DATABASES FOR PROMOTION OF RESEARCH: THE CTGA DATABASE FOR GENETIC DISORDERS IN ARABS

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A US army-wide measles outbreak in 1917 resulted in more than 95,000 cases and more than 3,000 deaths. The outbreak sparked a broad-interdisciplinary research effort with hundreds of military and civilian physicians and scientists representing disciplines such as internal medicine, pathology, microbiology, radiology, surgery, preventive medicine, and rehabilitation medicine.
THE EPIDEMIC THAT CHANGED MEDICINE

This forgotten epidemic created the blueprint for the military response to the 1918 Spanish H1N1 influenza pandemic.

Elsewhere, the pandemic infected 500 million people across the world and resulted in the deaths of 50-100 million (3-5% of the world's population).
Communicable Diseases

Non-Communicable/Genetic Diseases

Healthcare

Molecular Genetics

Clinical Genetics
Proper practices linked to vaccination, nutrition, medicine (1950s).

Decreasing focus of public health measures on communicable diseases.

Increasing attention towards research on non-communicable chronic diseases; many include genetic conditions.

Improved genetics curricula in medical education.
Communicable Diseases

Non-Communicable/Genetic Diseases

Healthcare

Molecular Genetics

Clinical Genetics
GENETIC VARIABILITY

THE BLOOD GROUPS OF THE PEOPLE OF EGYPT.
Donegani JA, Ibrahim KA, Ikin EW, Mourant AE.
Heredity (Edinb). 1950; 4(3):377-82. PMID:14802994

Congenital malaria in the eastern Mediterranean basin (Lebanon, Syria, Palestine); study of clinical genetics.
Feghali A.
Sem Med. 1951; 27(54):650-2. PMID:14892846

AN INVESTIGATION OF GENETIC VARIABILITY AMONG SUDANESE.
Rife DC.

Thalasso-drepanocytosis in a young Algerian.
Genetic study of 3 generations.
Gillot F, Bigorie, Medioni B.
CLINICAL GENETICS

The blood groups of the people of Egypt.
Donegani JA, Ibrahim KA, Ikin EW, Mourant AE.
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CONGENITAL MALARIA IN THE EASTERN MEDITERRANEAN BASIN (LEBANON, SYRIA, PALESTINE); STUDY OF CLINICAL GENETICS.
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An investigation of genetic variability among Sudanese.
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THALASSO-DREPNOCYTOSIS IN A YOUNG ALGERIAN.
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GENETIC DISORDERS IN ARABS

Description of 1000s of families with pathogenic characters.

Large number of genetic disease entities (1398).

Monogenic and polygenic disorders:

- Hemoglobinopathies
- Cardiovascular diseases
- Cystic fibrosis
- Diabetes
- FMF
- Hypertension
- G6PD
- Cancers

Rare metabolic and congenital disorders.
One Thousand and One Genetic Tales

100s of private disorders and clinical subtypes.

Shared characteristics:

- Early onset
- Autosomal recessive
- Element of surprise
- High recurrence in consanguineous families.
INCOMPLETE STORIES

Analysis confined to clinical assessments result in 301 genetic disorders.

Minimal intervention.

Many affected members in single tribes or families.

Extremely local.

Local problems that need local solutions.
ARAB MOLECULAR GENETICS RESEARCH

[13.1.2016; PubMed > Mutation AND ***]
DROWNING IN A RISING INFORMATION SEA
RISING SEA OF UNANSWERED QUESTIONS
Prof. Ahmad Teebi and Mr. Saeed Teebi established the Arab Genetic Disease Database (AGDDB), a curated catalog of genetic disorders found in Arab populations.

The first online release of the database was populated with information from the textbook ‘Genetic Disorders Among Arab Populations’, co-authored by Prof. Teebi and Dr. Talaat Farag in 1997.
THE AGDDDB DATABASE

AGDDB was composed of data elements including clinical, genomic, reference, and population frequencies of genetic disorders.

After initial indexing in 2002, AGDDDB contained over 1000 unique disorder entries.

The database was freely accessible at www.agdddb.org until in 2004 it went offline because of technical problems.
Offline tabular lists of genetic disorders described in Arab individuals with corresponding references.

Using this strategy, 374 entries for genetic disorders in Arabs were recorded in 1999.

An update early in 2004, 752 entries.

In March 2004, the name ‘Catalogue of Transmission Genetics in Arabs’ (CTGA) was coined for any online database that may materialize out of this survey.
CTGA DATABASE

Catalogue of Transmission Genetics in Arabs.

Launched on the 30th of November 2004.

A continuously updated catalogue of bibliographic material and observations on human gene variants and inherited, or heritable, genetic diseases in Arab individuals.

www.cags.org.ae
CTGA DATABASE WORKFLOW

1. International / Regional Literature Survey
   - Direct Submissions
2. Literature Collection
3. Digitization
4. Editing
5. Literature Review
6. CAGS Library
7. Data Curation
8. Database Testing
9. Database Online Upload
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GENETIC DISORDERS IN ARABS

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Total: 688 (2005)
GENETIC DISORDERS IN ARABS

Total: 777 (2006)
GENETIC DISORDERS IN ARABS

Total: 841 (2007)
GENETIC DISORDERS IN ARABS

Total: 897 (2008)
GENETIC DISORDERS IN ARABS

Total: 936 (2009)
GENETIC DISORDERS IN ARABS

Total: 955 (2010)
GENETIC DISORDERS IN ARABS

Total: 991 (2011)
GENETIC DISORDERS IN ARABS

Total: 1041 (2012)
GENETIC DISORDERS IN ARABS

Total: 1099 (2013)
GENETIC DISORDERS IN ARABS

Total: 1188 (2014)
GENETIC DISORDERS IN ARABS

Total: 1258 (2015)
GENETIC DISORDERS IN ARABS

Total: 1398 (2016)
<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital malformations &amp; chromosomal abnormalities</td>
<td>35.8%</td>
</tr>
<tr>
<td>Endocrine, nutritional, &amp; metabolic diseases</td>
<td>18.0%</td>
</tr>
<tr>
<td>Diseases of the nervous system</td>
<td>11.4%</td>
</tr>
<tr>
<td>Diseases of the blood &amp; the immune mechanism</td>
<td>6.5%</td>
</tr>
<tr>
<td>Diseases of the eye &amp; adnexa</td>
<td>4.5%</td>
</tr>
<tr>
<td>Neoplasms</td>
<td>4.4%</td>
</tr>
<tr>
<td>Diseases not elsewhere classified</td>
<td>2.6%</td>
</tr>
<tr>
<td>Diseases of the ear &amp; mastoid process</td>
<td>2.4%</td>
</tr>
<tr>
<td>Diseases of the circulatory system</td>
<td>2.4%</td>
</tr>
<tr>
<td>Diseases of the skin &amp; subcutaneous tissue</td>
<td>2.3%</td>
</tr>
<tr>
<td>Mental &amp; behavioural disorders</td>
<td>1.9%</td>
</tr>
<tr>
<td>Diseases of the musculoskeletal system</td>
<td>1.8%</td>
</tr>
<tr>
<td>Diseases of the digestive system</td>
<td>1.8%</td>
</tr>
<tr>
<td>Diseases of the genitourinary system</td>
<td>1.6%</td>
</tr>
<tr>
<td>Diseases of the respiratory system</td>
<td>0.6%</td>
</tr>
<tr>
<td>Symptoms, signs and abnormal clinical and laboratory...</td>
<td>0.4%</td>
</tr>
<tr>
<td>Certain conditions originating in the perinatal period</td>
<td>0.4%</td>
</tr>
<tr>
<td>Infectious &amp; parasitic diseases</td>
<td>0.4%</td>
</tr>
<tr>
<td>Pregnancy, childbirth, &amp; the puerperium</td>
<td>0.2%</td>
</tr>
</tbody>
</table>
GENETIC DISORDERS IN ARABS

Common (51 - >100 cases/100,000 live births)

1. Anencephaly
2. Breast Cancer
3. Celiac Disease
4. Coarctation of Aorta
5. Colorectal Cancer
6. Deafness, Autosomal Recessive
7. Dermatitis, Atopic
8. Diabetes Mellitus, NID
9. Down Syndrome
10. Familial Mediterranean Fever
11. Febrile Convulsions, Familial, 1
12. Glucose-6-Phosphate Dehydrog.
13. Gordon Syndrome
14. Graves Disease
15. Hashimoto Thyroiditis
16. Hemoglobin - Alpha Locus 1
17. Hemoglobin - Beta Locus
18. Homocystinuria due to CBS Deficiency
19. Hydrocephalus
20. Hypercholesterolemia, AD
21. Hypertension, Essential
22. Lung Cancer
23. Myocardial Infarction, Suscept. to, 1
24. Orofacial Cleft 1
25. Osteoarthritis Susceptibility 1
26. Polycystic Kidneys
27. Preeclampsia/Eclampsia 1
28. Sickle Cell Anemia
29. Sjogren Syndrome
30. Spondyloarthropathy, Suscept. to, 1
31. Stroke, Ischemic
32. Takayasu Arteritis
GENETIC DISORDERS IN ARABS

Rare (11-50 cases/100,000 live births)

1. Adrenal Hyperplasia, Congenital, due to 21-Hydroxylase Deficiency
2. Antiphospholipid Syndrome, Familial
3. Choanal Atresia, Posterior
4. Diaphragmatic Hernia, Congenital
5. DiGeorge Syndrome
6. Dystrophia Myotonica 1
7. Fragile X Mental Retardation Syndr.
8. Hemophilia A
9. Hirschsprung Disease, Suscept. to, 1
10. Hodgkin Lymphoma
11. Hyperinsulinemic Hypoglycemia, Familial, 1
12. Kawasaki Disease
13. Meckel Syndrome, Type 1
14. Muscular Dystrophy, Duchenne Type
15. Nephrotic Syndrome, Steroid-Resistant, Autosomal Recessive
16. Neurofibromatosis, Type I
17. Patent Ductus Arteriosus
18. Pierre Robin Syndrome
19. Pneumothorax, Primary Spontan.
20. Prostate Cancer
21. Protein S
22. Spinal Muscular Atrophy, Type I
23. Systemic Lupus Erythematosus
24. Total Anomalous Pulmonary Venous Return 1
25. Tuberous Sclerosis
26. Vitiligo
## GENETIC DISORDERS IN ARABS

**Fairly Rare** (6-10 cases/100,000 live births)

| 1. Bardet-Biedl Syndrome               | Glomerulonephritis, X-Linked |
| 2. Bartter Syndrome, Type 3           | 9. Phenylketonuria           |
| 3. CHARGE Syndrome                    | 10. Prader-Willi Syndrome    |
| 5. Diarrhea 1, Secretory Chloride,    | 12. Testicular Tumors       |
|     Congenital                        | 13. Thrombocytopenic Purpura, |
| 6. Jejunal Atresia                    |     Autoimmune              |
| 7. Leukemia, Acute Lymphoblastic      | 14. Thyroid Carcinoma, Papillary |
| 8. Membranoproliferative              |                             |
GENETIC DISORDERS IN ARABS

Very Rare (2-5 cases/100,000 live births)

1. Angelman Syndrome
2. Behcet Syndrome
3. Cholestasis, Progr. Fam. Intrahep., 1
4. Citrullinemia, Classic
5. Common Variable Immunodeficiency
6. Cornelia de Lange Syndrome
7. Cri-Du-Chat Syndrome
8. Glutaric Acidemia I
9. Guillain-Barre Syndrome, Familial
10. Hydrocephalus due to Congenital Stenosis of Aqueduct of Sylvius
11. Leigh Syndrome
12. Leukemia, Acute Myeloid
13. Metachromatic Leukodystrophy
14. Moyamoya Disease 1
15. Multiple Pterygium Syndrome,
16. Mus. Dyst., Cong. Merosin-Def., 1A
17. Ocular Cicatricial Pemphigoid
18. Optic Atrophy 1
19. Osteopetrosis, AR 1
20. Pemphigus Vulgaris, Familial
21. Poland Syndrome
22. Polycystic Kidney Disease, AR
23. Rheumatic Fever-Related Antigen
25. Robinow Syndrome, AR
26. Spinal Muscular Atrophy, Type II
27. Thrombophilia
28. Thyrotoxic Periodic Paralysis
29. Van der Woude Syndrome
30. Von Hippel-Lindau Syndrome
GENETIC DISORDERS IN ARABS

Extremely Rare (<1 case/100,000 live births)

2. Acrofrontofacialasal Dysostosis, Severe
3. Arthropathy, Progressive
   Pseudorheumatoid, of Childhood
4. C Syndrome
5. Cerebr. Palsy, Spastic, Symmetric, AR
8. Diamond-Blackfan Anemia
9. Dysplasia Epiphysealis Hemimelica with
   Chondromas & Osteochondromas
10. Ehlers-Danlos Syndrome, Type VI
11. Hemolytic Uremic Syndr., Atypical
12. Hyperoxaluria, Primary, Type I
13. Hypertelorism, Teebi Type
14. Laron Syndrome
15. Laurence-Moon Syndrome
16. Leukemia, Chronic Myeloid
17. Lipoid Proteinosis of Urbach and Wiethe
18. Lymphoma, Non-Hodgkin, Familial
19. Macroosmia & Microphthalmia, Lethal
20. Maple Syrup Urine Disease
21. Microcephaly with Chorioretinopathy, AR
22. Nijmegen Breakage Syndrome
23. Osteoporosis-Pseudoglioma Syndr.
24. Persistent Mullerian Duct Syndrome, I & II
26. Sjogren-Larsson Syndrome
27. Spinal Muscular Atrophy, Type III
28. Tay-Sachs Disease
29. Thrombotic Thrombocytopenic Purpura,
   Congenital
30. Trigeminal Neuralgia
31. Weaver Syndrome
GENETIC DISORDERS IN GCC

Total: 550+

Saudi Arabia: 539
Kuwait: 332
Qatar: 141
Bahrain: 115
Oman: 326
UAE: 326

Overlapping cases:
Kuwait and Oman: 18
Kuwait, Oman, and UAE: 18
Disease of faulty synthesis of hemoglobin

**Poly A signal mutation** in alpha 2-globin gene (86.7%), -alpha (3.7 Kb deletion; 10%), alpha-5nt alpha (3.3%; Adekile et al., 1994).

12,220 infants > **prevalence: 28%** in Qatif, 16.3% in Al Hasa (Nasserullah et al., 1998). Hb Setif [alpha 94(G1)Asp----Tyr] (Abdo, 1989).


1,702 nationals > trait in 8% (Fawzi et al., 2003).

**Comorbidity** w/ SCD or dilated cardiomyopathy (Fawzi et al., 2003; El-Menyar et al., 2006).


Most common: **3.7 Kb deletion** (68.6%). Four non-deletional mutations > ~6% of cases: alpha-PA-1, alpha-PA-2, HbCS, alpha-5nt del (El-Kalla and Baysal, 1998). **Poly A-1 mutation** [alpha-PA-1 (AATAAA-AATTAAG)] is most common (47.4%; Baysal, 2001).
GENETIC DISEASE MODES OF INHERITANCE

OMIM: 8,327  Recessive: 51%  Dominant: 47%

CTGA: 1,398  Recessive: 61%  Dominant: 28%
GENETIC DISEASE MODES OF INHERITANCE

KSA: 539 disorders  
AD: 28%  
AR: 62%

UAE: 326 disorders  
AD: 28%  
AR: 63%

OMAN: 326 disorders  
AD: 32%  
AR: 56%

KUWAIT: 332 disorders  
AD: 35%  
AR: 52%

QATAR: 141 disorders  
AD: 42%  
AR: 50%

BAHRAIN: 115 disorders  
AD: 38%  
AR: 44%
GENETIC DISEASE MODES OF INHERITANCE

**KSA**: 539 disorders  
AD: 28%  
AR: 62%

**UAE**: 326 disorders  
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AR: 63%

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AD: 32%  
AR: 56%

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AR: 52%

**QATAR**: 141 disorders  
AD: 42%  
AR: 50%

**BAHRAIN**: 115 disorders  
AD: 38%  
AR: 44%
GENE VARIATION IN ARABS: HBB > IVS-II-1
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• β-thalassemia mutant
• Homozygous state > intermediate phenotype
• Association w/ -588 (A>G) & -158 (C>T)
• XmnI Gγ polymorphisms causing high HbF
Communicable Diseases

Non-Communicable/Genetic Diseases

Healthcare

Molecular Genetics

Clinical Genetics
SIGNIFICANCE OF CTGA
A long-term and multidisciplinary research program that will cover several aspects of genetic diseases in Lebanon.

- Regional distribution of GDs
- Impact of consanguinity as a selective force
- Molecular etiologies and Lebanese Variome
- Database platforms
- Supporting families at-risk through proper genetic counseling methods
Communicable Diseases

Non-Communicable/Genetic Diseases

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