COLLECTION "SECTORS AT GENOPOLE"

1 INNOVATIVE BIOTHERAPIES
2 COMPUTATIONAL GENOMICS
3 THE BIOECONOMY

By combining the worlds of business, academic research and professional training, Genopole is helping to build three of tomorrow's industrial sectors.

RESEARCH & PLATFORMS
recherche.plateformes@genopole.fr

ENTERPRISES
entreprises@genopole.fr

BUSINESS & PARTNERSHIP
international@genopole.fr

MARKETING
& COMMUNICATION
communication@genopole.fr

GENOPOLE
INNOVATION TODAY, EVERY DAY

CONTACT OUR TEAMS
20 rue Henri Desbruères
91030 Évry-Courcouronnes Cedex
France
WWW.GENOPOLE.FR

INNOVATIVE BIOTHERAPIES AT GENOPOLE

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The number of clinical trials in biotherapeutics is growing continuously. As a pioneer in the sector, France must defend its place in the worldwide race for new treatments. The nation aims to guarantee patient access to the high-tech therapies resulting from this future-looking sector and defend its independence therein. Genopole contributes actively to those goals.

NATIONAL ISSUES IN BIOTHERAPEUTICS

BUILD A NATIONAL BIOTHERAPEUTICS SECTOR

DEVELOP A FRENCH ADVANCED THERAPY MEDICINAL PRODUCTS INDUSTRY

SUPPORT THIS EMERGING MARKET

POSITION FRANCE AS A EUROPEAN LEADER

GENOPOLE: A MAJOR ACTOR IN GENE AND CELL THERAPIES IN FRANCE

The Genopole model is unique in France. Located in Évry-Courcouronnes, within the greater Paris area, the biocluster unites academic research laboratories, innovative businesses, university-level training programs and a hospital. Genopole is a center of excellence in biotechnologies. It is the leader in Europe and a leader in the world for the development and production of advanced therapy medicinal products.

BIOTHERAPIES AT THE HEART OF ITS HISTORY

Genopole is renowned for its scientific excellence in biotherapies. It is home to two French pioneers in the sector: Genethon for gene therapies in rare diseases, and I-Stem for the study of human pluripotent stem cells and their use in cell therapies. Indeed, Zolgensma, the first gene therapy to be approved for the childhood neuromuscular disease spinal muscular atrophy, was the fruit of research done at Genethon.

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A FERTILE ECOSYSTEM

The model developed by Genopole, that is, a biocluster uniting research, entrepreneurship, training and medicine, has shown its potential. An industrial biotherapies sector has come to be at Évry-Courcouronnes in partnership with national, European and global networks. Today, the value chain is complete, from R&D through to GMP production: initial and continuous training, academic research, technology transfer accelerator for rare and common diseases, businesses providing R&D and services, a stem cell bank under construction and a gene therapy production facility.

GENE THERAPY

Gene therapies treat diseases by inserting functional genes in cells to correct for the missing or dysfunctional genes in the genome. The introduced gene is, itself, the active pharmaceutical ingredient of the therapy.

CELL THERAPY

Also called regenerative medicine, cell therapies employ cellular grafts developed from stem-cell technologies to restore the functions of tissues or organs affected by disease, injury or age.

ISSUES IN BIOTHERAPIES: A THIRD REVOLUTION IN THERAPEUTICS

The initial successes in clinical trials and the market arrival of the resulting therapeutic innovations for both rare and common diseases have laid a path for no less than a third revolution in medicine.

Genopole and its actors are able and willing to accompany this revolution and bring answers to the challenges within it. They are helping to build a biotherapies sector.

GENE THERAPIES

MEDICAL AREAS

- **Rare genetic diseases** (immunodeficiencies, neuromuscular diseases, metabolic disorders, diseases of the blood, vision, liver, skin, etc.)
- **Cancers** (lymphoma, leukemia)
- **Neurological diseases** (Parkinson's disease, etc.)
- **Cardiovascular diseases**
- **Infectious diseases** (AIDS, etc.)
- **...**

SCIENTIFIC AND TECHNOLOGICAL ISSUES

- **Identification of defective genes**
- **Delivery of therapeutic genes** (conception of viral vectors, etc.)
- **Effective targeting**
- **Durable function of the therapeutic gene**
- **Risk management** (immune reactions, genotoxicity, etc.)

ETHICS ISSUES

- **Genetic modification** of treated cells
- **Respect of regulations for germline gene therapies**
- **Transmission of deleterious genes**

GENERAL CONCERNS

LEGAL ISSUES

- **Specific regulations** (European directives)

SOCIOECONOMIC ISSUES

- **Still a fledgling market**
- **Treatments currently very expensive**
- **Access for as many as possible**
- **Pharmacoeconomic approach** (social organisms, mutuals, etc.)

INDUSTRIAL ISSUES

- **Complex medicines** with challenging reproducibility issues
- **GMP production, quality, purity**
- **Optimization, standardization** for industrialization processes

CELL THERAPIES

MEDICAL AREAS

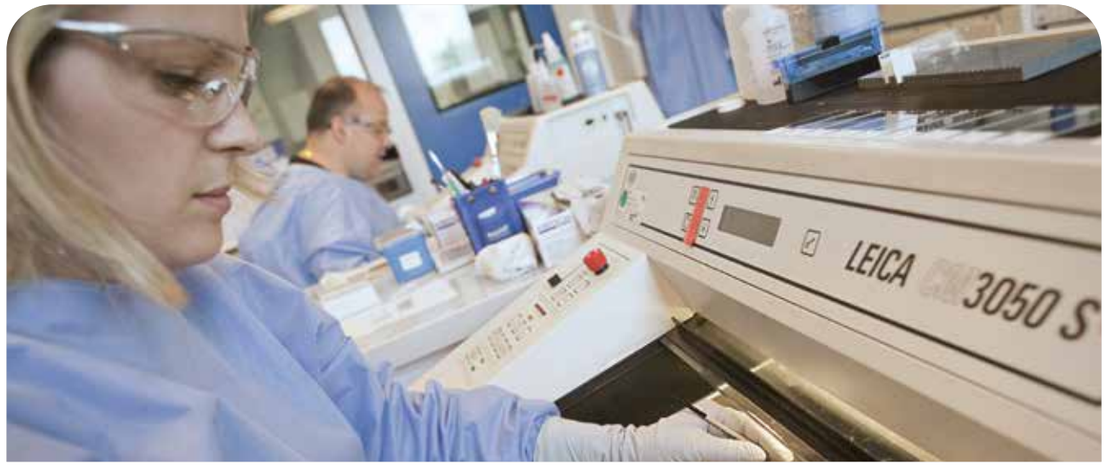
- **Degenerative diseases** (retinal degenerative diseases, arthrosis, Parkinson's and Huntington's diseases, myopathies, etc.)
- **Heart failure**
- **Skin ulcers**
- **Diabetes**
- **Blood cancers**
- **Etc.**

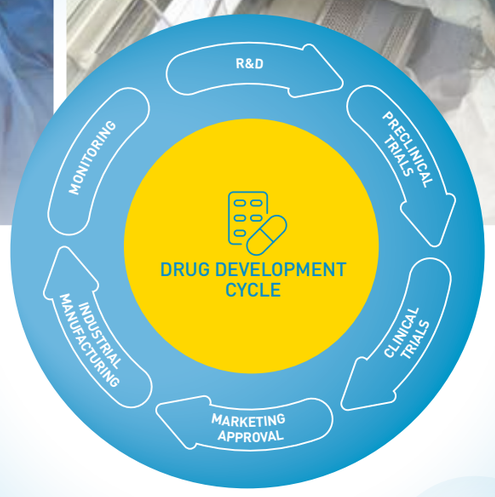
SCIENTIFIC AND TECHNOLOGICAL ISSUES

- **Stem cells**
  - adult: in blood, skin, intestine, etc. for autologous grafts
  - embryonic: great therapeutic promise because of their pluripotency
  - iPS: laboratory-produced via induction of pluripotency
- **Differentiation processes** for cells with therapeutic interest
- **Risk management** (carcinogenicity, immune reactions, etc.)

ETHICS ISSUES

- **Embryonic stem cells** (no longer intended for a parenting project and destined for destruction)
- **Cell donations for iPS lines** (consent framework as the lines are potentially immortal)
- **Research involving embryonic stem cells** (subject to bioethics laws)
- **International regulatory divergences** (stem cell tourism)





LIVING MEDICINES

Research in gene and cell therapies has led today not only to unprecedented treatments for previously untreatable rare diseases such as immunodeficiencies or serious childhood myopathies, but also to novel treatments for frequent diseases such as cancers (leukemia among others). These breakthroughs and others like them are called “advanced therapy medicinal products” (ATMPs) and subjected to specific and strict regulations to guarantee patient safety.

In addition to the medical challenges and regulatory constraints, there are also technological, economic and industrial challenges to overcome on the path to clinical trials and thereafter for the large-scale, economically-viable production of these complex biodrugs. Furthermore, it is vital to guarantee national healthcare independence for these treatments and fair access to them for all patients.

INDUSTRIALIZING BIOPRODUCTION

Like all other medicines, ATMPs, gene therapy viral vectors and stem-cell-derived cell sheets for cell therapies must be produced using Good Manufacturing Practices (GMP) in pharmaceutical establishments. This is true both for product batches meant for clinical research and those produced industrially for commercialization. Getting treatments to as many patients as possible requires consequential process upscaling (bioreactor-based production facilities, controlled atmospheres, management of supplies, stocks and human resources, etc.).

Whether for gene therapy viral vectors or therapeutic stem cells, the passage to large-scale production is a major challenge to meet.

MAKING BIOTHERAPIES ACCESSIBLE

Several ATMPs count among the most expensive medicines ever marketed. For example, the inherited retinal dystrophy treatment Luxturna costs €700,000 for a single treatment, but even it pales in comparison to Zolgensma, a treatment for spinal muscular atrophy, which is the world’s most expensive therapeutic at close to €2 million per patient. For the pharmaceutical companies, such prices are justified not only by the cost of ensuring the reproducible manufacturing of these living and complex therapeutics but also by the radical improvement they bring to patient life expectancy and/or quality of life and furthermore the reduction of the use of other expensive therapies. The questions of pricing and health systems sustainability must be addressed to guarantee wide patient access to these novel therapies. Otherwise, certain areas of the world may find themselves effectively excluded from access to them.

In gene therapy, the viral vectors used to deliver the gene API to cells are manufactured using cell lines cultured in bioreactors. In cell therapy, the unlimited proliferative ability of pluripotent stem cells enables the production of great quantities of cellular therapeutics from clinical-grade cells maintained in cell banks. Those banked cells must be sufficiently diverse to ensure immune compatibility with the greatest number of people possible.

THE VALUE CHAIN

GENOPOLE: HELPING TO BUILD AN INNOVATIVE BIOTHERAPIES SECTOR

INITIAL AND CONTINUOUS TRAINING

UNIVERSITY OF ÉVRY-PARIS SACLAY
Master 1 and 2 Tissue, Cell and Gene Biotherapies

IMT GROUP - ÉVRY SITE
Professional training in bioproduction for the cosmetics and pharmaceutical industries

SUPPLIERS / SERVICES

NEW ENGLAND BIOLABS
Reagent discovery, production and supply

ABCELL-BIO
Isolation of human hematopoietic stem cells and primary cells from cord blood and tissue, cell culture media

GENOSAFE
Evaluation of the quality, safety and efficacy of advanced therapy medicinal products

TEXCELL
Assessment of virus safety, toxicology and immunology

SYNHELIX
Enzymatic production of DNA

RESEARCH / DISCOVERY / OPTIMIZATION

GENETHON
Gene therapies for neuromuscular diseases

INTEGRARE
Gene therapies for rare genetic diseases

I-STEM / CECS
Cellular models, therapeutic screening and cell therapies from human pluripotent stem cells

LGRK
Genomics and Radiobiology of Keratinopoiesis Laboratory - skin stem cells, biology and pathologies

WHITELAB GENOMICS
Artificial intelligence to accelerate the development of gene & cell therapies

POLYTHERAGENE
Polymers for gene therapies and the bioproduction of therapeutic proteins

EUKARYS
Gene therapies for liver diseases and cancers, bioproduction of proteins and recombinant viruses

STEMSELECT
Isolation of stem cells from adipose tissue for therapeutics

DNA AND CELL BANK
Preparation and preservation of DNA, lymphocytes, myoblasts, fibroblast, etc. for research in rare diseases

BIOBANK **BIOPROCESSES**
HIGH THROUGHPUT SCREENING
3 associated platforms: cell bank storage, automated production of stem cells and research for active compounds

NGS & GENOMICS ANALYSES
Sequencing and genomic and bioinformatic analyses

PRECLINICAL AND CLINICAL RESEARCH

CERFE
Functional exploration and research

HISTOLOGY

ANATOMICAL PATHOLOGY / CYTOPATHOLOGY
Preparation, staining and microscopic study of tissues

OCCIGEN
Imaging and cytometry for research ranging from the single cell to the entire living organism

TRANSLATIONAL RESEARCH / PROCESS DEVELOPMENT

ART-TG
Genomic Therapy Technology Research Accelerator

CITHERA
iPS cell engineering, production of a bank of clinical-grade iPS cell lines

MAGENTA
Manufacture and control of innovative cellular products and lentivirus vectors for gene therapies; label shared by ART-TG and Cithera

BIOPRODUCTION / INDUSTRIALIZATION

YPOSKESI
Production of gene therapies

A SECTOR REPRESENTING:

> 600
JOBS IN CLOSE TO 20 LABORATORIES AND BUSINESSES

8
TECHNOLOGICAL PLATFORMS WITH A €600,000 ANNUAL BUDGET (EXCLUDING SPECIFIC OPERATIONS)

≈ 10
FAMILIES OF DISEASE (RARE GENETIC MUSCLE DISORDERS, DISEASES OF BLOOD, VISION, THE LIVER, ETC., CANCERS, INFECTIOUS DISEASES)

- Laboratory
- Business
- Technological platform
- Training
- "Industrial Integrator" label

INNOVATIVE BIOTHERAPIES AT GENOPOLE

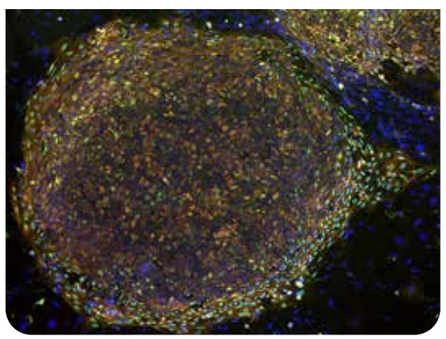
PROVIDING TRAINING FOR CAREERS IN BIOTHERAPIES

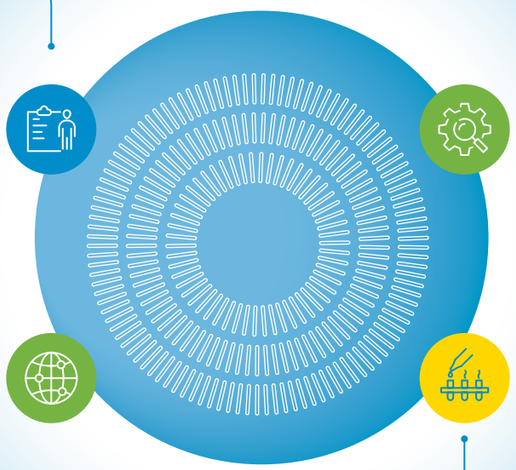
The **IMT Group** at Genopole is a professional training center for careers in bioproduction and galenic formulations. It contributes to the rapid development of the biotherapies sector and supports the pharmaceutical industry's evolution toward the new technologies associated with that sector. The establishment occupies 700 m² at Genopole, 400 m² of which is a technical facility for professional simulation training to acquire specific competencies. Notably, it furnishes a professional technician certification for industrial bioproduction. That certification can be accessed through both the French program for the allocation of undergraduate places in higher learning (Parcoursup) and the French personal continuous professional training account program (CPF; *compte personnel de formation*).

ESTABLISHING THE FRENCH CLINICAL-GRADE IPS CELL BANK

It was in 2012 that Professor Shinya Yamanaka earned the Nobel Prize in Medicine for his discovery of how to genetically reprogram any cell, for example a fibroblast, back to the pluripotent state of embryonic stem cells. These reprogrammed cells, called induced pluripotent stem (iPS) cells, can thereafter be guided into differentiating into nearly any type of human cell. When produced from diseased patients, iPS cells are valuable cellular models to better understand pathologies and enable the screening of potential therapies. When produced from healthy people, they collectively constitute a constellation of cell lines with great potential in regenerative medicine.

Indeed, it is possible to create banks of iPS cells that largely respond to the immune compatibility needs of a population. This is the goal of the clinical-grade iPS bank project underway at Genopole under the direction of **the innovation center Cithera.**





ACCELERATING CLINICAL AND INDUSTRIAL DEVELOPMENT FOR THE GOOD OF PATIENTS

The Genomic Therapy Technology Research Accelerator (ART-TG, Inserm) facilitates research on and the clinical development & industrial deployment of gene therapies for rare and common diseases, notably in the fields of immunology and hematology. ART-TG and the laboratory Cithera (also at Genopole) pilot **Magenta, an Industrial Integrator** within the Biopharmaceuticals category of the French Government's Major Challenges program. Magenta is focused on the bioproduction and control of next-generation cellular products and lentiviral vectors for gene therapies.

LEADING VIRAL VECTOR PRODUCTION IN EUROPE WITH YPOSKESI

With its suites for manufacturing and packaging, **Yposkesi** currently benefits from 5,000 m² of space at Genopole and will soon have more. The company was created by AFM-Téléthon and Bpifrance's SPI investment fund. Yposkesi develops small to large-scale bioproduction processes, manufactures clinical lots of gene therapy vectors and furnishes regulatory affairs services.

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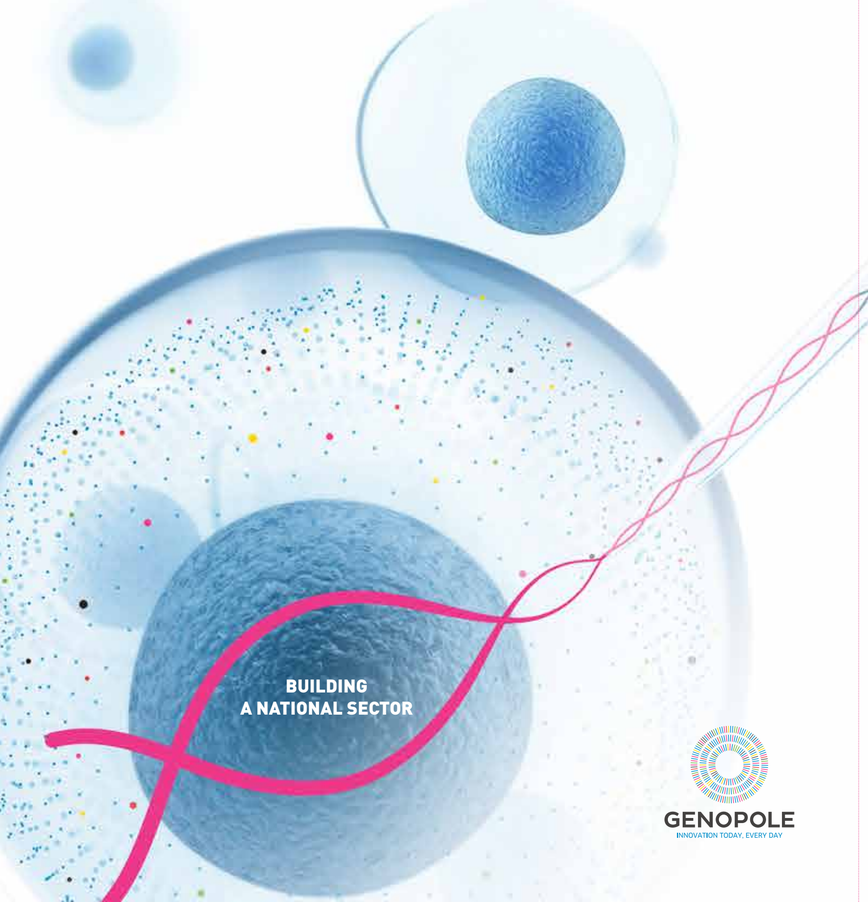

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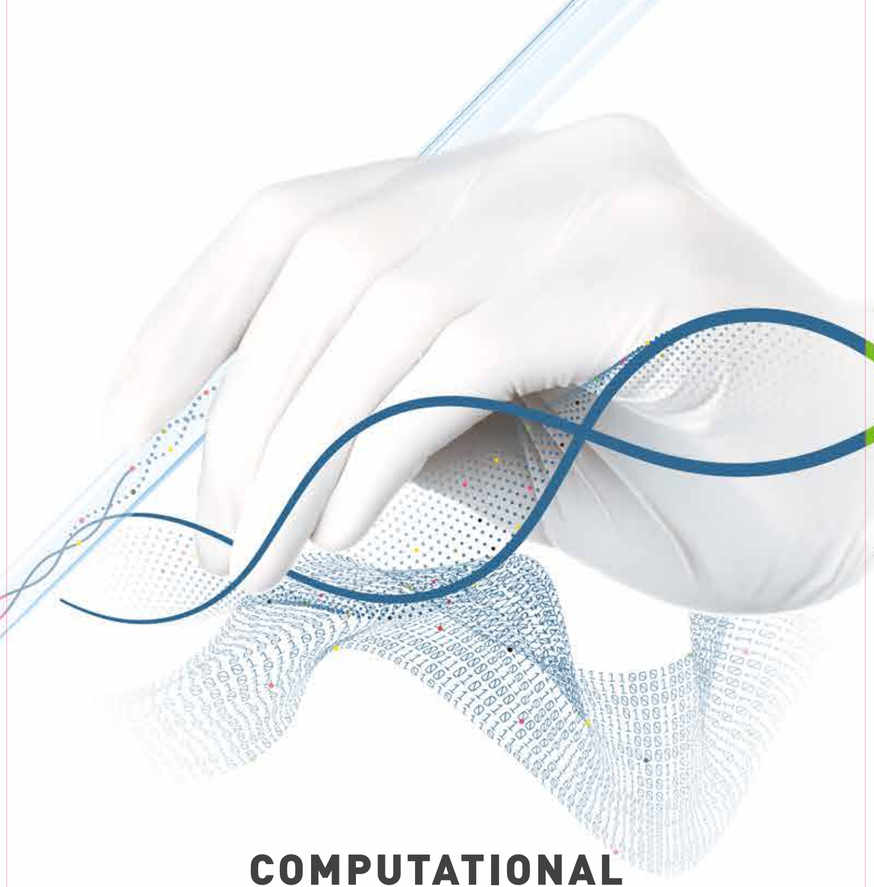

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