HEALTH

AGIR UR UPJV 4294
Infectious agents, resistance & chemotherapy

KEYWORDS

- Animal models
- Antibiotherapy
- Antibiotic resistance
- Anti-infectious
- BK virus / *polyomaviridae*
- Cell culture and prokaryotic models
- Clinical research
- ESKAPEE bacteria / nosocomial infections
- Genome analysis
- Heterocyclic and asymmetric synthesis
- Molecular modelling
- Mycobacteria / tuberculosis
- Peptide synthesis
- *P. falciparum* / malaria
- Pharmacokinetics
- SARS-CoV-2 / COVID-19
- Viral infections

A FEW THOUGHTS FROM THE DIRECTOR

"With the emergence of multiple bacterial resistances, antibiotherapy is going through a global crisis in the 21st century, with dramatic consequences for public health. In the European Union, antibioresistance is estimated to be responsible for 25,000 deaths per year, with an overall annual cost to society of €1.5 billion (source: ECDC 2007). The lack of knowledge and the emergence or re-emergence of certain viral infections are also acute public health problems.

As one of the major issues in anti-infectious treatments, the fight against resistance phenomena is at the heart of our laboratory's objectives. AGIR designs and evaluates new anti-infectious molecules to better fight against malaria, tuberculosis, nosocomial infections and viral infections in immunocompromised patients. At the same time, the team is investigating the physiopathological mechanisms of these infections."

Professor Pascal SONNET, Director
Professor Sandrine CASTELAIN, Deputy Director

FIELDS OF RESEARCH

AGIR focuses its research on the resistance developed by these 4 groups of pathogens:

- ESKAPEE bacteria, which are at the origin of numerous nosocomial infections causing more than 700,000 deaths per year throughout the world;
- Mycobacteria responsible for tuberculosis, the second most deadly infectious disease after HIV;
- *Plasmodium falciparum*, the parasite responsible for malaria (228 million cases and 405,000 deaths worldwide in 2018);
- The BK virus, which is responsible for 10 to 15% of rejection in patients with kidney or bone marrow transplants.
- The laboratory is also working on the SARS-CoV-2 virus which is at the origin of the COVID-19 epidemic (see "Research projects").

AGIR develops and studies new anti-infectious molecules according to a global and multidisciplinary scientific approach:

- Epidemiology and clinical research: characterisation of the biomolecular targets of pathogens;
- Pharmacochemistry: design and synthesis of anti-infectious molecules;
- Physicochemistry and Bioinformatics: study of structure-activity relations *in silico*;
- Microbiology and Molecular Biology: *in vitro* biological evaluation, development of cellular models and biomolecular study of mechanisms of action;
- Pharmacokinetics and *ex vivo / in vivo* biological evaluation in animal models.

FIELDS OF APPLICATION

- Pharmacochemistry: synthesis of new anti-infectious heterocyclic and/or peptidic molecules
- Physicochemistry
- Microbiology
- Molecular modelling
- Clinical biology
- Epidemiology
- Molecular biology
- Cell Biology
- Genomics

RESEARCH PROJECTS

- **SEAPAL Project "Synthesis and study of new enantiomerically pure antipaLudic drugs"**
  Synthesis and evaluation of new amino-alcohol derivatives with a quinoline structure potentially active to counter resistance phenomena in *Plasmodium falciparum.*
- **SYNETUBER project "Synthesis and study of new antituberculosis drugs"**
  Synthesis and evaluation of the activity of new antituberculosis drugs (heterocyclic derivatives and/or AMP (AntiMicrobial Peptides))
- **SASAB project "Synthesis and study of analogues of siderophores with a broad antibacterial spectrum"**
  Synthesis and study of new analogues of siderophores (iron carriers), vectors of antibiotics (**"**Trojan horse strategy**"**)
- **BKSTRIP project "Development of a rapid BK virus urine test for the benefit of the patient"**
  Development of a strip urine test for early detection of the reactivation of the BK virus for better management of patient follow-up in the post-transplant period.

COVID-19 PROJECTS

- **CORONADE Project:** Study of the facilitation of infection by antibodies and critical forms of COVID-19
- **NEUTRALCOV Project:** Study of the kinetics and quantification of neutralising antibodies in patients with COVID-19
- **SALICOV Project:** Evaluation of the performance of a salivary sample versus a nasopharyngeal sample in the diagnosis of SARS-CoV-2 by RT-PCR
- **AMBUCOVID Project:** Therapeutic trial evaluating the efficacy and tolerance of azithromycin in pauci-symptomatic forms of the disease in outpatient care.

AGIR also participates in other clinical and biological research projects on COVID-19:
COVIDIAG, SALICOV-ID, SERCOVAL, SEROLOGIES PASTEUR, CORSER, COVID-OLD, COVIDOSE, CORIMUNO19-ECU, DISCOVERY, FRENCH COVID, HYCOVID, SEQ-COV, OSCAR.

EQUIPMENT

- Peptide synthesizer on solid support Liberty 1 (CEM)
- Circular dichroism apparatus J-815 (Jasco)
- Cluster of computers for scientific calculations (worth 100 KE)
- Biosafety level 3 laboratory
- Ultracentrifuge
- Fluorescence microscope with motorised platform for medium-flow screening in biosafety level 2 laboratory (L2)

INDUSTRIAL REFERENCES

- FAVI
- JANSSEN
- SANOFI - AVENTIS
- Start-up: Pharmamems, Pharm'Aging
- SERVIER
- THERANEXUS

Success Story

The AGIR research unit has proven expertise in the synthesis and evaluation of new pharmacological molecules.

In 2011, the laboratory has developed the enantioselective synthesis of new anti-malarial molecules analogous to mefloquine, with a 4-aminoquinoline methanol scaffold and active on the parasite. This new technology was the subject of a European patent application in 2011, extended internationally in 2012. The team noted that the S configuration enantiomers of these molecules are significantly more active against malaria, while those of the R configuration seem to be responsible for the side effects of anti-malarial treatments. This discovery led to a maturation project funded by SATT Nord, the SEAPAL project, which in turn led to the development of a promising new family of aminopyridinemethanol derivatives and the filing of a European patent in 2017, extended internationally in 2018.

In addition, a previous collaboration with SATT Nord led to the filing of an international patent in 2016 for the laboratory's design of new multifunctional anti-AGE/ALE diamines (Advanced Glycation Endproducts / Advanced Lipid peroxidation Endproducts), active against carbonyl and oxidative stress. These innovative molecules are used in dermo-cosmetics by Pharm'aging, which has signed an exclusive operating licence with SATT Nord.

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