	22105	Foudil	0??	3	oui								
244	ICH		BOU	23050	Louaoui	2	4	?								

Mutations in ichthyin on 5q33

- 9 consanguineous families
- 12 patients
- Collodion baby : 9

- a new gene on chromosome 5q33
  - NBCIE:N=6/12
  - LI: N=6/12

Mutations in ichthyin on 5q33 Clinical pecularities

- More important lesions on the neck N=5
- Keratoderma with respect of the center of palms N=6/12 (3IL, 3 EICS)
- Keratoderma with respect of internal part of soles N=6/12

Mutations in ichthyin on 5q33 Genetic study

- 5 homozygote missense mutations in the ichthyin gene in 9 algerian families
- Ichthyin encodes a protein with several transmembrane domains which belongs to a new family of proteins of unknown function localized in the plasma membrane (PFAM: DUF803), with homologies to both transporters and G-protein coupled receptors. This family includes NIPA1, in which a mutation was recently described in a dominant form of spastic paraplegia (SPG6). We propose that ichthyin and NIPA1 are membrane receptors for ligands (trioxilins A3 and B3) from the hepoxilin pathway

C.Lefèvre, B.Bouadjar, Aysen Karaduman ,JF.Prud'homme, J.Fischer **Mutations in *ichthyin* a new gene on chromosome 5q33 in a new form of autosomal recessive congenital Ichthyosis** *Hum. Mol. Genet. 2004. vol.13, N°20, 2473-2482*

Mutations in ABCA12 on 2q33-35

- 4 consanguineous families
- 8 patients.
- Collodion baby : N=8

- LI : N=6/8
- NBCIE : N=2/8

- Clinical pecularities:
  - Distorsion of hands N=3/8

Mutations in ABCA12 on 2q33-35

- Homozygote missense mutations in 4 algerian families in ABCA12
- The ABCA12 protein belongs to a superfamily of membrane proteins that translocate a variety of substrates across extra- and intracellular membranes

C. Lefèvre, S.Audebert, F.Jobard, B.Bouadjar, JF.Prud'homme, J.Fischer **Mutations in the transporter ABCA12 are associated with lamellar ichthyosis type 2** *Hum Mol. Genet. , 2003, vol. 12, N°18 2369-2378*

Mutations in ALOXE3 and ALOX12B on 17

- 3 consanguineous families
- 4 patients
- Collodion baby N=4

- Mutations in ALOXE3 and ALOX12B on 17
  - NBCEI:N=4

Mutations in ALOXE3 and ALOX12B on 17

- These two genes belong to lipoxygenases family and are expressed in the keratinocytes

Novel mutations in ALOX12B in patients with autosomal recessive congenital ichthyosis and evidence for genetic heterogeneity on chromosome 17p13
Lessueur B, Bouadjar B, Fisher J.
1: J Invest Dermatol. **2007** Apr;127(4):829-34. Epub 2006 Nov 30.

F.Jobard, C.Lefèvre, A.Karaduman, JF.Prud'homme,J.Fischer **Lipoxygenase-3 (ALOXE3) and 12(R)-lipoxygenase (ALOX12B) are mutated in non-bullous congenital ichthyosiform erythoderma (NCIE) linked to chromosome 17p13.1** *Hum. Mol. Genet. , **2002**, vol.11, N°1 , 107-113* .

Mutations in TGM1 on 14q11

- 3 consanguineous families
- 3 patients
- Collodion baby : 3

- LI : N=2
- NBCEI : N=1

Mutations in cytochrome p450 gene in 19p32

- 11 consanguineous families
- 18 patients.
- Naissance : Collodion baby : N=9
- Genetic study:
  - LI : N=17
- Clinical peculiarities:
  - Hyperkeratosis on elbows and knees N=10/14
  - Palmar hyperlinearity N= 10/15
  - PKK more marked on heels and part in front of foot N= 10/15

Caroline Lefe`vre, Bakar Bouadjar, Ve´ronique Ferrand, Gianluca Tadini, Andre Megarbane, Mark Lathrop, Jean-Franc¸ois Prud'homme and Judith Fischer **Mutations in a new cytochrome P450 gene in lamellar ichthyosis type 3** Human Molecular Genetics, **2006**, Vol. 15, No. 4

Deletions in STS on X p22

- 15 families
  - Consanguinity : 4
  - 24 patients

- Birth : normal

- Respect of fold
- Respect of palms and soles
- Respect dorsum of feet and hands

Mutations in CGI-58 on ch3
Chanarin Dorfman syndrome

- 3 consanguineous familles
- 4 patients
- Birth : BBC : N=4
- NBCEI
- Strabism: N=3/4
- Lipid droplets in granulocytes

Mutations in CGI-58 on ch3 Chanarin Dorfman syndrome

- The CGI-58 protein belongs to a large family of proteins characterized by an alpha/beta hydrolase fold. CGI-58 contains three sequence motifs that correspond to a catalytic triad found in the esterase/lipase/thioesterase subfamily

C. Lefèvre , B.Bouadjar, JF.Prud'homme, J.Fischer **Mutations in *CGI-58*, the gene encoding a new protein of the esterase/lipase/thioesterase subfamily, in Chanarin -Dorfman Syndrome** Am. J ; Genet. 69 :1002-1012, 2001

Mal de Meleda
65 cases

Main clinical features

- Beginning before age of 5 months
- First manifestation : erythema of the palms and soles
- Followed rapidly by roughning and thickening of the skin
- Hyperkeratosis varied from less marked to massive and yellowish
- Transgressive pachyderma (before age of 3 years)
- Sharply outlined brownish red and scaly border
- Trichophyton rubrum : cultured

B.Bouadjar, S.Benmazouzia,JF.Prud'homme,J.Fischer, Clinical and genetic studies of 3 large, consanguineous, Algerian families with Mal de Meleda
Archives of Dermatology 2000,136,10,1247-1252

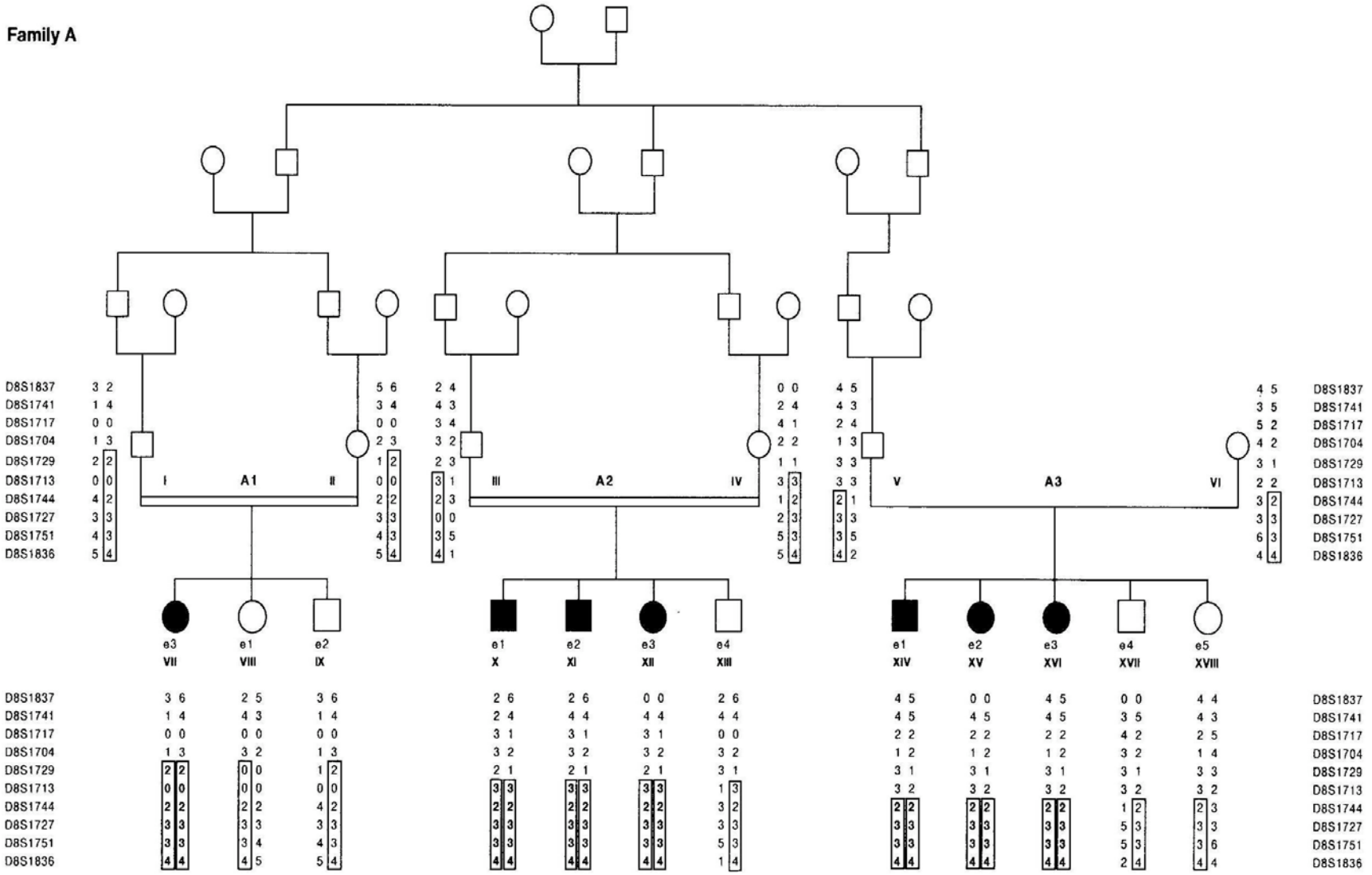
Other features

- Pseudo-ainhum : 25 patients
- Conical distal phalangia : 18 patients
- Brachytelephalangia (Vth) : 17 patients
- Contractures : 26 patients
- Angular cheilitis : 22 patients
- Keratotic plaques on knees and elbows
  14 patients

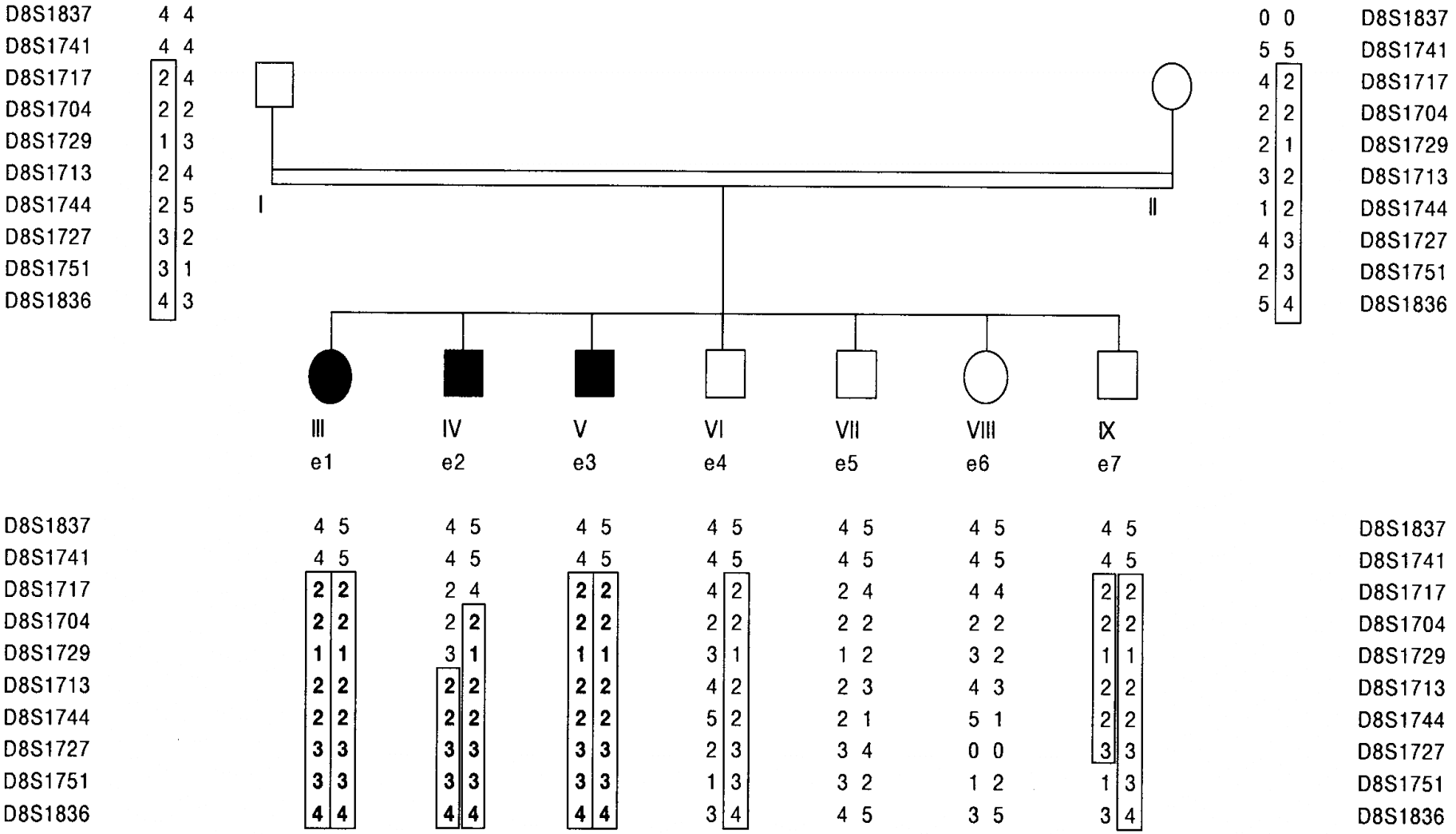
Linkage and haplotype analysis

- Linkage analysis performed in 2 large consanguineous algerian families led to the first localization of the MdM gene on 8qter
- A common haplotype was observed in these two families, suggesting a founder effect.
- Morever, a same geographical origin and an ancestral relationship cannot be excluded.

J.Fischer, B.Bouadjar,R.Heilig, C.Fizames, JF.Prud'homme, J.Weissenbach
Genetic linkage of Meléda disease to chromosome 8qter
European Journal of Human Genetics (1998), 6, 542-547


Family A
D8S1837
D8S1741
D8S1717
D8S1704
D8S1729
D8S1713
D8S1744
D8S1727
D8S1751
D8S1836
I
A1
II
III
A2
IV
V
A3
VI
e3 VII
e1 VIII
e2 IX
e1 X
e2 XI
e3 XII
e4 XIII
e1 XIV
e2 XV
e3 XVI
e4 XVII
e5 XVIII

Family B


D8S1837 4 4
D8S1741 4 4
D8S1717 2 4
D8S1704 2 2
D8S1729 1 3
D8S1713 2 4
D8S1744 2 5
D8S1727 3 2
D8S1751 3 1
D8S1836 4 3
0 0 D8S1837
5 5 D8S1741
4 2 D8S1717
2 2 D8S1704
2 1 D8S1729
3 2 D8S1713
1 2 D8S1744
4 3 D8S1727
2 3 D8S1751
5 4 D8S1836
I
II
III
IV
V
VI
VII
VIII
IX
e1
e2
e3
e4
e5
e6
e7
D8S1837 4 5 4 5 4 5 4 5 4 5 4 5 4 5 D8S1837
D8S1741 4 5 4 5 4 5 4 5 4 5 4 5 4 5 D8S1741
D8S1717 2 2 2 4 2 2 4 2 2 4 4 4 2 2 D8S1717
D8S1704 2 2 2 2 2 2 2 2 2 2 2 2 2 2 D8S1704
D8S1729 1 1 3 1 1 1 3 1 1 2 3 2 1 1 D8S1729
D8S1713 2 2 2 2 2 2 4 2 2 3 4 3 2 2 D8S1713
D8S1744 2 2 2 2 2 2 5 2 2 1 5 1 2 2 D8S1744
D8S1727 3 3 3 3 3 3 2 3 3 4 0 0 3 3 D8S1727
D8S1751 3 3 3 3 3 3 1 3 3 2 1 2 1 3 D8S1751
D8S1836 4 4 4 4 4 4 3 4 4 5 3 5 3 4 D8S1836

Mutation analysis

- The interval of 8qter is refined using a combination of homozygozity mapping and linkage disequilibrium analysis in 19 families(12 from Algeria and 7 from Croatia).

- Mutations analysis of candidate genes in the interval revealed three different homozygous mutations in the *ARS* (*component B*) gene, encoding SLURP-1(secreted Lymphocyte antigen 6 urokinase-type PAR related protein 1) in these families.

J.Fischer, B.Bouadjar, R.Heilig, M.Huber, C.Lefèvre, F.Jobard, D.Hohl, JF.Prud'homme Mutations in the gene encoding SLURP-1 in Mal de Meleda *Human Molecular Genetics, 2001, vol.10, N°8*

Social action

Cancer, hepatitis, orphelin diseases .
Algeria expends 10 milliards of algerian dinars
CANCER, HEPATITE, MALADIES ORPHELINES
L'Etat débourse 10 milliards de dinars

Par: H. ***Barti***

Publié le: 03/04/2007

“The third category of diseases that has to gain a part of this budget (about 2 milliards DA , equivalent to 25.516.000 dollars) is what it is called orphelin diseases or rere diseases whom the cost of treatment stays excessively expansive to be supported by the patient , has underlined the health minister“

Genodermatoses
Budgetary expectations

Spéciality	Chronic diseases	Parmaceutic products		Estimation de Prévalence	Number of treated cases/year	Financial Estimation (dollars)	Registration		Repayment		Observ.
		Médications	Consomable				Oui	Non	yes	No	
Dermatology	Xeroderma Pigmentosum	Retinoïds (Acitretine) Photo-protectors	Photoprotector	400	200	78356	X	X	X	X	-
Dermatology	Ichthyosis	Retinoïds Emollients.		440	220	168767	X	X	X	X	-
Dermatology	Psoriasis	Retinoïds Immuno-modulators (Efalizumab) Dermo-corticoids.		900	200 100 600	73972 821917 2465	X X X		X X	X	- hospital
Dermatology	Palmoplantar keratoderma	Retinoïds (Acitretin) Emollients.		240	50 100	18473 684	X	X	X	X	
Dermatology	Hereditary epidermolysis bullosa		hydrocolloïds dressings Cicatriising cream	80	50	1712	X			X	

Pathology	Number of cases	Budget (dinars)	Budget (dollars)
Xeroderma pigmontosum	**200**	**5 720 000**	**78.356**
Ichthyosis	**220**	**12 320 000**	**168.767**
Palmoplantar keratoderma	**150**	**1 400 000**	**19.178**
Hereditary Epidermolysis bull	**50**	**125 000**	**1712**
Sclérose en plaques	508	396 480 000 DA	
Infirmité motrice cérébrale	20	150 000 000	
Mayasthénie	57	27 360 000	
Maladie de Gaucher	05	35 000 000	
Maladie de Wilson	200	4 065 312	
Maladie de Maroteaux Lamy	20	1 880 000	
Choléstase	200	2 267 280	
Plyradiculonévrite sévère	07	6 000 000	
Hémophilie	1000	940 000 000	
Béta thalassémie	566	340 180 000	
Total	**3203**	**1 862 617 592**	**25.515.308**

Prevalent Orphelin diseases
Budget imputed

- This budget was finally accorded on April 2009 by the director of finances in health minister to the 2 main hospitals in Algiers to buy drugs .

- It will be renewable each year.

- With possibility to increase this amount if necessary

Laboratories

- New : a second budget was also attributed to cover needs of laboratories involved in orphan diseases in terms of diagnosis or genetic studies
- This budget included equipment and reagent
- We will focus mainly on antenataldiagnosis in XP ++
- *Thanks to Dr Zghal for his help in evaluation of budget*

List of equipment and reagent for antenatal diagnosis in XP 125.000 euros

- Clean Bench (Haute aspirante avec filtre 0.2 micron, source UVC (pour la stérilisation), pompe à vide, bec de benzène) (12 000 Euros
- Incubateur CO^2 (12 000 E)
- Haute aspirante standard pour autoradiographie (3000 E)
- Pipette électrique (1000 E)
- Compteur de cellule (3000 E)
- Centrifugeuse (3000 E)
- Congélateur -80°C (10 000 E)
- 2 Container d'Azote liquide pour la conservation des cellules (6 000)
- Container de transport d'Azote liquide (2000 E)
- Boite de tube fluorescent UVC (2 000 E)
- Appareil de mesure les UV (3 000 E)
- Microscope inversée (5 000 E)
- Microscope à émersion + appareil photo digital (10 000 E)
- Autoclave (4 000 E)
- 10 Pipette digital (5 000 E)
- PC (1000 E)
- Compteur manuel (100 E)
- Boite noire (400 E)
- Appareil pour la distillation et la déonisation de l'eau (6 000)
- Matériel à usage unique : boite de pétri, boite de culture, pipette… (10 000 E /an)
- Consommable : produits chimies, milieu de culture, Thymidine radioactive, émulsion photographique, Filtres…… (25 000 E/an)

Psoriasis: Algerian network

Login

Groupe Algérien du Psoriasis

Groupe Algérien du Psoriasis

- Accueil du site
- Conseil scientifique
  - Membres du conseil scientifique :

[s'inscrire]
[mot de passe oublié ?]

Login (e-mail)

MISSIONS

- Promouvoir les connaissances sur le psoriasis auprès des médecins
- Faire le point sur la situation du psoriasis en Algérie
- Effectuer des études et des travaux sur le psoriasis
- Organiser des rencontres sur le sujet
- Encourager l'organisation d'associations pour les patients

Ce groupe est administré par un conseil scientifique composé de ***10 membres***

L'adhésion à ce groupe en tant que membre est ouverte à l'ensemble des dermatologues algériens

Associations

Associations

- **Association of Parents of Patients with Metabolic Diseases (APPMM) (Phenylcetonuria ++)**
  - Created in 1999
  - More than 100 patients repertoried
  - Difficulties: No milk adapted, No specific food
- **Association of Patients with Psoriasis**
  - Created in 2006
  - National
  - Scientific patronage: Prof. Benkaidali

Le Souk

- Created in 1985 with 100% students under 25 years mainly medical students .
- Help children with chronic diseases
- Activities:
  - Visits to parks
  - Paint, music and drawings workshops
  - Masqued ball for1000 children
  - **Program for Moon chidren: Visits in the evening on June to Cap Caxine and to attraction parc**

Amine Association of Bab El Oued , Algiers

- Created in 1997
- Place: Dpt of Pediatrics , CHU Bab El Oued , Algiers
- First named Alouane (=COLORS) according to the association mission: give colors and joy in the life of hospitalized patients. Then Amine,from the name of a young patient died at the beginning of activity of this association
- Activities
  - At first: drawings and music for children. A choir was created only with hospitalized patients and named « The voice of Amine » . This choir is now invited in the galas and a lot of artistic manifestations.
  - Then , education for patients with chronic diseases