INSTITUT PASTEUR IN MOROCCO

Missions

- Promote and develop basic and applied research
- Bring on contractual basis a contribution of expertise, biological analysis and advice to any individual, any business, administration and other regional institutions, national or international
- make or have made, import and export, distribute all vaccines, serums, biologicals for therapeutic and diagnostic
- Contribute to the teaching of biological disciplines related to these activities

RESEARCH & TEACHING

Research
The research department consists of two divisions,

- the first is focused on research on communicable diseases,
- the second division includes laboratories whose work is carried on non-communicable diseases, the genetic disease occurrences, the noninfectious cancers, and the scorpion and ophidian poisoning.

the staff of the research department consists of 39 researchers and research assistants, including 31 biological teachers, 1 doctor, 1 engineer and 6 masters holders assistants

Education
Staying true to the Pasteur tradition, the department of research and education involved in teaching and multidisciplinary continuing education by organizing scientific events (Congresses, seminars, workshops etc ..), supervision of research students, residents in medicine, pharmacy, engineering, and laboratory technicians.

HUMAN GENETICS

Human Genetics Laboratory
Dr.BARAKAT Abdelhamid

The Human Molecular Genetics laboratory work on two research programs that form part of an overall theme, on the genetic diversity and population health.
- The first program “Medical Genomics” has a genomic approach to identify the molecular basis of monogenic and multifactorial diseases in the Moroccan population.
- The second program “Development biology” concerns the genetic study of sexual development disorders and the genetic diversity of the Moroccan population.
In both programs, the investigation of targeted diseases is multidisciplinary involving several disciplines such as biochemistry, cytogenetics, and molecular genetics. Research on genetic diseases aims to develop serious tools for screening and prevention of disability of genetic origin.

**Title: Hereditary deafness in Morocco**

Team of Human and Molecular Genetics Laboratory described the contribution of ten genes, GJB2, GJB6, GJB3, MYO7A, ESPS, MTRNR1, LRTOMT, TPRN, TMPRSS3 and CLDN14 in the occurrence of hereditary deafness in various of the patient’s Moroccan population.

**Title: Bioinformatics**

- Analysis of sequencing
- Development of diseases database in the Moroccan population. (MFMD)

The Mediterranean Founder Mutation Database (MFMD) is a comprehensive database created to provide online access to the data of founder mutations of the Mediterranean population. The database provides an overview of the range of founder mutations found in the Mediterranean population in the scientific community. In addition, MFMD help scientists develop more effective diagnostic tests and provides useful information to understand the history and migration events of the Mediterranean population.

**Title: MEDIGENE**


The Mediterranean basin has for millennia been the home of many historical migrations. For example, the Albanians have emigrated to North Italy and Greece, forming a large Turkish community in Lyon (France), the Romanian exceptionally sedentary for thousands of years who have recently immigrated to Spain and North African immigrants such as Algerians, Tunisiens and Moroccans. Many of these people are sensitive - protected - metabolic syndrome, obesity and diabetes due to unknown factors. Modern migrations are extraordinary sources to understand the collision between genetic factors and lifestyle or dietary MEDIGENE of populations is a research program funded by the European community, its purpose is to study the genetic and environmental determinants of metabolic syndrome in Mediterranean populations immigrants. The basic idea is the use of the genetic architecture of Mediterranean populations to better stratify populations in large Genome association studies (GWAS). GWAS Strategies will be improved by taking into account not only the frequency of single nucleotide polymorphisms (SNPs), as well as combinations of haplotypes and phylogeny.

**GENETICS OF DEVELOPMENT AND REPRODUCTION**

- **Title: Disorder of Sexual Development (DSD)**
  - Genetic and biochemical analysis of patients with DSD remains an essential tool to open the way for further studies that will lead to their purpose in diagnostic and therapeutic solutions.

- **Title: Genetic and epigenetic control of spermatogenesis**
  - First, we look for abnormalities in the AZF region of the Y chromosome (AZFa, AZFb, AZFc) known to be associated with infertility.

- **Title: Genetic Diversity of the Moroccan population**
Moreover, the results also are a source of very interesting data for the reconstruction of their life history that may supplement the information may be available from the paleontological studies, language, or their written or oral history.

**MICROBIOLOGY**

**Molecular Bacteriology**
Description in preparation

**Chlamydia, Mycoplasma**
Dr.RADOUANI

The *Chlamydioses* and *Mycoplasmoses* are among the most common infectious diseases. These are intracellular bacteria responsible for severe and extremely varied pathological manifestations as well in humans as in many animal species, according to the infecting species and the infected site. *Chlamydia trachomatis* and *urogenital mycoplasma* are the first sexually transmitted infections throughout the world, in most cases asymptomatic and unapparent. Infection with *C. trachomatis* may be complicated in women of ectopic pregnancy or infertility due to inflammation and tubal obstruction.

In humans, it can be responsible for urethritis which complicate prostatitis and epididymitis. However, infection with Mycoplasma urogenital can cause abortions. Chlamydia and mycoplasma are involved in especially genital pathologies, but some strains are responsible for eye diseases, respiratory diseases and may be involved in cardiovascular disease.

**Missions**
- Securing the diagnostic activity of these infections
- Undertake research report with Chlamydia, Mycoplasma and the diseases associated with them in order to:
  - Establish Monitoring programs
  - Adopt A management strategy and control of these infections to limit their development and dreaded complications

**Work in progress:**

- **project 1**
  - **Title:** Study from *Chlamyphilia pneumoniae* infection in Cardiovascular Diseases
    - **Objective:** Evaluation of the degree of association with a case study / witnesses and molecular characterization of circulating strains.

- **project 2**
  - **Title:** The *Urogenital mycoplasma* in genital infections: Prevalence and Antibiotic Susceptibility
    - **Objective:** The main purpose of this study is to evaluate the rate of infection by Mycoplasma urogenital, studying the antibiotic susceptibility of circulating strains and perform a molecular study of resistance genes.

**Meningococcal**
Dr.Aziza RAZKI

- monitoring the epidemiology of meningococcal thanks to phenotypic and genotypic markers;
**Work in progress**

**Title: Epidemiological Surveillance of Invasive Meningococcal Infections**

Invasive meningococcal disease is a serious infection that occurs worldwide. *Neisseria meningitidis (Nm)* remains a **leading cause of bacterial meningitis** in all ages, mostly in **children**. Meningococcal disease is considered one of the **main causes of death**. In Morocco the fatality rate exceeds **20%**.

Invasive meningococcal infections (IMD) is mandatory and represent a major public health problem worldwide. The objective of the laboratory of the Pasteur Institute of Morocco meningitis is **monitoring** the epidemiology of meningococcal thanks to phenotypic and genotypic markers; complete characterization.

The study includes three axes:

- To describe prospectively the **epidemiological** profile of Meningococcal PCR and monitor its resistance to antibiotics for therapeutic and prophylactic purposes.
- Describe the **genetic diversity** by **MLST** of Men B and whole genome sequencing.
- Test expression and cross-reactivity of vaccine antigens by the antigen or MATS typing system (**Meningococcal Antigen Typing System**)

**Food Microbiology**

Dr. Brahim Bouchrif

**Salmonellosis** is a disease caused by **enteric bacteria** of the genus Salmonella.

Each year the laboratory expertise of 80 to 150 Salmonella strains from private laboratories City (**laboratory microbiological analysis of food**), laboratories of hospitals, fisheries research institutes and veterinary laboratories. His role, **monitoring** the emergence of **multi-resistant strains** participating in the **epidemiological** investigation by performing **serotyping, molecular typing** of bacterial strains, it analyzes the monitoring of **antibiotic sensitivity** of Salmonella over time, it adapts to new molecular tools for tracking bacterial strains and is working with the National Reference Centre for Escherichia coli, Shigella and Salmonella (**CNR**) and the microbiology laboratory CHU Casablanca.

**Work in progress:**

- **Title: Molecular typing** by pulsed field gel electrophoresis (PFGE) of Salmonella Infants isolated in Casablanca Morocco.
- **Title: Prevalence, sensitivity to antibiotics** and isolated Salmonella virulence genes of laying hen farms in Morocco.
- **Title: The first postponement of SHV-12 Producing isolates of Salmonella serovar Agona from turkey meat (Meknes - Morocco).
- **Title: Participation in genomic analysis sequencing whole thrust by strains of Salmonella chester**
- **Title: Study of the isolated strains of Escherichia coli food.**
- **Title: Antimicrobial resistance in Salmonella isolated from shellfish in mediterranean coast, Morocco**

**Gastric pathology Oncology**

Dr. Fatima MAACHII

**Helicobacter pylori and Gastric Cancer:**

H. pylori is a gastric carcinogen class 1 (WHO, 1994). The infection contracted in childhood, usually before 10 years, persists in most individuals all life in the absence of treatment. Currently, with infection rates reaching **50%** of the world population,
Work in progress:

- **Title:** Resistance to treatment and failure of *H. pylori* eradication Genotypic detection methods and mechanism of resistance
- **Title:** Study of proinflammatory host factors
  - Study The role of SNPs in the TNF-alpha promoter and TNFRI in carcinogenesis
- **Title:** Prevalence of infection of *H. pylori* in the oral cavity
  - The objectives of this project are:
    - Check if the oral cavity is the second tank of *H. pylori* by the detection of *H. pylori* in dental plaque
    - To determine the prevalence and risk factors of *H. pylori* infection in the oral cavity

**ONCOLOGY AND CELL THERAPY**

**Oncovirology**

Dr. Meriem Khyatti

The laboratory's activities include the study of cancers associated with viruses that exist in a high prevalence or are specific to Morocco, such as:

- The nasopharyngeal cancer: cancer associated with Epstein-Barr virus, which is the first cancer ENT
- Cervical cancer: cancer associated with HPV, which is the second cancer site in women.
- Breast cancer: study of viral and genetic etiology of breast cancer is the first cancer in women in Morocco.

Work in progress:

- **Title:** Study of genetic, immunological & viral nasopharyngeal cancer(NPC)
  - As part of this project we are interested in:
    - Evaluate The prognostic value of plasma viral load in the EBV followed post treatment of NPC patients
    - The Effectiveness of certain types of chemotherapy or radiation therapy requires a good quality of immune response
    - Replication Study based on Chinese GWAS meta-analysis hits were North African population.

- **Title:** Evaluation of breast cancer biomarkers: genetic approach & viral etiology
- **Title:** Project EUNAM: EU and migrants from North African origin: health and care systems

**Cell therapy**

Dr. Loubna Mazini

Work in progress:

- **Title:** skin regeneration in patients with non-ulcer scar after autologous stem cells derived from adipose tissue
- **Title:** Involvement of mesenchymal stem cells in wound healing in chronic and acute brules
Parasitology
Dr. Meryem Lemrani

Leishmaniosis is a public health problem in Morocco, not only because of the number of cases reported each year, but also because of the wide distribution of the disease on Moroccan territory, the diversity of Leishmania species and the diversity of forms clinical.

Work in progress:
- Title: Cutaneous Leishmaniosis, Leishmania major Zoonotic: Diversity parasite Genetic and Immune Response impact on the patient
- Title: Role of climate, environmental factors and host interaction -parasite in determining local epidemiology and incidence of cutaneous leishmaniasis in Leishmania tropica in Morocco
- Title: Study of the genetic susceptibility to visceral leishmaniasis and phylogenetic and evolutionary analysis of the population of strains of Leishmania

Vector diseases
Dr. M'hammed Sarih

The growing importance of emerging and re-emerging vector-borne diseases is observed in animal health and public health. Climate change could have a direct impact on the bio-ecology and Arthropods promote the proliferation, the appearance or disappearance of certain species that may be causing the re-emergence or the emergence of vector-borne diseases such as dengue fever, Rift valley fever, West Nile (West Nile Virus), chikungunya, Malaria, borreliosis tick, and Rickettsiose. Thus, the study of the ecology of vectors (ticks, mosquitoes), population genetics, sensitivity status to different families of insecticides and their vector competence, are of paramount interest to understand the epidemiology of these diseases.

Work in progress:
- Title: Characterization of molecular mechanisms of resistance to insecticides of Culex pipiens complex and study of the effect of resistance on vector competence vis-à-vis the West Nile virus and fever of the valley Rift.
- Title: Susceptibility of Plasmodium falciparum and insecticide susceptibility of Anopheles sergentii Morocco
  - In Morocco, Plasmodium vivax and P. falciparum are the main species affected by malaria.

Toxins and Venoms
Dr. Noreddine Ghalim

This laboratory research area focusses on:
- the biochemical, immunological and pharmacological study of venoms of the most dangerous snakes and scorpions in Morocco by using the most modern tools such as mass spectrometry.
- Improvement of immunotherapy is the only treatment specific and this by producing antibodies having great power neutralizing
Work in progress:

- Development and validation of quantitative and qualitative determination of the venom of scorpions in the blood of poisoned patients to:
  - Show correlation between the amount of circulating venom and severity of clinical symptoms to optimize treatment.
  - Determine the type of offending scorpion (Buthus or Androctonus)
  - Clinical and biological studies in the poisoned patients
- Physio-pathological study of both venoms of scorpions Buthus occitanus and roctonus mauretanicus and comparative study
- Development of new generations of anti-venom vaccines, nanobodies, ...
- Research, design and development of antitumor molecules, anti-angiogenic and/or proapoptotic

VIROLOGY

Immuno-virology
Dr. Lahcen Wakrim

The laboratory's activity is focused in part on clinical research on the issue of HIV and AIDS, mainly, molecular epidemiology of HIV infection and the other on environmental research by studying contamination of surface waters in many regions of the kingdom by enteric viruses.

Work in progress:

- Title: Epidemiological Monitoring of genetic variability of HIV-1 circulating in Morocco and the development of resistance to anti-retrovirals.
- Title: Study of genetic polymorphism of DC-SIGN, the HLA-B*40 and HLA-A*11 in patients infected with HIV and their impact on susceptibility to AIDS and tuberculosis.
  - Co-infection with HIV and Mycobacterium tuberculosis is a major public health problem worldwide. Tuberculosis (TB) is the most common opportunistic infection in people living with HIV. It is one of the main factors of AIDS mortality. At least one in four deaths among HIV-positive is attributed to tuberculosis. In Morocco, tuberculosis is responsible for 35% of AIDS deaths.
  - Among the best studied factors, it was shown that DC-SIGN protein adhesion and HLA-B*40 molecules are associated with progression to AIDS and TB while the HLA-A*11 molecule is associated with resistance to both diseases
- Title: Evaluation of the presence of enteric viruses in surface water and seafood in the Moroccan coast.

ANALYSIS & ORGANIC FOOD SAFETY

Pathology

Head: Dr. Hakima BENOMAR

Presentation of d.Anatomo-Cytopathology Laboratory (ACP):
The d.ACP responds to requests from examines pathological hospital-centers academics, d.hôpitaux regional, and private sector (clinics and laboratories). These applications relate to all medical and surgical disciplines.

The Cytopathology (ACP) is a medical specialty at the intersection of **clinical, surgical, imagery, biology** and **research**.

L.ACP uses fundamental knowledge anatomy, histology and normal cytology to recognize macroscopic and microscopic morphological abnormalities associated with the disease.

**Laboratory Activities Anatomy pathological:** the two core activities of the pathological laboratory of the department of anatomy, are firstly the diagnostic activity and also the research activity, which follows from the first due the importance and the variety of pathologies.

**Diagnosis activity** the primary activity is related to the nature of pathological anatomy, medical discipline that includes the study of all observable lesions in a patient at three levels.

Macroscopic examination or study at the bare it histological and cytological study under the microscope specialized analyzes using advanced techniques of cell biology, histological and cytological study under the microscope:

- histochemistry
- immunohistochemistry
- skin Immunofluorescence
- HercepTest (HER2 / neu)
- Fluorescence in situ hybridization (CISH)

**Technical Platform** The laboratory hosts advanced equipment:

- **Cytology**: single-layer system: Novacyte (Novaprep)
- **Histology**: Automate to inclusion, coating Station, Microtome, Optical microscopes with camera.
- **Immunohistochemistry**: Auto-Stainer
- cutaneous **Immunofluorescence**: Cryostat
- **in situ hybridization** (CSA): Hybridizer

**Quality approach:**
Placing it’s assurance quality system assessment by technical protocols and interpretation the results of different structures (Registration AFAQAP).

**Scientific Research:** It aims to evaluate new methods of diagnosis and treatment, allowing futures to pass certain techniques in routine activity and improve the diagnostic operations and / or prognostic for the benefit of patients.

**Immunohistochemistry on frozen sections**

- Development of **molecular biology techniques** for the **diagnosis** and the identification of **therapeutic targets** "Kras, Braf, NRAS, EGFR, Pi3AKT, p65, NFkB" in **digestive cancers, lung, prostate** and **melanoma**.
- **Typing HPV** Test and p16INK4a (ASCUS, LSIL)
- Development of technical TMA (Tissue Microarray)
- Development d.une tumor bank

**Bacteriology**
Leader: Dr. Mohamed EL AZHARI
Service Overview:
The bacteriology department, parasitology and medical mycology aims to diagnose bacterial, parasitic and fungal human.
Microbiological samples are collected under the supervision of medical biologists. They are mostly made on site, quickly routed to the service, and in case of culture, they soon seeded on specific media, then observed under the microscope with or without specific staining.

The service includes three units:
- L. unité Bacteriology: it ensures the analysis of biological products in the context of diagnostic activities.
- L. unité Parasitology: it ensures detecting parasites in the feces (parasite coprology), urine and blood (parasites).
- L. unité Mycology: it ensures the skin samples and appendages in search of yeasts or filamentous.

Training and Mentoring students:
The laboratory also trains many students from various universities in the kingdom

Biochemistry and immunochemistry

It performs a wide range of analysis that helps general practitioners and specialist guide or consolidate their diagnosis, to monitor response and/or changing the recommended treatment.

Diagnostic Activity

Dosage of the following:
- Substrates: Urea, blood sugar, creatinine, uric acid, bilirubin, cholesterols (total, HDL, LDL), triglycerides, serum and urine protein ...
- Enzymes: Transaminases (AST, ALT), alkaline phosphatase, amylase, lipase, lactate dehydrogenase, GGT
- Ions: Calcium, Magnesium, Phosphorus, Sodium, Potassium, Chlorine, Ammonia
- FIBROTEST
- HBA1c

Quality approach:
The biochemical laboratory is involved in quality management process. Referent service quality:

Molecular biology
Leader: Dr Abdelouaheb Benani

Molecular Biology Laboratory plays a very important role in the diagnosis and therapeutic monitoring of infectious diseases, especially in the field of viral hepatitis, tuberculosis and STI Chlamydia trachomatis.

Diagnostic Activity

- Measurement of the viral load hepatitis virus B (HBV) by real-time PCR,
- Measurement of the viral load hepatitis virus C (HCV) by real-time PCR,
- HBV genotyping,
- Genotyping HCV,
- HPV genotyping,
- Search of Mycobacterium tuberculosis by real time PCR,
Chlamydia trachomatis search by real-time PCR.

Public Health Activity

In collaboration with the Directorate Epidemiology and Fight against Disease (MLED), the Laboratory of Molecular Biology of IPM is the reference laboratory of the Greater Casablanca from southern Morocco in the plan National fight against viral hepatitis through the RAMED program.

Currently, a national strategy for prevention and control of viral hepatitis 2016-2021, is being elaboration the Ministry of Health.

Cytogenetics and genetic counseling

This laboratory is composed of a specialized technical platform, consisting of two coupled microscopes capture systems and image processing, two bathrooms, culture and genetic counseling room.

Hematology

The hematology / coagulation laboratory allows through experienced staff and by all analyzes conducted to meet the demands and requirements of clinicians prescribing.

Diagnostic Activity

- Complete blood count
- Médullogramme
- The rate of sedimentation
- The blood grouping in ABO RH1
- Coombs tests direct and indirect
- Search irregular antibodies
- Hemostasis: bleeding time (BT), activated partial thromboplastin time (aPTT) and prothrombin rate (TP).
- the test of the globular resistance.

Hormonology tumor-markers

Leader: Dr Benabdelljalil NADIA / Dr AINAHI ABDELHAKIM

The laboratory has its performance art equipment allowing it executer most hormonology applications and tumor markers in a limited time and in conditions of optimum quality.

L.i1000SR is a multiparameter analyzer capable immunology effector Justus 100 tests per hour. It uses the micro particle immunoassay technology by chemiluminescence (CMIA) for the presence antigens, ant corps or analytes in the samples analyzed.

Diagnosis of Activity The CMIA diagnostic technique exploration of:

- **endocrine** pathologies:
  - biological explorations Thyroid FT4, TSH, ATPO, ATG.
  - biological exploration of Fertility: FSH, LH, PRL, E2, PG, Testosterone, Beta HCG.
  - biological exploration of the adrenal gland: Cortisol (8 am, 16 pm) serum and urine.

- **Oncological** pathologies:
  - biological explorations of tumor markers: CEA, CA125, CA15-3, CA19-9, total PSA, free PSA, AFP.
Public Health Activity

Hormonology Laboratory is involved in the implementation of the national neonatal screening for congenital hypothyroid program at the Grand Casablanca region.

**Immuno-histo-compatibility**

Leader: Dr Siham Bennani

This activity is organized around 3 axes:

- **Transplant** balances of hematopoietic stem cells
- **transplantation**
- organs association **HLA polymorphism** and disease

HLA class typing analyzes I (HLA-A, HLA-B, HLA-C) and II (HLA-DRB, HLA-DQB,) are made with the following techniques:

- microlymphocytotoxicity (HLA class I), Luminex technology (research and identification of HLA typing and HLA I and II antibodies by PCR-SSO),
- technical HLA typing class I and II PCR-SSP

**Diagnostic activity**

- **kidney** Has Registry
  - TYPING HLA Class I / Class II
  - Cross match
  - HLA antibody screening
- **Bone Marrow** Registry
  - HLA Class I / Class II
- **associated HLA Diseases**
  - Becher’s disease: HLA B5
  - rheumatoid spondylitis HLA B27
  - Celiac disease: HLA DQ
  - Rheumatoid arthritis: HLA DR

**BIOLOGICAL ANALYZES AND FOOD SAFETY**

**Immunology & Serology**

It consists of four units:

- **Autoimmunity**
- **Immuno-pathology**
- **Allergology**
- **Serology and Immunoochemistry.**

**Diagnostic Activity**

- Diagnosis and monitoring of patients with monoclonal gammopathy.
- Diagnosis and monitoring of allergic diseases.
- Diagnosis and monitoring of autoimmune diseases whether systemic (connective) or organ specific.
- Diagnosis and serological monitoring infectious diseases that are bacterial, parasitic or viral.
PHARMACEUTICAL ACTIVITIES

Head Pharmacist Dr Hasnaa EL MELLOUKI RIFFI

The Institute Pasteur in Morocco is a public institution, compared to a pharmaceutical industrial, power to carry out manufacturing operations, import and marketing of serums, vaccines, biological products and immunological products.

Currently, to meet the national need, IPM relies on the expertise of its partners in the production of serums, vaccines and biological products to offer its range of products which represents a major public health issue.

Products

Sanofi:
- Stamaril - Vaccine live attenuated against yellow fever
- Typhim Vi - Vi Capsular Polysaccharide Vaccine purified against typhoid fever
- Vaxigrip - inactivated split virion influenza vaccine
- Verorab - inactivated rabies vaccine for the prevention of purified rabies before and after exposure

Serum Institute of India (SII):
- Tetanus Serum (SAT) - Prophylactic use in people at risk of infected wounds
- BCG Vaccine - Active immunization against tuberculosis
- Diphtheria and Tetanus (DT) - Primo vaccination and revaccination in adults, adolescents and children over 7 years
- Onco BCG - Treatment of carcinoma of urinary bladder endothelium

Statent Serum Institut (SSI):
- Tuberculin PPD - Tuberculin test
- Culture BCG SSI - treatment of carcinoma of urinary bladder endothelium

Bharat Serum and Vaccines:
- Equirab - rabies serum for passive immunization against rabies

GSK:
- Mencevax - Meningococcal polysaccharide groups A, C, W135 and Y conjugate not against meningitis
- Engerix B - Vaccine Hepatitis B recombinant adsorbed against the infection caused by the hepatitis B virus (HBV)

In addition, IPM is spirited to study the possibility of locally resume production of serums, vaccines and biological products including tetanus antitoxin, rabies serum, anti-venom serums, BCG and living BCG and tuberculin.