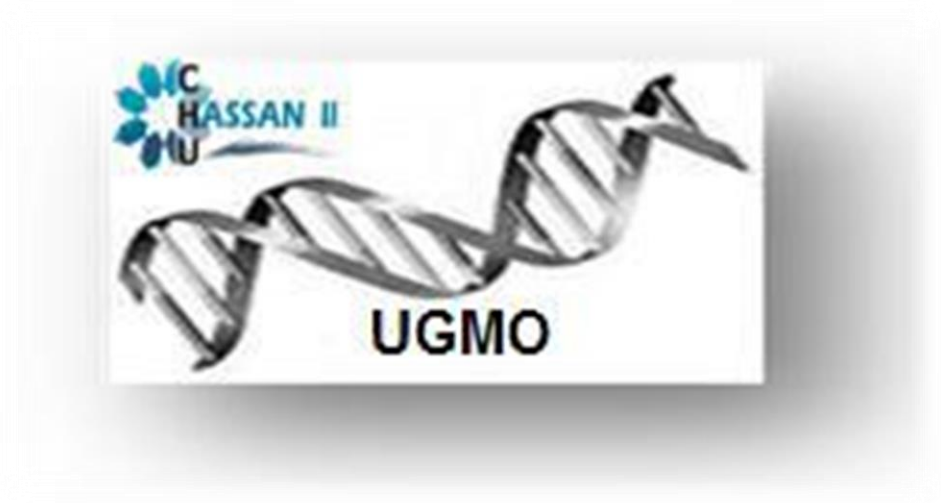
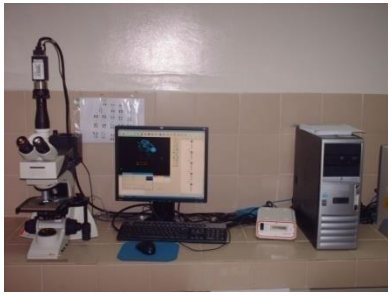
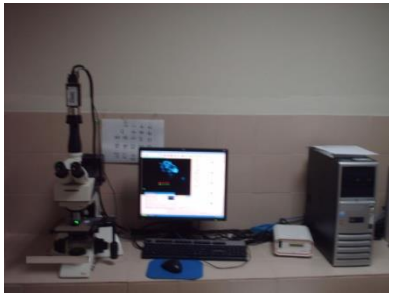
Central Medical Analysis Laboratory

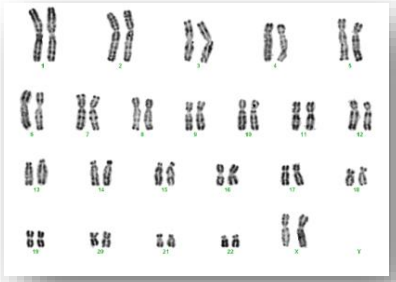
MEDICAL GENETICS AND ONCOGENETICS UNIT-CHU HASSAN II-FES

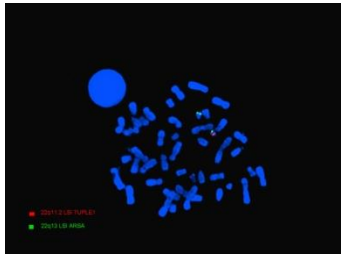


South-North and South-South collaborations in medical genomic research in Africa





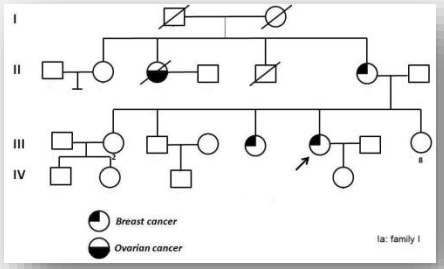




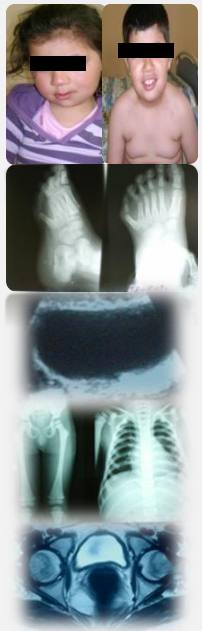
Medical Genetics and *oncogenetics CHU Hassan II-Fez*

Clinical Genetics

Genetic consuling

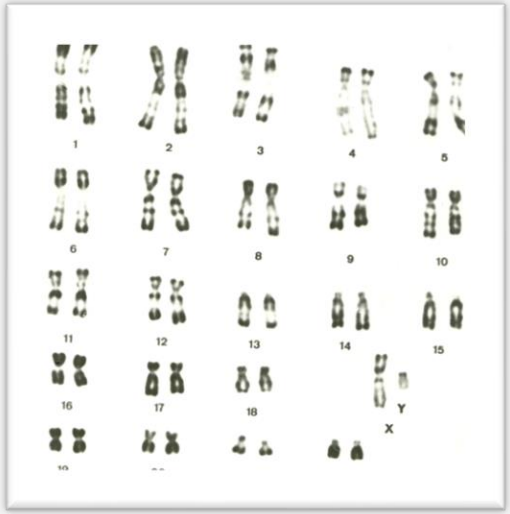


Clinical Diagnosis

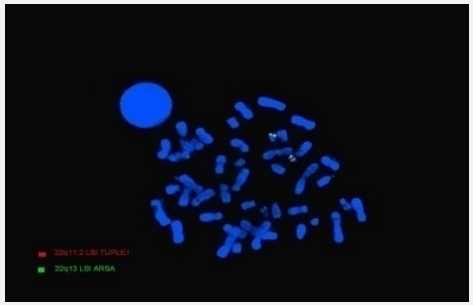


Cytogenetics

Karyotype

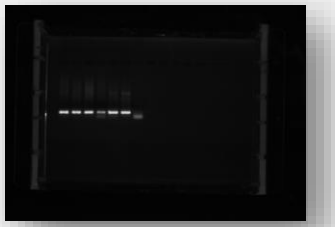


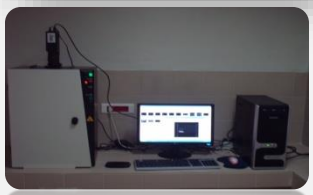
Molecular Cytogenetics



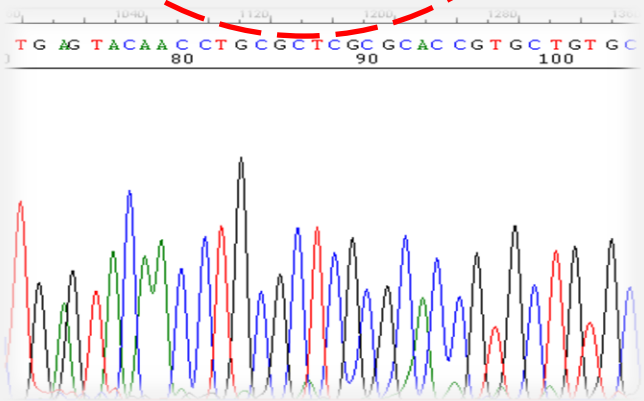
Molecular diagnosis

PCR



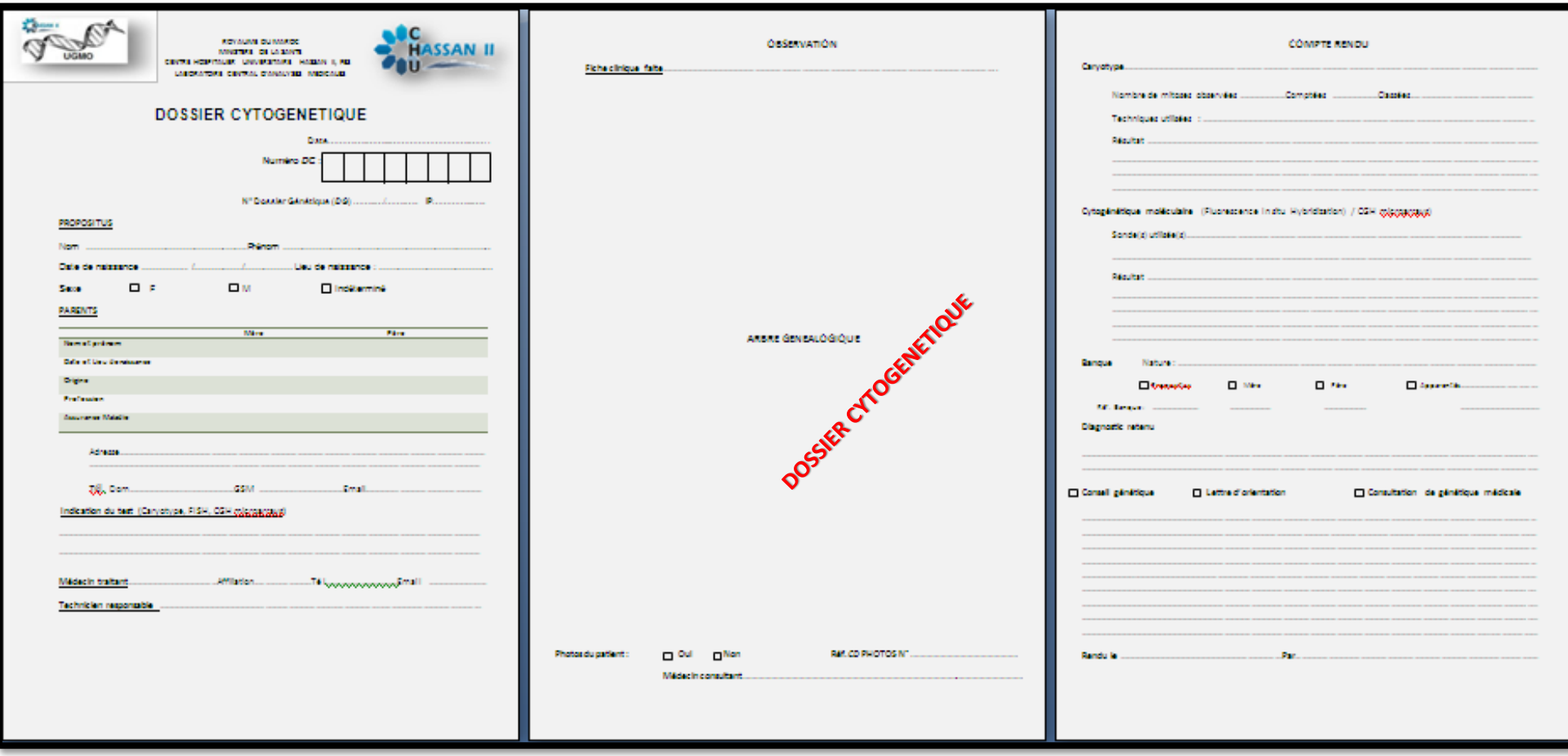


Sequence analysis



- The staff includes:
  - 3 Biologists,
  - 7 residents in training
- Drains all of northeastern Morocco.

Medical genetics consultation



INDICATION → **Genetic exploration**

**** Constitutional postnatal karyotype**

**** Oncohematology karyotype**

**** Post natal FISH:**

- 22q11 microdeletion syndrome
- Williams syndrome
- Wolf hirschhorn syndrome
- Prader willi syndrome
- Angelmann syndrome
- Sotos syndrome
- Miller-diecker syndrome
- Smith magenis syndrome
- Rubinstein taybi syndrome
- CEPX / SRY probe

**** FISH oncohematology:**

- BCR-ABL probe
- CSF1R / D5S23 / D5S21 probe: exploration of chromosome 5
- D7S522 / CEP7 probe: exploration of chromosome 7
- TP53 / CEP17 probe
- MLL break apart probe

** Antenatal FISH

- Screening for the main aneuploidies: 13, 18,21, X, Y

Molecular biology tests

- SRY gene analysis (Pcr multiplex and sequencing)
- AZF region deletion in male infertility
- Search for the V617F mutation of the JAK2 gene, sequencing of exon 12
- Search for the deletion of exon 7 of the SMN gene
- Search for the 525delT mutation in the LGMD2C gene
- Search for major mutations in the MEFV gene (exons 2.10)
- NEM type 2, search for mutations in the RET gene (exons 10 and 11)
- Testing for the 35delG mutation of Connexin 26
- Search for mutations in exon 10 of the CFTR gene
- Search for the c.1601G> A mutation in Leiden Factor V
- Sequencing of exon 9 of the CALR gene
- Thrombophile by G20210 mutation of the prothrombin gene

Molecular biology tests

- Molecular study of the PTPN1 gene in noonan syndrome
- Search for major mutations in familial hypercholesterolemia
- Search for major mutations in the MYH gene
- Search for the c.1643_1644delTG mutation of the XP gene
- Study of deletions of the dystrophin gene in duchenne myopathy
- Search for G380R and N540K mutations of the FGFR3 gene (Achondroplasia / Hypochondroplasia)
- Search for recurrent mutations in the HF2 gene Hemochromatosis
- Search for recurrent mutations in the G6PC Glycogenosis type Ia
- Search for the c.144delC mutation of the AURKC gene
- Search for the c.3233C> G mutation of the IDUA gene (howling)
- Sanfilippo disease Search for recurrent mutations in the HGSNAT gene

Molecular biology tests

- Distal renal tubular acidosis with deafness by sequencing of exon 12 of the ATP6V1B1 gene
- Search for deletions of the NPHP1 gene in nephronophthisis
- Tubulointerstitial nephropathies associated with the UMOD gene
- Molecular diagnosis of hyperoxaluria by study of the AGXT gene
- Analysis of the NPHS2 gene in patients with Corticosteroid-Resistant Nephrotic Syndrome
- Monogenic diabetes (mody2)
- Monogenic diabetes (mody2 and mody5)
- Study of the MECP2 gene in RETT syndrome
- Methyl PCR Angelman / Prader-Willi X fragile
- Search for major mutations in the HBB gene (beta thalassemia, sickle cell disease and hemoglobinosis C)
- Multiplex RT-PCR of bcr-abl transcripts
- Real-time quantitative PCR (RQ-PCR) residual disease
- Search for resistance mutations to tyrosine kinase inhibitors
- Search for the recurrent m.3243A> G mutation in mitochondrial diseases

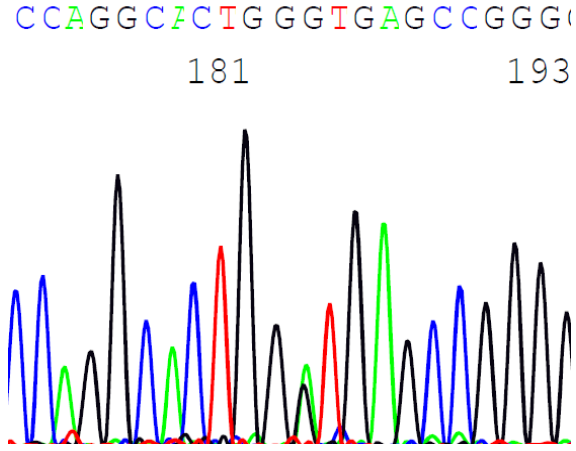
Molecular biology tests

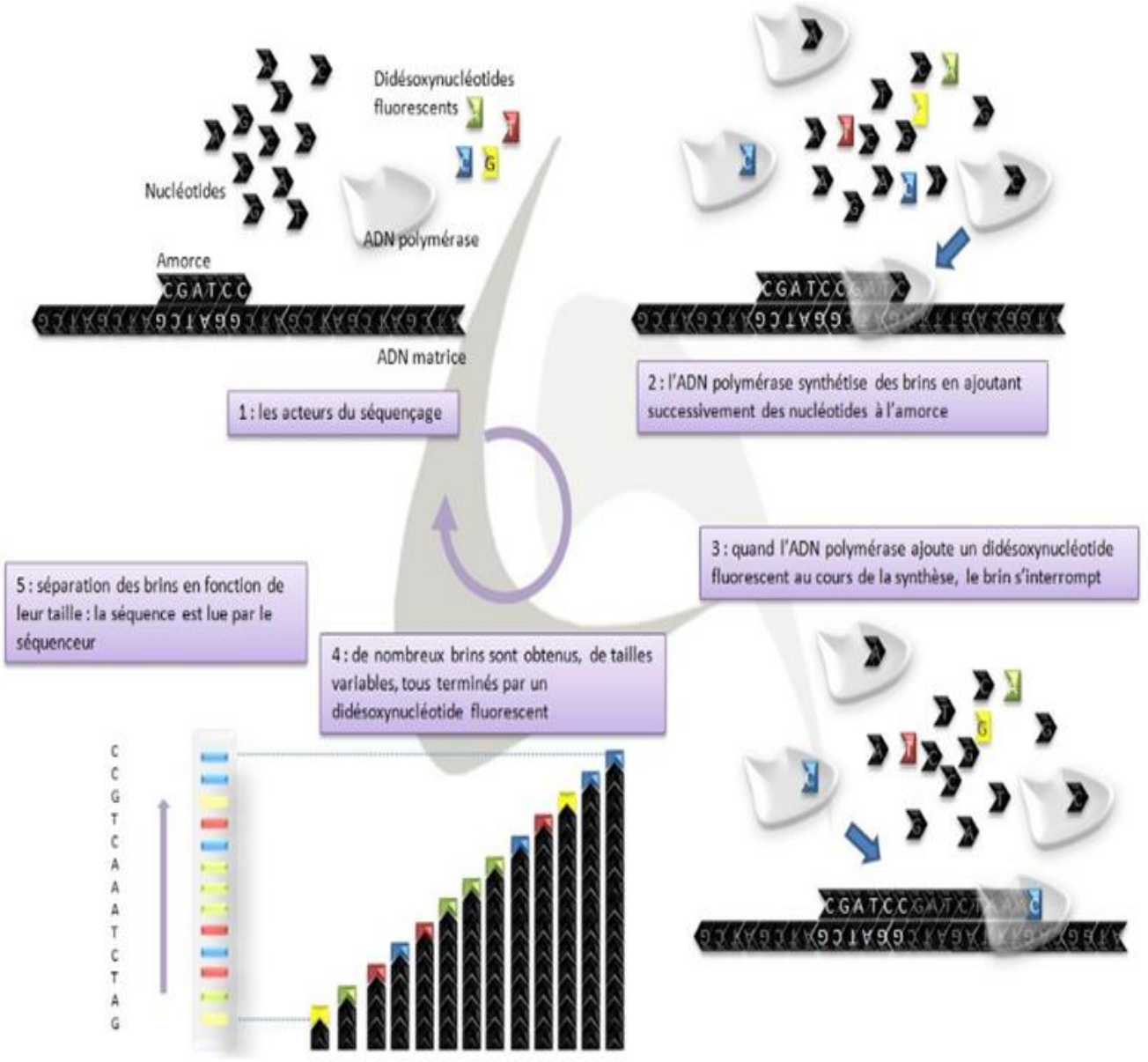
- Oncogenetic : tests for targeted therapy
  - ✓Full ras mutation for colorectal cancer
  - ✓CKIT and PDGFR mutation in GIST
  - ✓EGFR mutation in metastatic lung cancer

Molecular biology tests

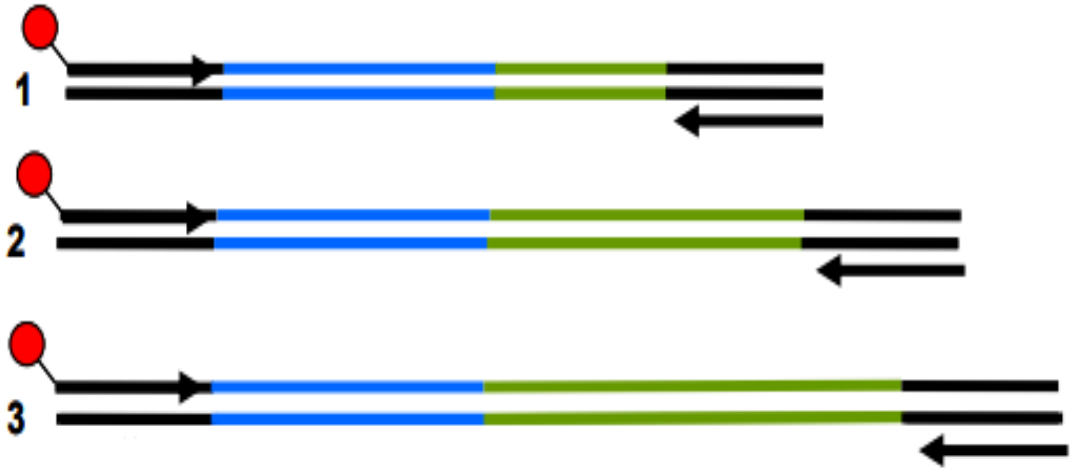
- Pharmacogenetics :
  - Polymorphisms of the VKORC1 gene
  - Polymorphisms of the TPMT gene
  - Polymorphisms of cytochrome P450 2C19
  - Polymorphism of the DPYD gene

sequencing

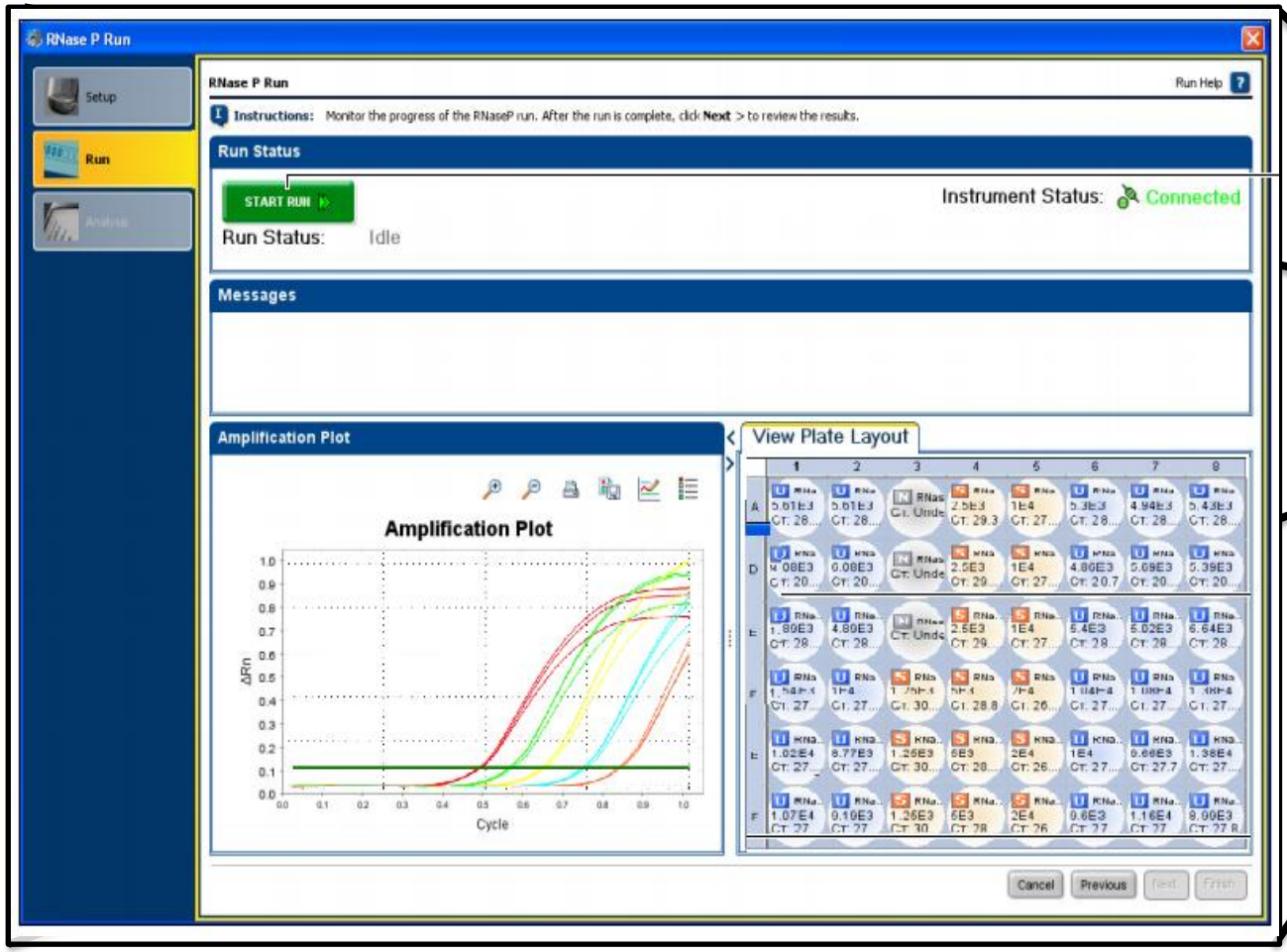

CCAGGCACTGGGTGAGCCGGG
181
193


Didésoxynucléotides fluorescents
Nucléotides
ADN polymérase
Amorce
CGATCC
ADN matrice
1 : les acteurs du séquençage
2 : l'ADN polymérase synthétise des brins en ajoutant successivement des nucléotides à l'amorce
3 : quand l'ADN polymérase ajoute un didésoxynucléotide fluorescent au cours de la synthèse, le brin s'interrompt
4 : de nombreux brins sont obtenus, de tailles variables, tous terminés par un didésoxynucléotide fluorescent
5 : séparation des brins en fonction de leur taille : la séquence est lue par le séquenceur
C C G T C A A T C T A G

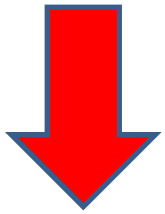
MLPA



ABI3500Dx (Applied Biosystems)


RNase P Run
Setup
Run
Analysis
RNase P Run
Run Help
Instructions: Monitor the progress of the RNaseP run. After the run is complete, click Next > to review the results.
Run Status
START RUN
Instrument Status: Connected
Run Status: Idle
Messages
Amplification Plot
Amplification Plot
ΔRn
Cycle
View Plate Layout
Cancel
Previous
Next
Finish

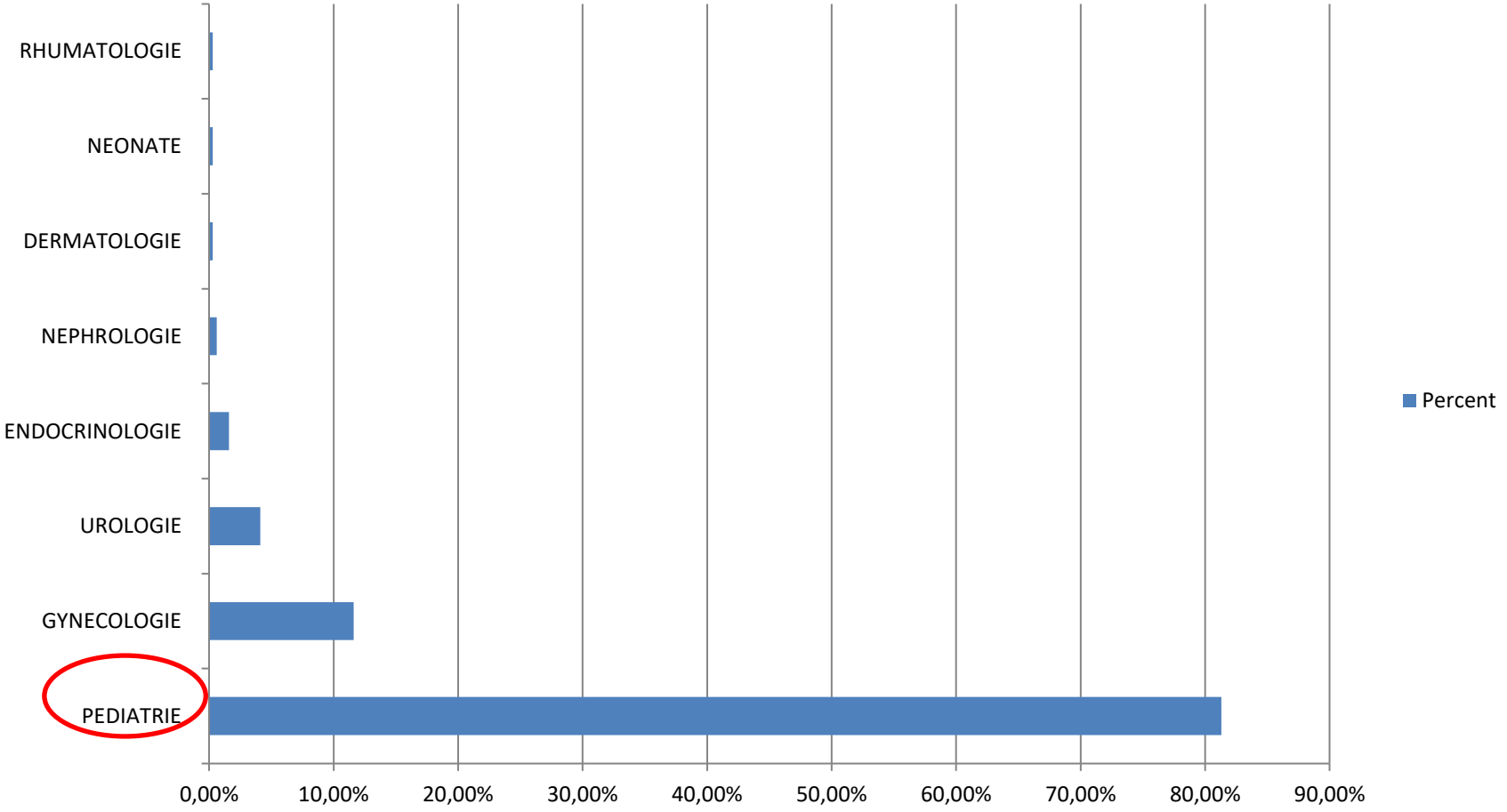
INDICATION : Cytogenetic exploration or molecular biology



6950 Cytogénétic tests

4680 Molecular biology tests

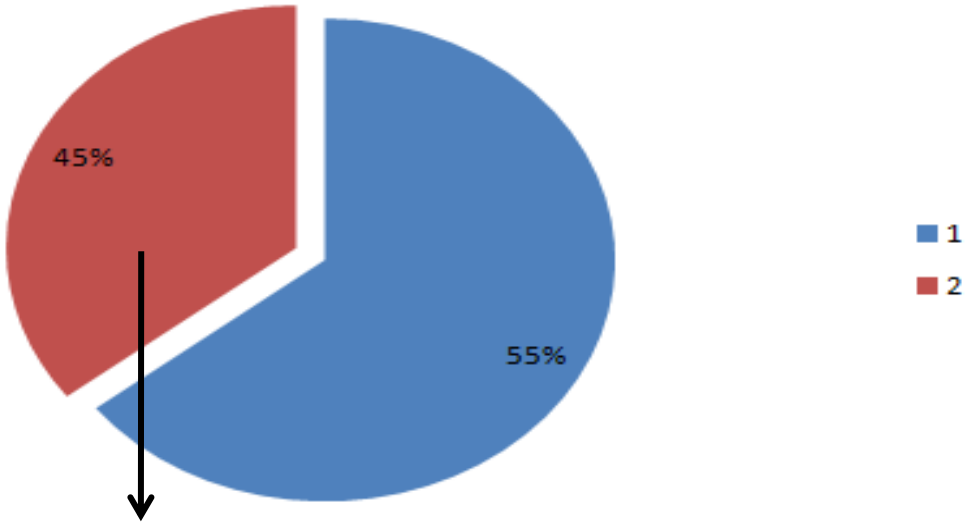
Résultats : Service référant



Consanguinité

NON Consanguineous marriages	77 %
Consanguinity	23%

Perspectives



- **Clinic, radiology ...**
- **Other exploration :**
  - CGH micro-arrays
  - Metabolic studies
  - **Next generation sequencing**

Accurate diagnosis | **adapted health care** | **Genetic counseling**

- master's and PhD thesis
- Project :

- Relationship between obesity and nutritional factors and risk of colorectal cancer as a function of BRAF status. Case control study.

  Project funded by MOFFIT center

  PI: Prof. BOUGUENOUCH Laila

- Classical and molecular cytogenetics of hematologic malignancies

  Project funded by the Faculty of Medicine and Pharmacy of Fez

  PI: Pr. EL AZAMI EL IDRISSI Mohammed , Pr. OULDIM Karim, Pr BOUGUENOUCH Laila

- Kras mutations and nutrition

  Project funded by MOFFIT center

  PI: Prof. OULDIM Karim, Prof. BOUGUENOUCH Laila

- Determinants of breast cancer in Morocco

  Project led by The International Agency for Research on Cancer (IARC), Lyon, France

- Molecular mechanisms of resistance to tyrosine kinase inhibitors

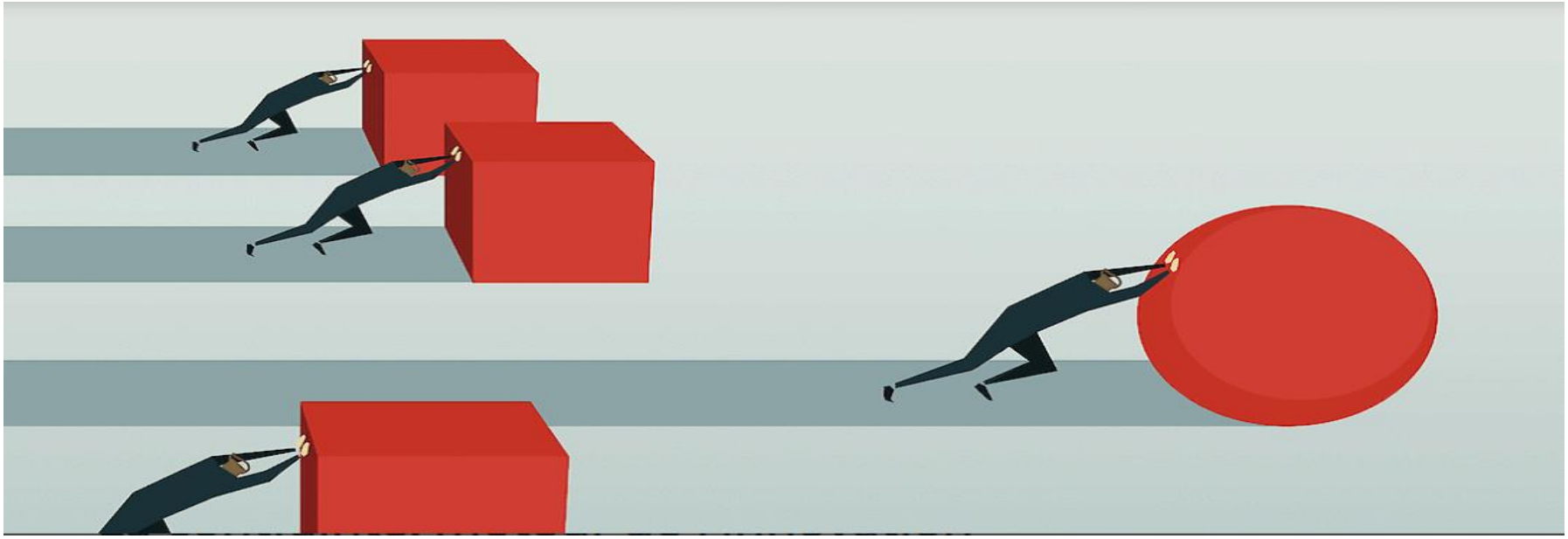
  PI: Pr. EL AZAMI EL IDRISSI Mohammed , Pr BOUGUENOUCH Laila

  Project funded by cancer research institute

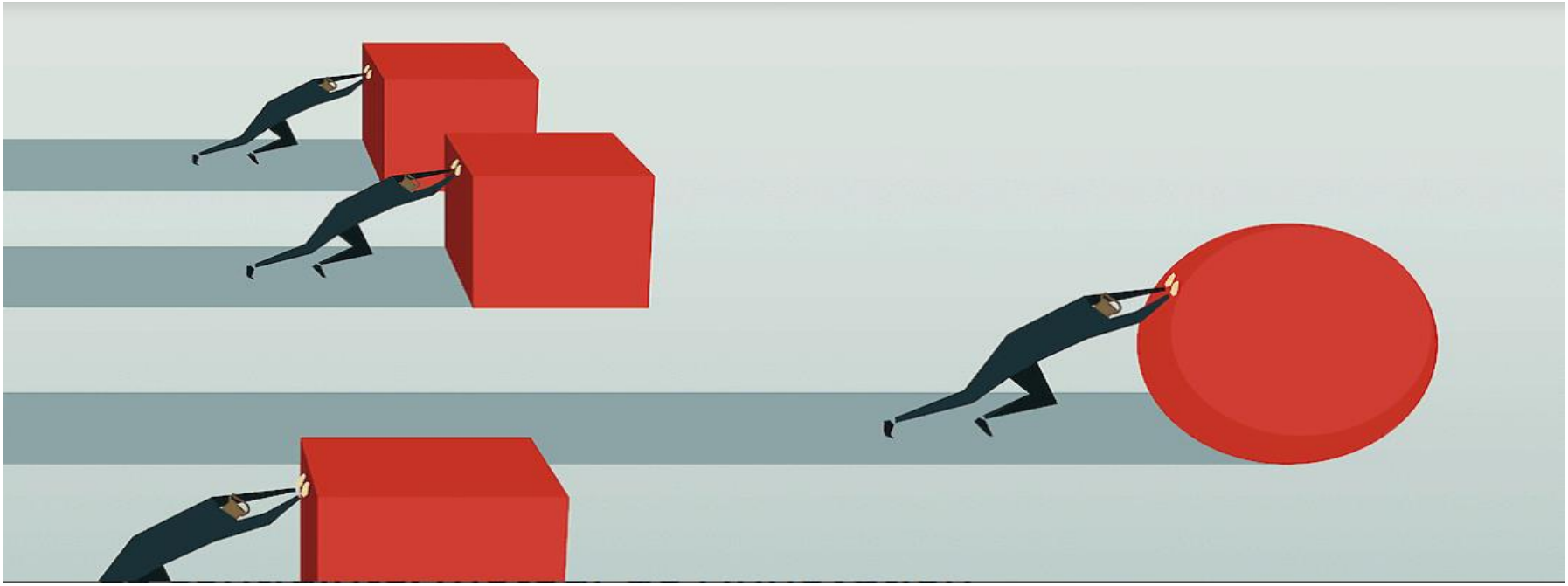
SMOG

Société Marocaine de Génomique et Génétique Humaine

SM2GH



- ✓ Lack of funding
- ✓ Limited research infrastructure
- ✓ High cost of reagent
- ✓ Lack of collaboration
- ✓ Limited data availability
- ✓ Lack of trained personnel



90% of pHd students abandon their thesis

- ✓ Lack of funding,
- ✓ Limited financial resources of PhD students
- ✓ Limited scholarships
- ✓ **Post**-doctoral qualification

THE COST OF PUBLISHING

JOURNAL PRICES VARY WITH INFLUENCE AND BUSINESS MODEL.

Price of prestige

Open-access prices correlate weakly with the average influence of a journal's articles.

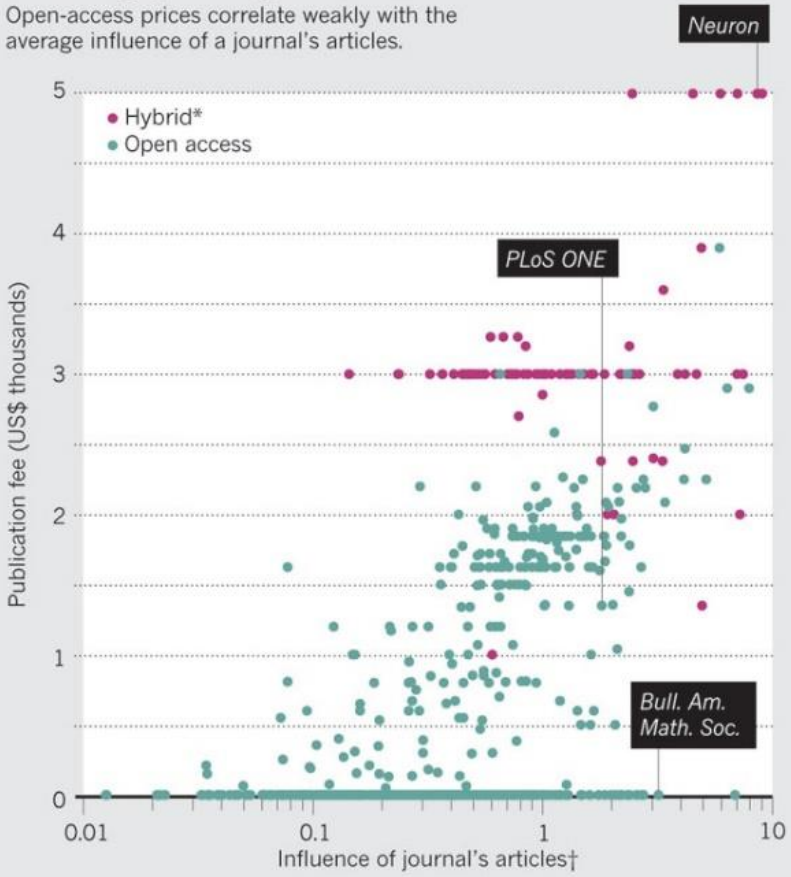


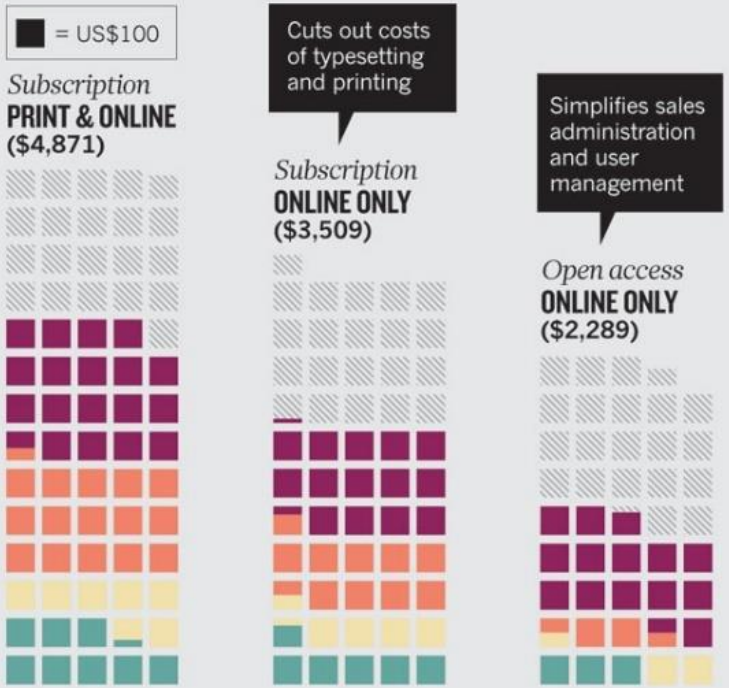
Chart omits open-access journals yet to receive an Article Influence® score.

*Subscription journals that give option of open-access publishing. †Relative score, in which 1 = global average.

The Article Influence score measures the relative importance of a journal, based on the average influence of an article in that journal over 5 years after publication, and normalized so that the global mean influence is 1. Like the impact factor, Article Influence is based on citation counts, but gives heavier weight to citations from papers in journals that are themselves highly cited. See www.eigenfactor.org/openaccess for more.

How costs break down

An economic model shows how switching from subscription to open access changes the costs of publishing.



Voluntary peer review (not counted in price)
Additional cost if reviewers were paid for their time.

Article processing
Administering peer review (assuming average rejection rate of 50%); editing; proofreading; typesetting; graphics; quality assurance.

Other costs
Covers, indexes and editorial; rights management; sales and payments; printing and delivery; online user management; marketing and communications; helpdesk; online hosting.

Management and investment
Includes cost to establish journal: assumed 20% subscription; 15% open access.

Margin
Assumed 20% subscription; 15% open access.

Data from J. Houghton *et al. Economic implications of alternative scholarly publishing models* (Joint Information Systems Committee, 2009). available at go.nature.com/uqrxqw.

Despite repeated calls and warning, genomics eurocentric bias is on the rise

2016

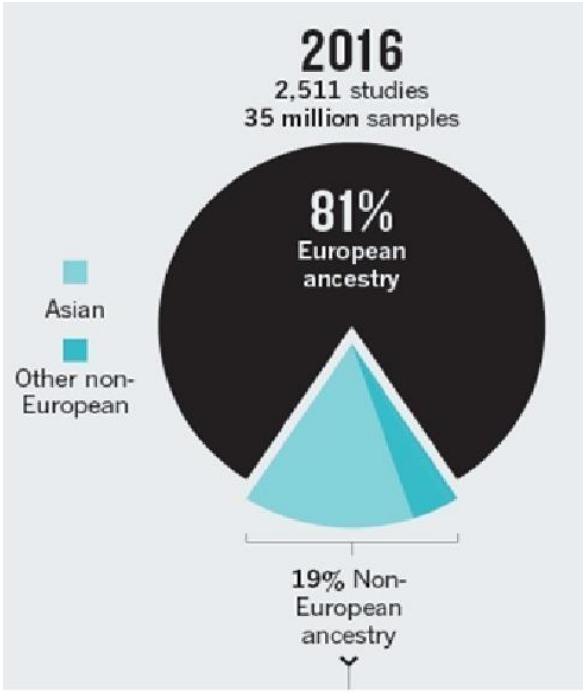
- Europeans: 81%
- Africans: 3%

2019

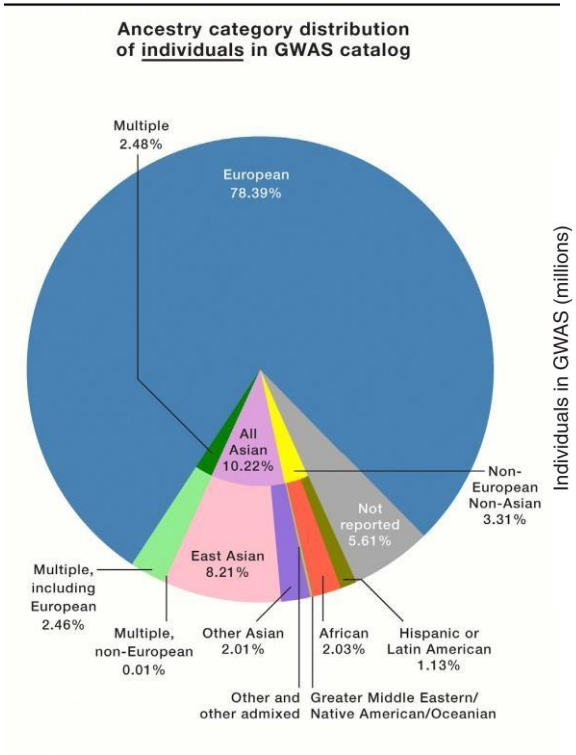
- Europeans: 78.39%
- Africans: 2.03%

2022

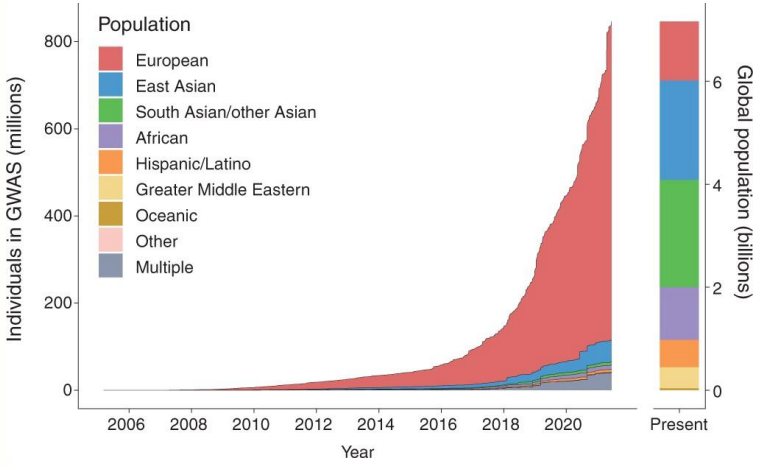
- Europeans: 86%
- Africans: 1.1%



Popejoy, A., Fullerton, S. 2016 *Nature* **538**, 161–164



Sirugo *et al.,* 2019. *Cell*, *177*(1), 26-31.



Fatumo *et al.,* 2022 *Nature Medicine*, *28*(2), 243-250.

Research funding is done by

- ✓ Global funding supported by the public
- ✓ Calls for projects

But Research funding remains very limited compared to other emerging countries.

In Morocco, the scientific research system is of recent creation and comes under the supervision of the Ministry of Education and Scientific Research

The national research strategy has planned several actions:

- ✓ The creation of a national science and technology ethics committee
- ✓ The creation of a scientific research coordination committee,
- ✓ The creation of a high committee in charge of monitoring the participation of Moroccan skills residing abroad in the scientific and technological development of our country

Scientific collaboration is a powerfull vector for developing the productivity and quality of research production:

- ✓ Increase research productivity
- ✓ Increase its visibility and the quality of publications
- ✓ Leverage other assets for research, including funding
- ✓ Increase resources and genomic data

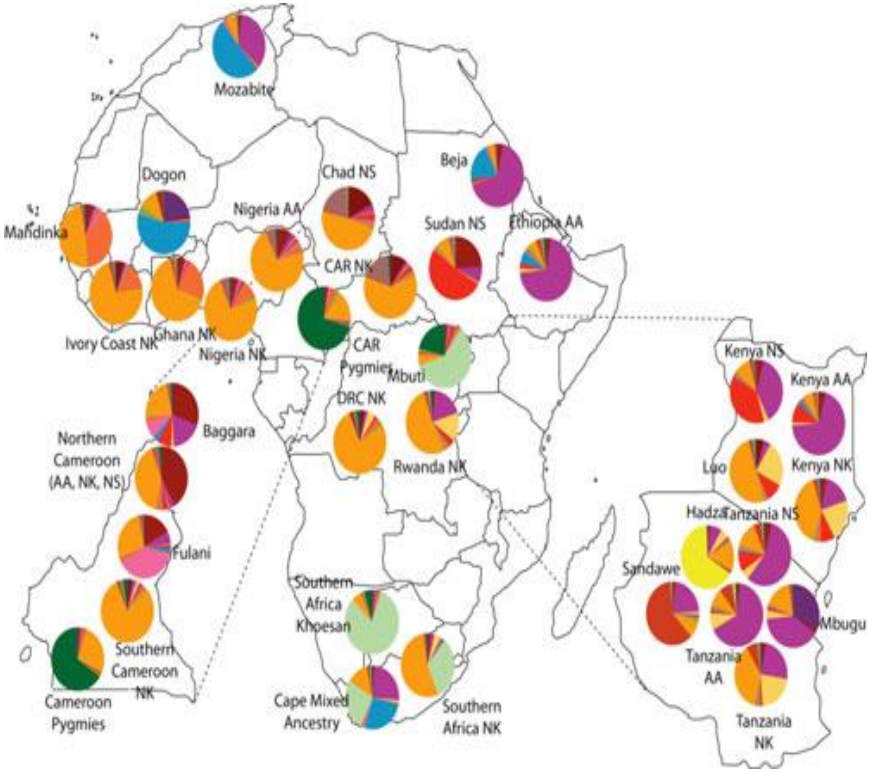
International collaboration south south or north south in genetics can be done through :

- ✓ The conventions and agreements signed by Morocco
- ✓ The conventions and agreements signed by the ministry in charge of scientific research
- ✓ The conventions and agreements signed by universities
- ✓ Driving to the base of personal contacts

- ✓ Establishment of partnerships:
- ✓ Exchange of Knowledge and Resource
- ✓ Progra
- ✓ Planning of commun projects
- ✓ Funding and support
- ✓ Publication and sharing of results
- ✓ Scholarships and training courses for young researchers
- ✓ Technology transfer

H3ABioNet

3MAG



Conclusion

Concerted effort from governments, institutions, and researchers to :

- ✓ Prioritize genetics research,
- ✓ Invest in infrastructure and technology,
- ✓ Promote collaboration and ethical research practices.