Recent Advances Relevant to Screening of Congenital Cardiomyopathy in Lebanon

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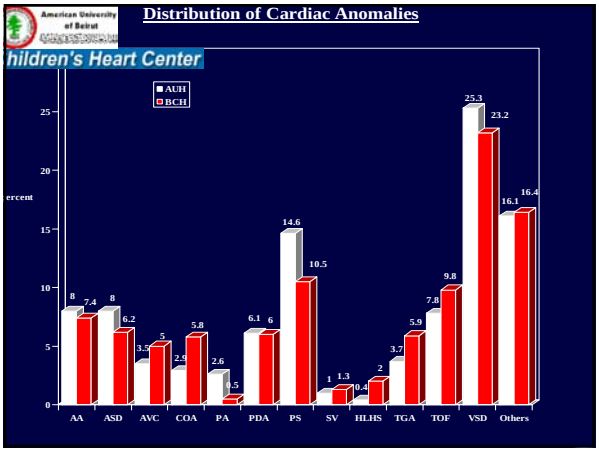


American Journal of Medical Genetics 116A:342–347 (2003)

Parental Consanguinity and Congenital Heart Malformations in a Developing Country

Mona M. Nabulsi,[1*] Hala Tamim,[2] Maha Sabbagh,[1] Mounir Y. Obeid,[3] Khaled A. Yunis,[1] and Fadi F. Bitar[1*]

American Journal of Medical Genetics 140(14):1524-30 (2006)

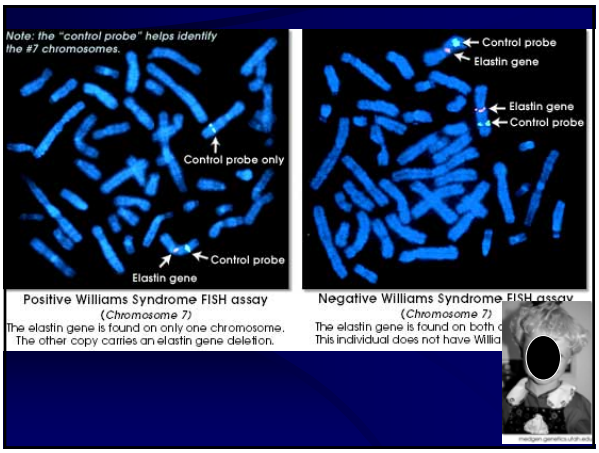
Consanquineous marriage and congenital heart disease : A case control study in the neonatal period.

Yunis KA , Mumtaz G, Bitar FF, Chamseddine F, Kassar M, Rashkidi J, Makhoul G, Tamim H .

TABLE III. Proportions of First-Cousin Mating in the Different Categories of Cardiovascular Malformations

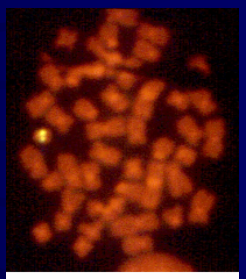
	Total no. (%)	Consanguinity no. (%)	Exact *P* value[a]	Exact *P* value[b]
Category I	3 (0.4)	2 (66.7)	0.05	0.02
Category II	144 (18.9)	30 (20.8)	0.009	<0.0001
Category III	41 (5.4)	11 (26.8)	0.017	0.0003
Category IV	138 (18.2)	26 (18.8)	0.056	<0.0001
Category V	328 (43.3)	60 (18.3)	0.006	<0.0001
Category VI	8 (1.1)	1 (12.5)	1.000	0.50
Category VII	97 (12.8)	23 (23.7)	0.004	<0.0001
Total	759 (100)	153 (20.2)	<0.0001	<0.0001

[a]Comparison is made to the highest proportion of first-cousin mating reported from the NCPNN database (13.2%; Bekaa subjects).
[b]Comparison is made to the adjusted proportion of first cousin mating of NCPNN database (8.19%).



22q Deletion

- This deletion involves some 30 or so genes.
- At least 1 – *TBX1*- appears to be important for outflow tract development.
- Several other syndromes are associated with this deletion e.g.Noonan & CHARGE.



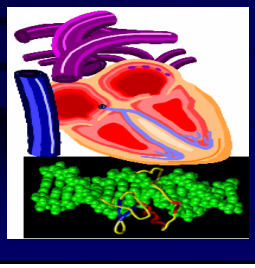
Deletion of genes in DiGeorge syndrome can be visualized by a fluorescent signal on only one of the two copies of chromosome 22.[Image credit: David Ian Wilson, University of Newcastle upon Tyne, UK.]

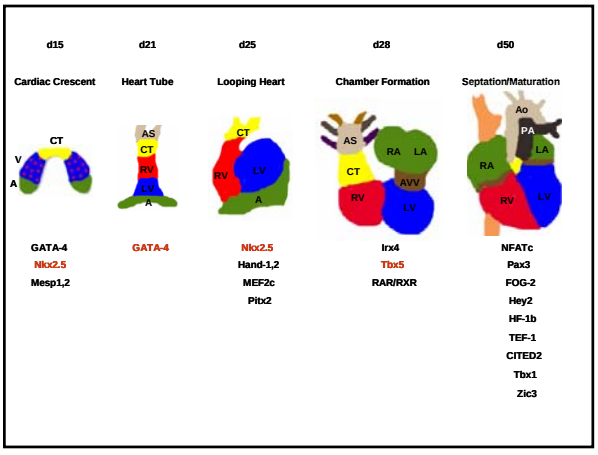
Genes

- Human genome and single Nucleotide polymorphism databanks
- So many genes are involved in programming heart development that, at present, it is difficult to see an immediate clinical application.

The Congenital Heart Disease Genetic Program

CHDGP





HUMAN MUTATION Mutation in Brief #881 (2006) Online

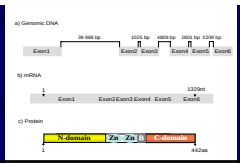
MUTATION IN BRIEF

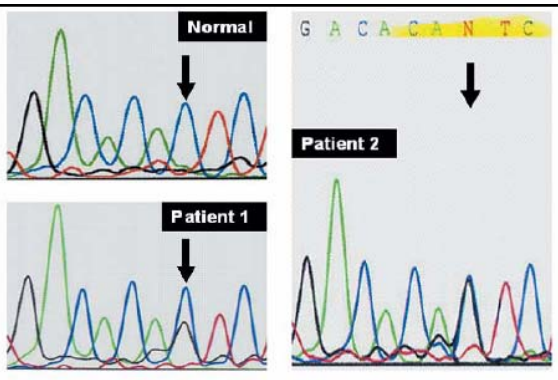
A Novel Mutation in the *GATA4* Gene in Patients With Tetralogy of Fallot

Georges Nemer[1,*], Fatimah Fadlalah[1], Julnar Usta[1], Mona Nemer[2], Ghassan Dbaibo[3], Mounir Obeid[3], and Fadi Bitar[3]

[1]Departments of Biochemistry and [3]Pediatrics, American University of Beirut (AUB),Beirut, Lebanon; [2]Laboratoire de Développement et Différenciation Cardiaques, Institut de Recherches Cliniques de Montréal, Montréal, Québec, Canada

Phenotype	n	C/G polymorphism
TOF	26	2
Other CHDs	94	0
Normal parents and/or siblings	223	0





Exon 2. Heterozygous mutation in 2 patients with TOF resulting in a E216D substitution. **A:** Three chromatograms showing the results of sequencing with the reverse primer of a normal individual, and the two patients with TOF in which a C is substituted by a G (arrow). The resulting codon GAC will encode an aspartic acid instead of glutamic acid (GAG).

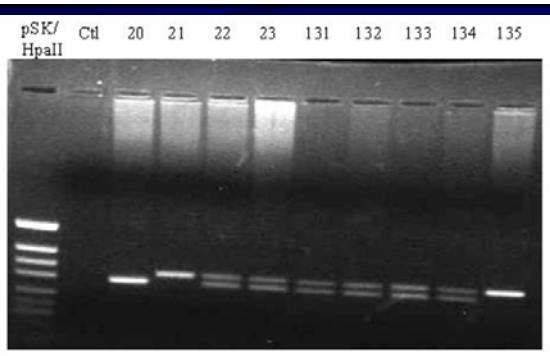
Differential Duplication of an Intronic Region in the NFATC1 Gene in Patients with Congenital Heart Disease

Running Title: **NFATC1 and CHD**

Amin Yehya[1], Ramzi Souki[1], Fadi Bitar[2], and Georges Nemer[1,*]

Genome **49**(9): 1092–1098 (2006)

	Homozygous normal allele	Heterozygous	Homozygous "variant" allele
Phenotypically Normal Parents/Sibs	16	15	0
PS	10	15	0
TA	4	8	0
Phenotypically Normal Parents/Sibs	17	15	3
VSD	10	9	2
Normal Unaffected	47	34	0

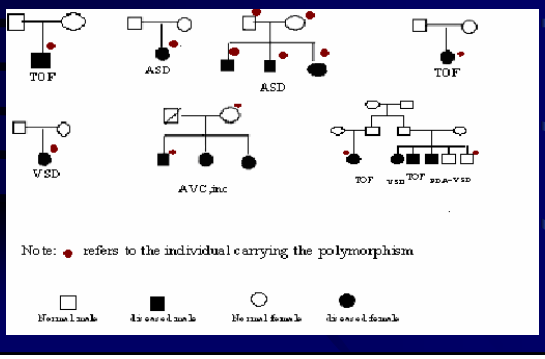


The amplification of the exon 7 region in patients with VSD and their parents shows differential expression of the two alleles.

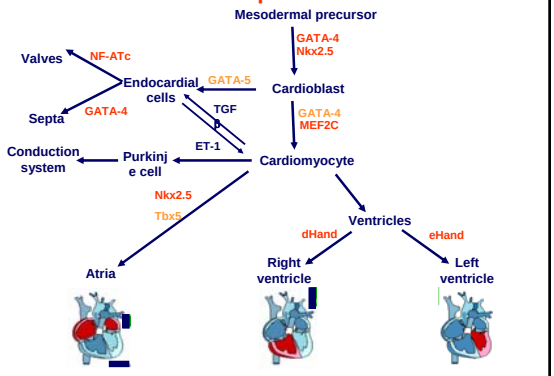
NFATC1 is a potential VSD-susceptibility gene

Odds ratio (OR) for the homozygous "variant" allele in VSD patients versus all other clinic ally healthy individuals (total 147) is calculated as follows: OR= (a/b)/(c/d) = 5.05.

Families with more than 3 children with CHD



Cardiac Transcription Factors in Early Heart Development

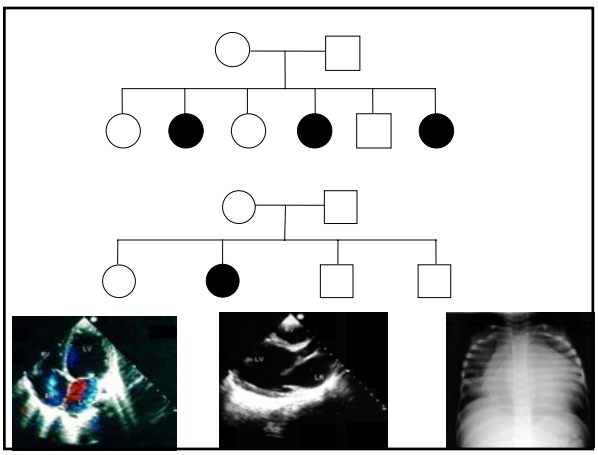


Congenital Cardiomyopathy

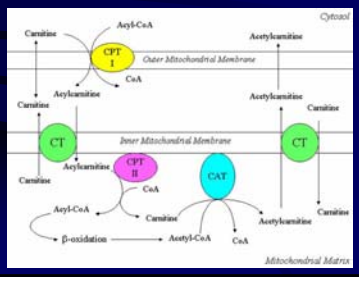
Exclusive cardiac dysfunction in two familial Primary Carnitine Deficiency cases

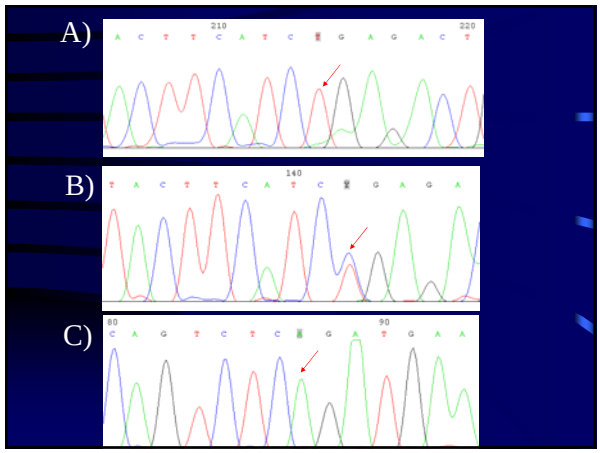
Abir A. Yamak, Fadi Bitar, Pascale Karam, and Georges Nemer

Clinical Genetics,2006



PCD is caused by mutations of the SLC22A45 gene that encodes the sodium-dependent organic cation transporter OCTN2 .R254X





CHD is a leading cause of death in the first year of life

However, just starting……

More Team Work , Research, Support and Collaboration are needed

Progress in Medical Genetics
ISBN : 1-59454-489-1

Molecular Markers of Congenital Heart Disease

By George Nemer and Fadi Bitar