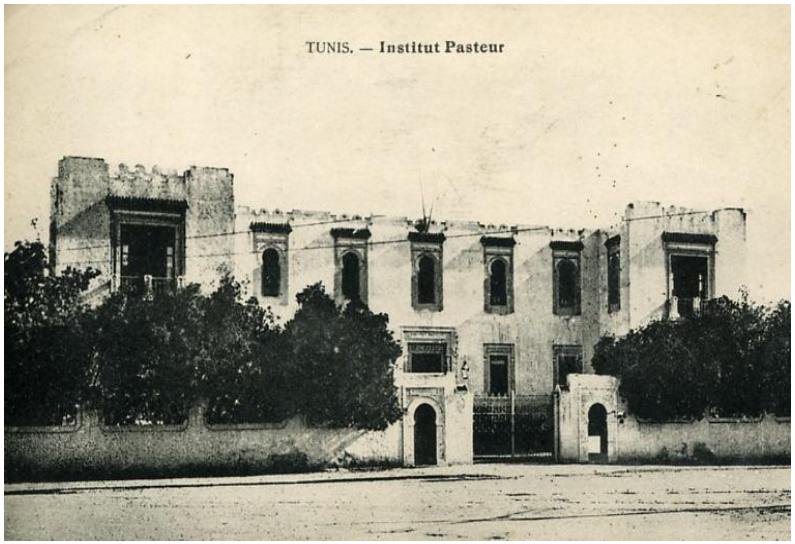
DNA typing for genetic diseases investigation and human identification



1893

2012

Institut Pasteur in Tunis

Rym KEFI
Associate Professor

www.pasteur.tn

Outline

I- Institut Pasteur in Tunis

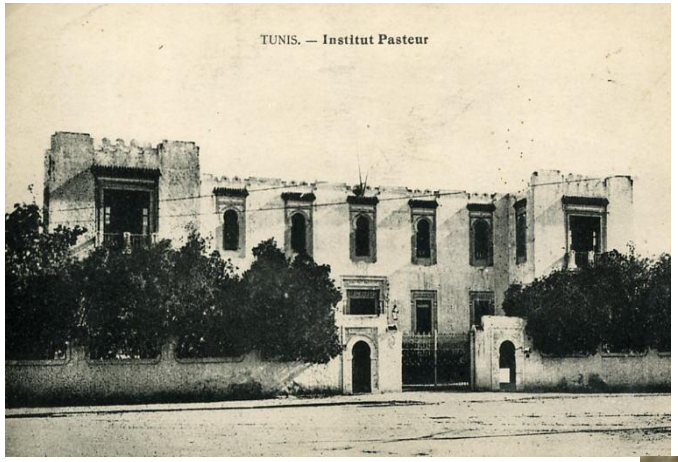
II- Laboratory of Biomedical Genomics and Oncogenetics:

- Molecular investigation of genetic disorders

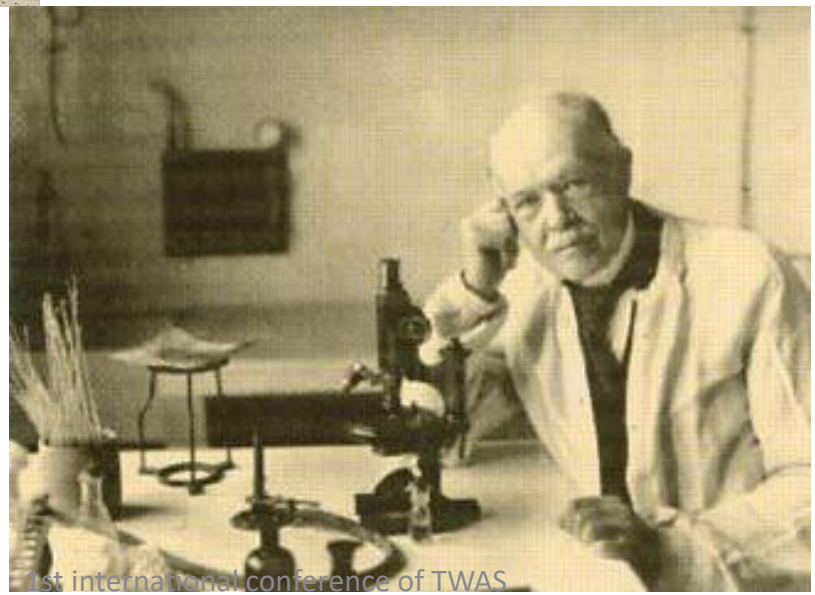
III- Genetic typing core facility

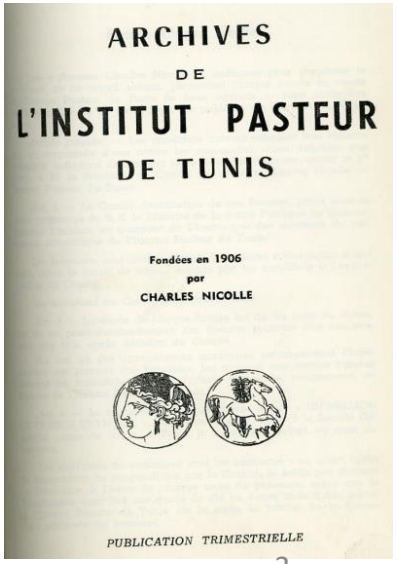
I- Institut Pasteur de Tunis

www.pasteur.tn



- **Founded in 1893 by Adrian Loir**
- **Directed from 1903 to 1936 by Charles Nicolle, Nobel Prize for Medicine in 1928**





Institut Pasteur International Network consists of 33 institutes throughout the world.

Missions of IPT (1)

1- To provide diagnostic services in human and animal pathology

18 laboratories: biochemistry, hormonology, toxicology, hematology, immunology, genetic diseases, cellular pathology and food control

- National and International reference centers in many diseases (Leishmaniasis, Measles, Poliovirus, HPV, Salmonella, Cholera, Rabies, Malaria).

- International Vaccination centre

- Anti-rabies vaccination center

Missions of IPT (2)

2- to product vaccines and therapeutic sera

- BCG
- anti- scorpion
- Anti-rabies

Mission of IPT (3)

3- to conduct research and training in the field of public health

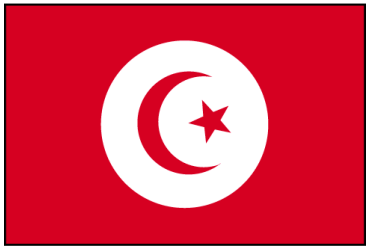
9 research laboratories in IPT

The present research activity focuses mainly on:

- *Epidemiology and* Immunology *of the infectious diseases (leishmanioses, tuberculosis, viral hepatites, rabies, papillomavirus, mycoplasmoses*)

- Molecular investigation in genetic disorders

- *Biotechnologic development (design of new vaccines and molecules therapeutic by the means of genetic engineering).*



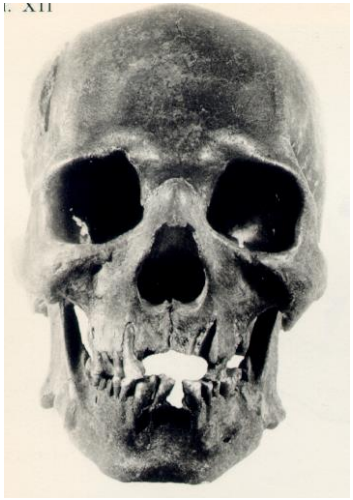
Population: 10, 67 millions (2011)

Tunisia is located at a crossroads of Europe, the Middle East, and sub-Saharan Africa.

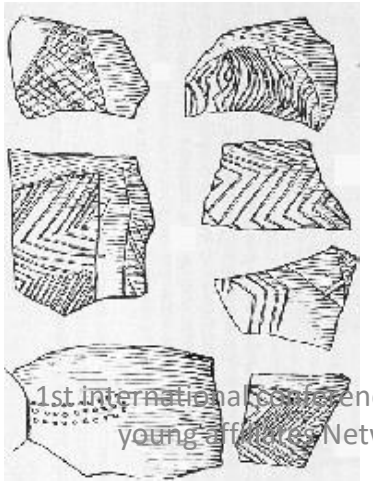
Prehistoric period (40.000 years BP)

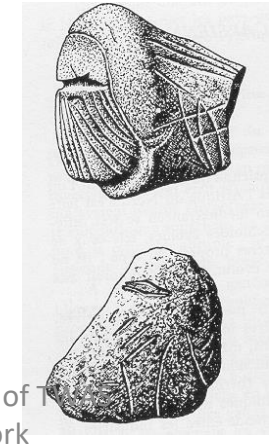
- Aterian civilization

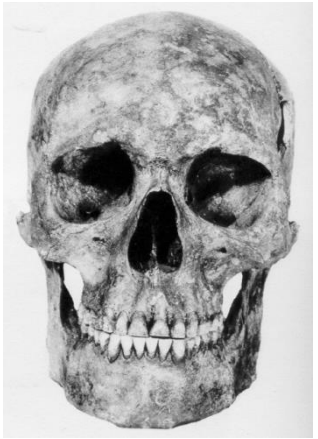
- the Iberomaurusian civilization



- The Capsian civilization







Historic period (3.000 years BP)

- **In the Historic period :** Berbers, called also “Imazighen”, belong to the most ancient group which seems to have Capsians as local ancestors

Along its 3000 years of history, Tunisia was successively under the reign of :

- the Phoenicians (3rd century),
- the Romans (starting from 154),
- the Vandals (beginning 6th)
- the Byzantine
- the Arab conquest (7th century)

Roman temple

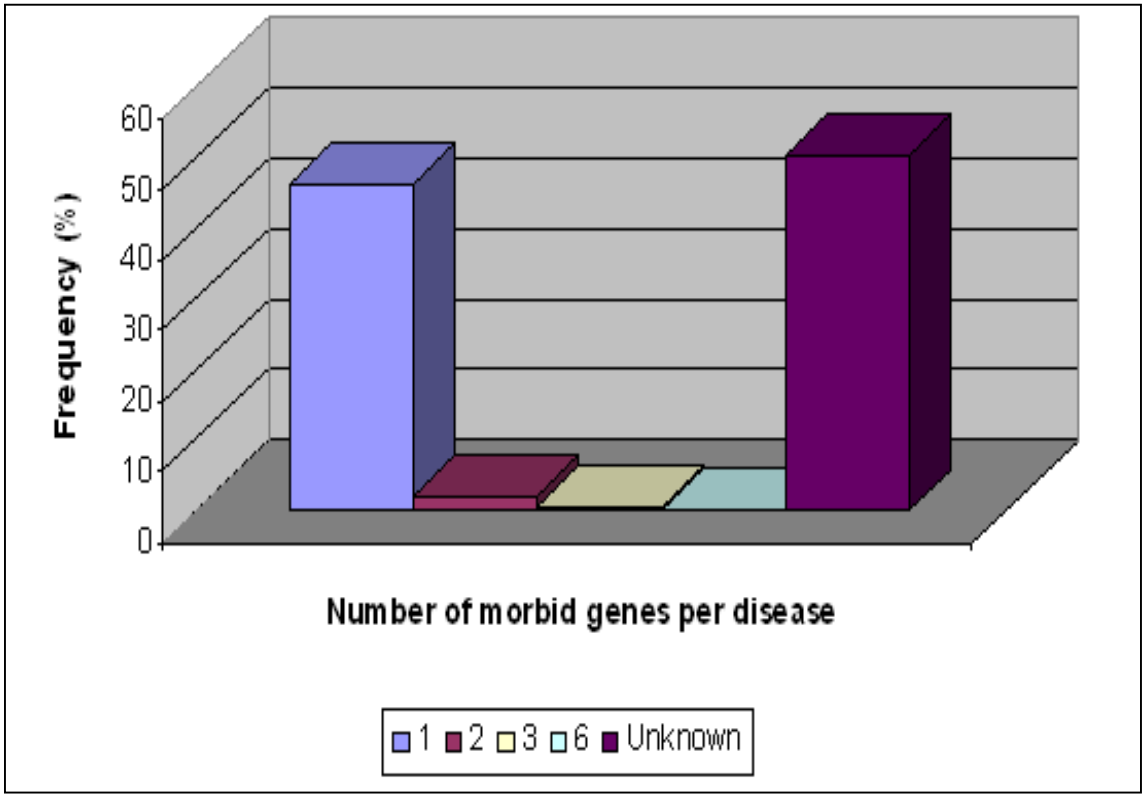
Currently Tunisia is witnessing an epidemiological transition.

- an improvement in the control of some infectious diseases
- decrease of child and maternal mortality.

- challenged by the increase of monogenic diseases

More than **340 genetic** diseases

For >50% the molecular basis is still unknown!



Romdhane and Abdelhak, Am. J Med. Genet. 2011.

+

T2diabetes 10 to 12 %

Metabolic syndrome 30%

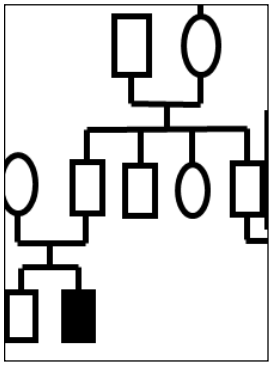
Fkih et al, 2013
IDF Atlas diabetes 2016
WHO reports

(1) Investigation of genetic disorders

Objectives

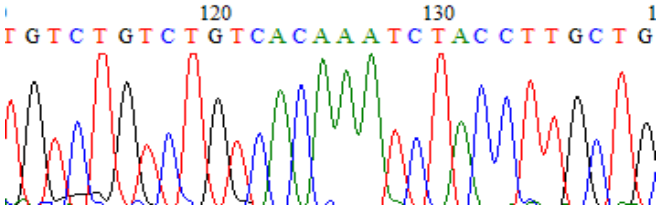
- Identification of mutations causing genetic disorders
- Development of simple molecular tools for the diagnosis of genetic diseases

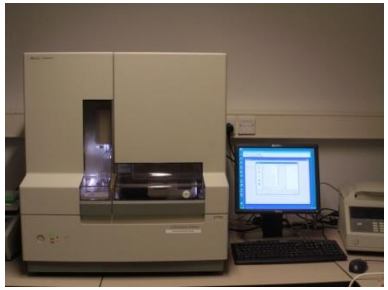
Strategy :

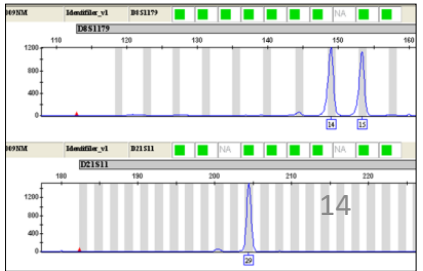


- Collection of clinical and genealogical data
- Collection of biological material

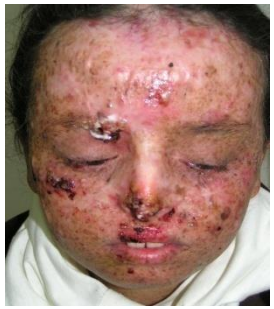
- Sequencing (classic or NGS)



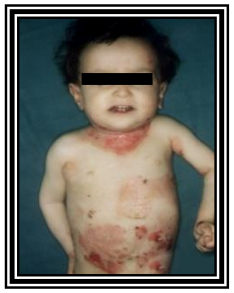




- Metabolic disorders:
  - *Glycogenosis: G6PC*
  - *Gaucher: GBA*
  - *Wilson: ATP7B*
- *Renal diseases:*
  - Distal renal tubular acidosis: ATP6V1B1, ATP6V0A4



- Genodermatosis and DNA repair diseases
  - *Xeroderma pigmentosum: XPA, XPC, POLH*
  - *Fanconi Anemia: FANCA*
  - *EBD: COL7A1*



- Neurosensory disorders.
  - Hereditary hearing loss: *GJB2, GJB6*

(2) Investigation of mutifactorial diseases

Objective:

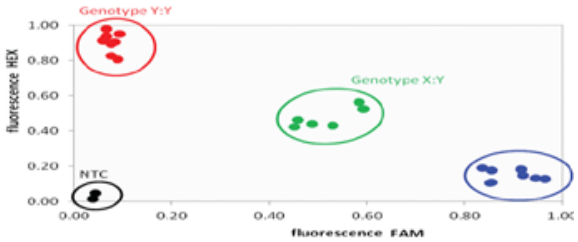
the genetic characterization of T2D and metabolic syndrome in the Tunisian and North African populations .

Strategy

340 patients

345 controls

Collection of clinical and genealogical data and biological material



Genotyping of SNP

Comparison of the allelic and genotype distribution between patients and controls using statistical tools.

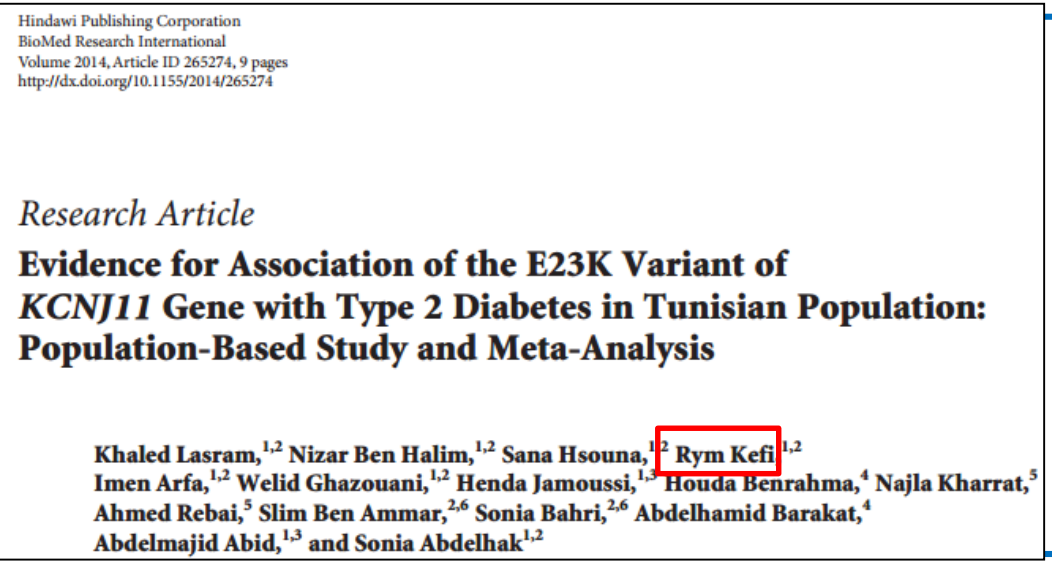
Results

- Variants in the KCNJ11 (ATP-sensitive potassium) gene and IGF2BP2 (Insulin Like Growth Factor 2 mRNA Binding Protein 2) increase the risk of T2D in Tunisia and Mauritania
  Risk factor from 2 to 3.6 .

- New candidate genes for MetS in the Tunisian population such as *FTO* (fat mass and obesity-associated gene)

- The genetic basis of this syndrome is depend on gender and geaographic origin

- Our study emphasizes the role of *APOA5* variants in the regulation of the triglycerides blood levels

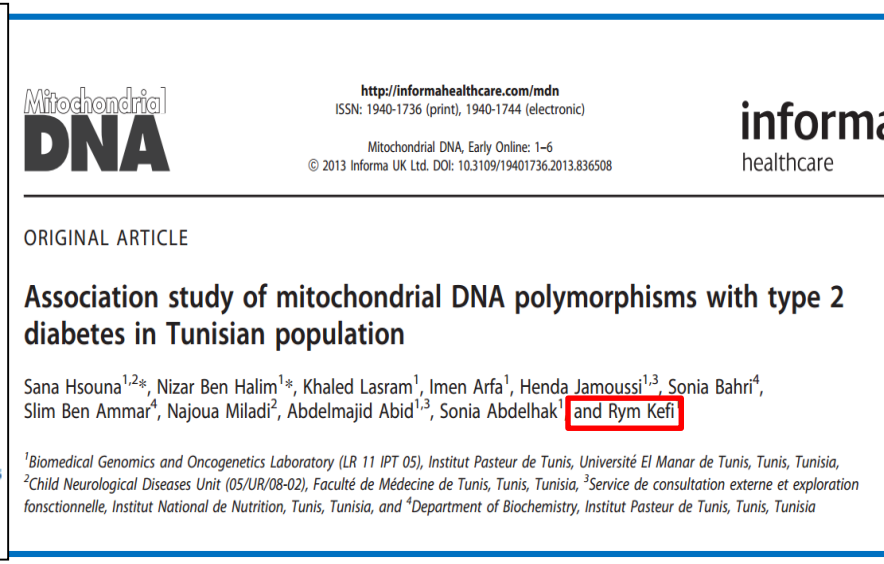


Hindawi Publishing Corporation
BioMed Research International
Volume 2014, Article ID 265274, 9 pages
http://dx.doi.org/10.1155/2014/265274

Research Article

Evidence for Association of the E23K Variant of *KCNJ11* Gene with Type 2 Diabetes in Tunisian Population: Population-Based Study and Meta-Analysis

Khaled Lasram,[1,2] Nizar Ben Halim,[1,2] Sana Hsouna,[1,2] Rym Kefi,[1,2] Imen Arfa,[1,2] Welid Ghazouani,[1,2] Henda Jamoussi,[1,3] Houda Benrahma,[4] Najla Kharrat,[5] Ahmed Rebai,[5] Slim Ben Ammar,[2,6] Sonia Bahri,[2,6] Abdelhamid Barakat,[4] Abdelmajid Abid,[1,3] and Sonia Abdelhak[1,2]



Mitochondrial DNA

http://informahealthcare.com/mdn
ISSN: 1940-1736 (print), 1940-1744 (electronic)
Mitochondrial DNA, Early Online: 1–6

DOI: 10.3109/19401736.2013.836508

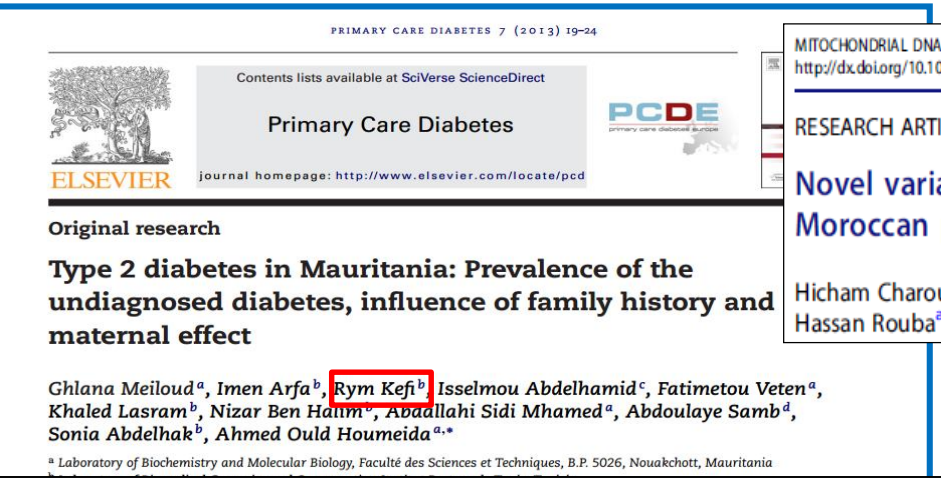
informa healthcare

ORIGINAL ARTICLE

Association study of mitochondrial DNA polymorphisms with type 2 diabetes in Tunisian population

Sana Hsouna[1,2]*, Nizar Ben Halim[1]*, Khaled Lasram[1], Imen Arfa[1], Henda Jamoussi[1,3], Sonia Bahri[4], Slim Ben Ammar[4], Najoua Miladi[2], Abdelmajid Abid[1,3], Sonia Abdelhak[1] and Rym Kefi

[1]Biomedical Genomics and Oncogenetics Laboratory (LR 11 IPT 05), Institut Pasteur de Tunis, Université El Manar de Tunis, Tunis, Tunisia, [2]Child Neurological Diseases Unit (05/UR/08-02), Faculté de Médecine de Tunis, Tunis, Tunisia, [3]Service de consultation externe et exploration fonsctionnelle, Institut National de Nutrition, Tunis, Tunisia, and [4]Department of Biochemistry, Institut Pasteur de Tunis, Tunis, Tunisia



PRIMARY CARE DIABETES 7 (2013) 19–24

ELSEVIER

Contents lists available at SciVerse ScienceDirect

Primary Care Diabetes

journal homepage: http://www.elsevier.com/locate/pcd

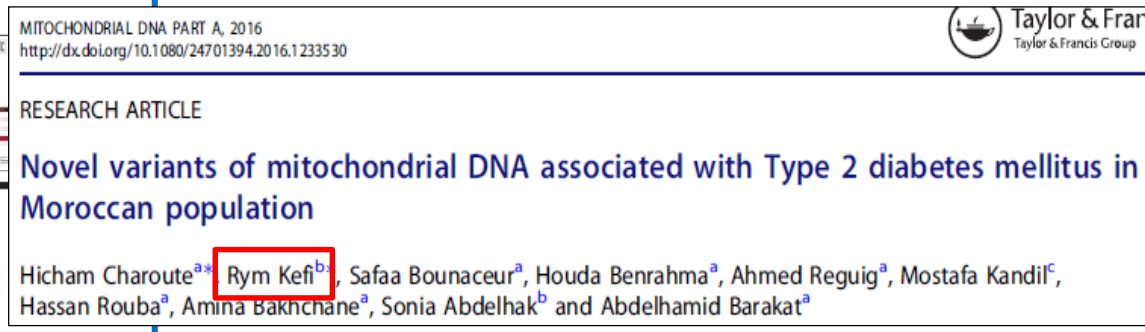
PCDE

Original research

Type 2 diabetes in Mauritania: Prevalence of the undiagnosed diabetes, influence of family history and maternal effect

Ghlana Meiloud[a], *Imen Arfa*[b], *Rym Kefi*[b], *Isselmou Abdelhamid*[c], *Fatimetou Veten*[a], *Khaled Lasram*[b], *Nizar Ben Halim*[b], *Abdallahi Sidi Mhamed*[a], *Abdoulaye Samb*[d], *Sonia Abdelhak*[b], *Ahmed Ould Houmeida*[a,*]

[a] *Laboratory of Biochemistry and Molecular Biology, Faculté des Sciences et Techniques, B.P. 5026, Nouakchott, Mauritania*



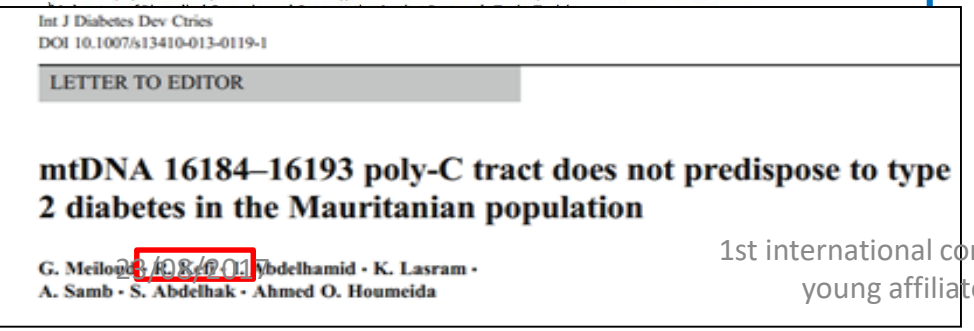
MITOCHONDRIAL DNA PART A, 2016
http://dx.doi.org/10.1080/24701394.2016.1233530

Taylor & Francis Group

RESEARCH ARTICLE

Novel variants of mitochondrial DNA associated with Type 2 diabetes mellitus in Moroccan population

Hicham Charoute[a]*, Rym Kefi[b]*, Safaa Bounaceur[a], Houda Benrahma[a], Ahmed Reguig[a], Mostafa Kandil[c], Hassan Rouba[a], Amina Bakhchane[a], Sonia Abdelhak[b] and Abdelhamid Barakat[a]

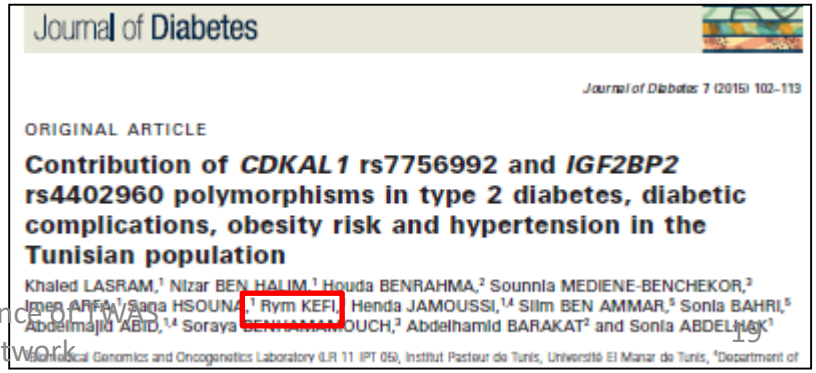


Int J Diabetes Dev Ctries
DOI 10.1007/s13410-013-0119-1

LETTER TO EDITOR

mtDNA 16184–16193 poly-C tract does not predispose to type 2 diabetes in the Mauritanian population

G. Meiloud · I. Arfa · Y. Abdelhamid · K. Lasram · A. Samb · S. Abdelhak · Ahmed O. Houmeida



Journal of Diabetes

Journal of Diabetes 7 (2015) 102–113

ORIGINAL ARTICLE

Contribution of *CDKAL1* rs7756992 and *IGF2BP2* rs4402960 polymorphisms in type 2 diabetes, diabetic complications, obesity risk and hypertension in the Tunisian population

Khaled LASRAM,[1] Nizar BEN HALIM,[1] Houda BENRAHMA,[2] Sounnia MEDIENE-BENCHEKOR,[3] Imen ARFA,[1] Sana HSOUNA,[1] Rym KEFI,[1] Henda JAMOUSSI,[1,4] Slim BEN AMMAR,[5] Sonia BAHRI,[5] Abdelmajid ABID,[1,4] Soraya [illegible],[3] Abdelhamid BARAKAT[2] and Sonia ABDELHAK[1]

[1]Biomedical Genomics and Oncogenetics Laboratory (LR 11 IPT 05), Institut Pasteur de Tunis, Université El Manar de Tunis, [4]Department of

METABOLIC SYNDROME AND RELATED DISORDERS
Volume 14, Number 2, 2016
Mary Ann Liebert, Inc.
pp. 1–8
DOI: 10.1089/met.2015.0090

ORIGINAL ARTICLE

Association of rs9939609 Polymorphism with Metabolic Parameters and *FTO* Risk Haplotype Among Tunisian Metabolic Syndrome

Sahar Elouej, PhD,[1,2,*] Hanen Belfki-Benali, PhD,[3] Majdi Nagara, PhD,[1,2,*] Khaled Lasram, PhD,[1,2] Redha Attaoua, PhD,[4,*] Om Kalthoum Sallem, MD,[1,5,*] Ines Kamoun, MD,[6,*] Mariem Chargui, MS,[1,*] Lilia Romdhane, PhD,[1] Henda Jamoussi, MD,[1,5,*] Zinet Turki, MD,[6,*] Abdelmajid Abid, MD,[1,5,*] Claude Ben Slama, MD,[6,*] Sonia Bahri, MD,[2,7] Sonia Abdelhak, PhD,[1,2,*] Florin Grigorescu, MD,[4,*] Habiba Ben Romdhane, MD,[3] and Rym Kefi, PhD[1,2,*]

Journal of Diabetes and its Complications 30 (2016) 206–211

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Association of genetic variants in the *FTO* gene with metabolic syndrome: A case-control study in the Tunisian population

Sahar Elouej [a,f,1], Majdi Nagara [a,f,1], Redha Attaoua [b,1], Om Kalthoum Sallem [a,c,1], Ins
Sana Hsouna [a,f,1], Khaled Lasram [a,f], Nizar Ben Halim [a,f], Mariem Chargui [a,1], Henda J
Zinet Turki [d,1], Ines Kamoun [d,1], Hanen Belfki-Benali [g], Abdelmajid Abid [a,c,1], Claude
Sonia Bahri [e,f], Dalenda Triki [h], Habiba Ben Romdhane [g,1], Sonia Abdelhak [a,f,1],
Rym Kefi [a,*,1], Florin Grigorescu [b,1]

Annales d'Endocrinologie

Volume 78, Issue 3, July 2017, Pages 146-155

Original article

Association of *apolipoprotein A5* gene variants with metabolic syndrome in Tunisian population

Étude d'association du gène *APOA5* au syndrome métabolique et à ses composantes dans la population tunisienne

Rym Kefi [a, b, 1], Meriem Hechmi [a, 1], Hamza Dallali [a, c, 1], Sahar Elouej [d, 1], Haifa Jmel [a, c, 1], Yossra Ben Halima [a, b, 1], Majdi Nagara [d, 1], Mariem Chargui [a, b, 1], Sihem Ben Fadhel [a], Safa Romdhane [a], Ines Kamoun [e, 1], Zinet Turki [e, 1], Abdelmajid Abid [a, e, 1], Sonia Bahri [f, 1], Afaf Bahlous [f, 1], Ramon Gomis [g, 1], Abdelhamid Baraket [h, 1], Florin Grigorescu [i, 1] ... Sonia Abdelhak [a, b, 1]

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Gender-specific associations of genetic variants with metabolic syndrome components in the Tunisian population

Sahar Elouej[a,b,†], Insaf Rejeb[a,b,†], Redha Attaoua[c,†], Majdi Nagara[a,b,†], Om Kalthoum Sallem[a,d,†], Ines Kamoun[e,†], Mariem Chargui[a,†], Henda Jamoussi[a,d,†], Zinet Turki[e,†], Abdelmajid Abid[a,d,†], Claude Ben Slama[e,†], Sonia Bahri[b,f], Habiba Ben Romdhane[g,†], Sonia Abdelhak[a,b,†], Rym Kefi[a,b,†], and Florin Grigorescu[c,†]

Regional collaborations

New Partnership for Africa's Development (NEPAD)
North Africa Biosciences Network (NABNet)
http://www.nrc.sci.eg/nepad/default.html

"Multidisciplinary investigation of the genetic risk factors of type II Diabetes and its complications in North Africa"

2008-2011

International collaboration

Identification: MEDIGENE – FP7-279171-1

Title: Genetic and environmental factors of insulin resistance syndrome and its long-term complications in immigrant Mediterranean populations

Duration: 56 months (January 2012-2016)

Countries: France, Italy, Spain, Turkey, Albania, Russia, Romania, Tunisia, Algeria, Morocco, Finland and Hungary

New project

Acronym: DiaBiomark

Title: Identification of biomarkers for Type 2 Diabetes through multidisciplinary investigations

Start: January 2018

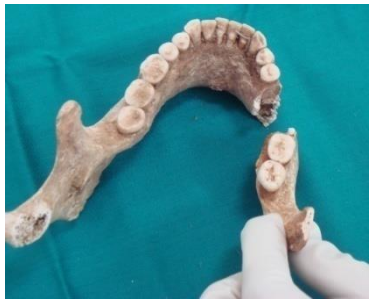
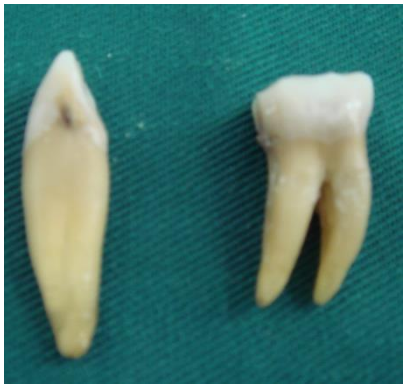
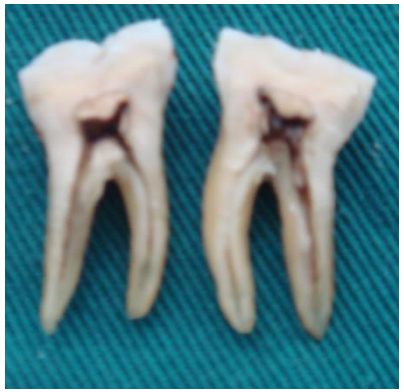
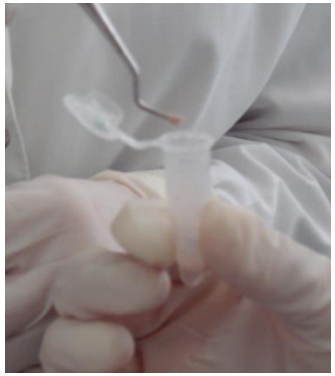
Genetic typing core facility

DNA typing (genetic profiling or genetic fingerprinting) is used :

- Paternity test
- to confirm the identity of living persons.
- To resolve criminal cases
- To identify victims of terrorist attacks both in Tunisia and Lybia

Human Identification in forensic

We have developed a rapid and effective molecular protocol for human body identification in forensic using dental pulp.

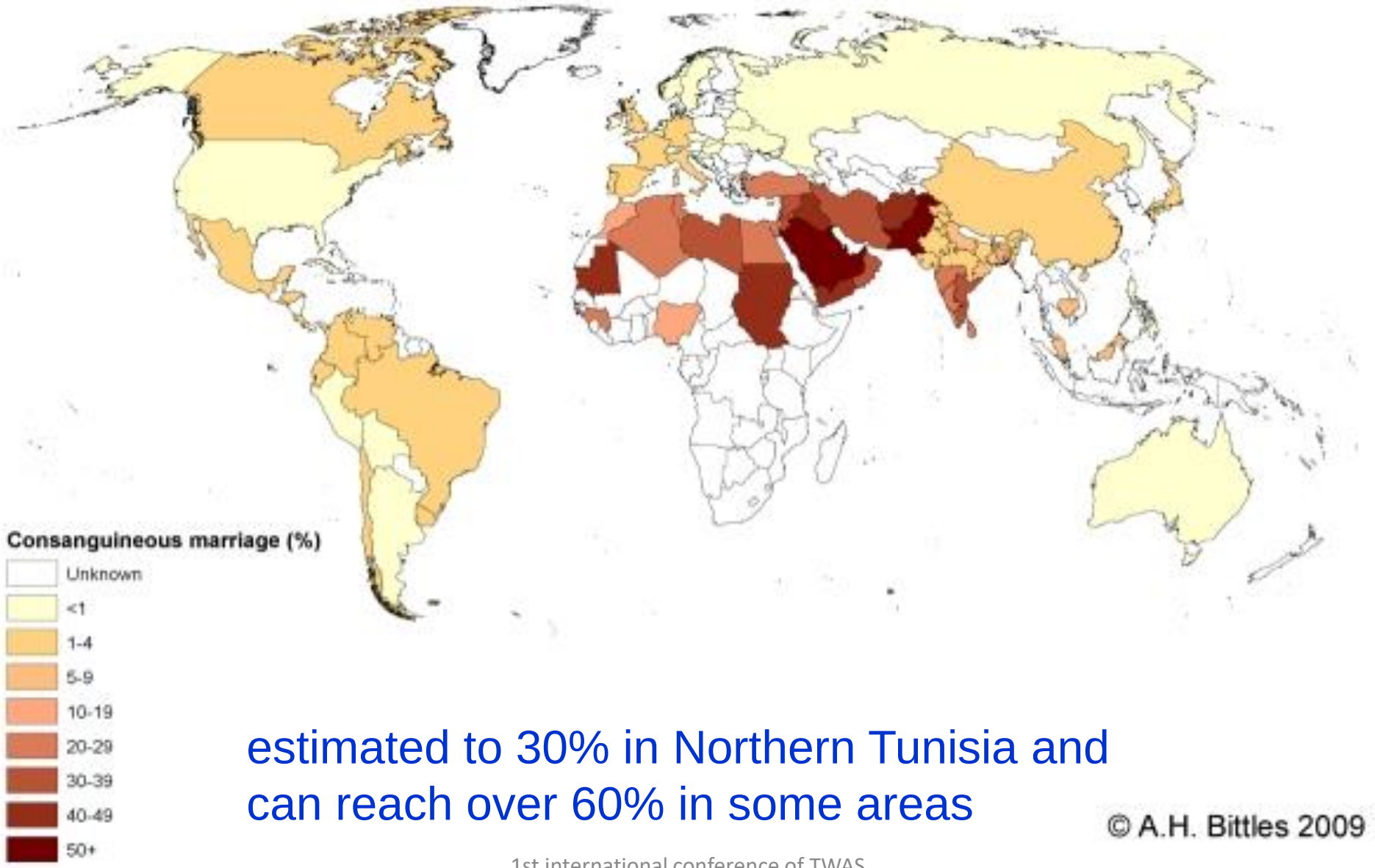





This protocol provides a sufficient quantity and a good quality of DNA to establish a genetic profile of victims.

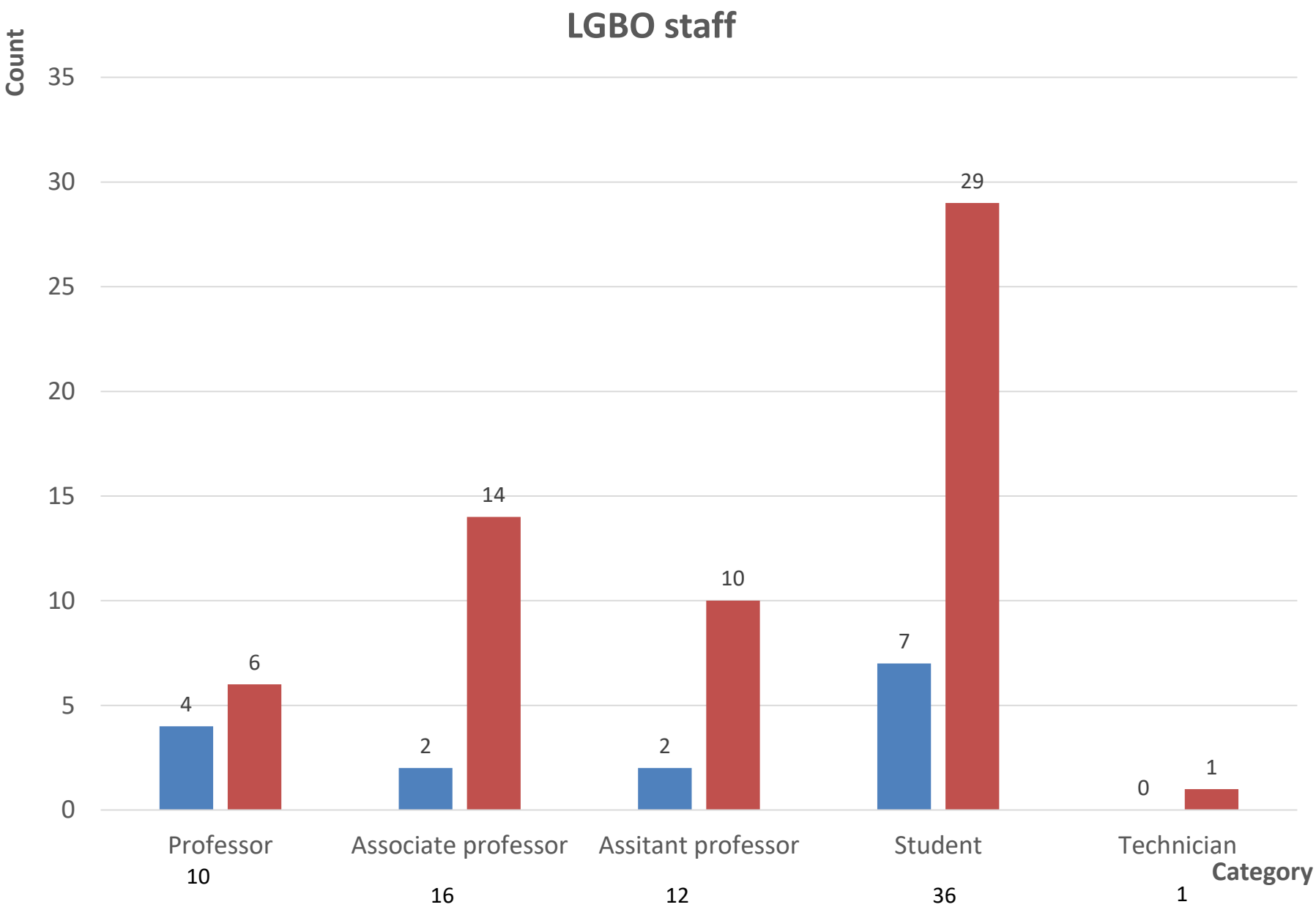
rym.kefi@pasteur.rns.tn

kefi_rym@yahoo.fr

➢High level of consanguineous marriages



estimated to 30% in Northern Tunisia and can reach over 60% in some areas


LGBO staff
Count
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Professor
Associate professor
Assitant professor
Student
Technician
Category
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16
12
36
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Men
Women