University of Zurich[UZH]

ITINERARE
Symposium
November 12th, 2021
University Children's Hospital
Zurich | 14:00 – 18:00

:magine

INSTITUT DES MALADIES GÉNÉTIQUES

Integrating research and care for rare genetic diseases:
the experience of the *Imagine* Institute (Paris) Stanislas Lyonnet

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS · Necker · MAIRIE DE PARIS · Inserm La science pour la santé From science to health · AFMTELETHON · INSTITUT CARNOT Imagine · INVESTIR L'AVENIR

GENETICS DISEASEs: CHALLENGES

>8,000 Rare diseases, 80% inherited

> 3 M
Individuals affected in France

> 60 M
In North America & EU

>1/3
OF PEDIATRIC EMERGENCIES

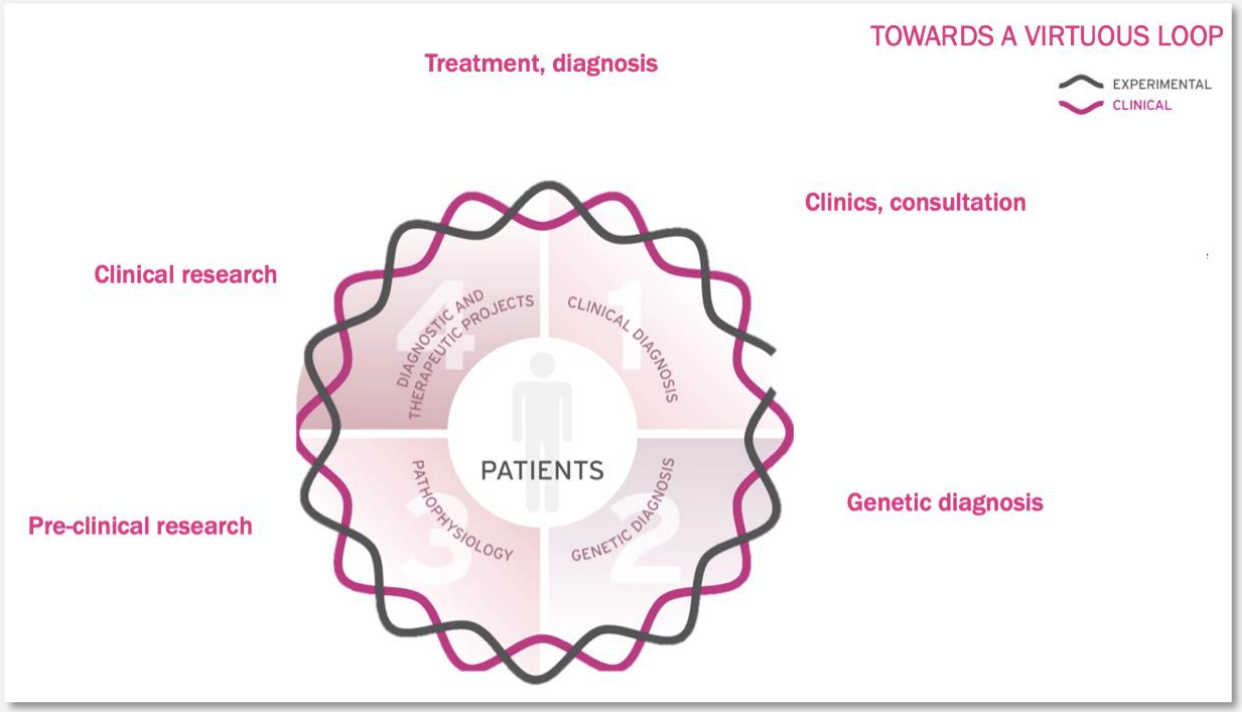
in the world involve genetic diseases

LIFE THREATENING / DISABLING

<10% Covered by treatments

>50% undiagnosed patients

TO CHANGE THE LIFE OF FAMILIES AFFECTED BY GENETIC DISEASES



TO NAME: Adequate and timely diagnostic → (40 to 80 %)

TO UNDERSTAND: Identify genes and mechanisms

TO TREAT: Innovative, transformative treatments →(10 to 20%)

TO DISSEMINATE and ADVOCATE: The knowledge in the field

Imagine was born to bring together in the same place all the forces to fight against genetic diseases.

On the campus of the Necker-Enfants malades, in the heart of Paris,

"*We imagined a place to bring together clinicians and researchers around patients*. »

Prof. Claude Griscelli,
1st President of the *Imagine* Foundation

Imagine: A brief (and recent) history…

2007

Imagine Foundation
Imagine CTRS

2008 - 2010

Details of the building
SAB meets
First core facilities

2011

Imagine becomes IHU
> University-Hospital Institute
First MD-PhD promotion

2012

First international call for lab directors

2014

Building opening and inauguration
Arrival of new teams

2015-2017

Heroes 1 & 2
Roadmap 2016-2025
Mid-term report ANR evaluation
Tremplin Carnot

2018-2019

HCERES assessment: UMR 1163
Heroes 3
Roadmap 2018-2028
Applies to IHU prorogation

IMAGINE's PEOPLE ans FIGURES 2020-2021

1,000
RESEARCH AND HEALTH STAFF GATHERED AROUND THE SAME CAUSE

24
BASIC AND TRANSLATIONAL RESEARCH GROUPS ON SITE

16
CORE FACILITIES

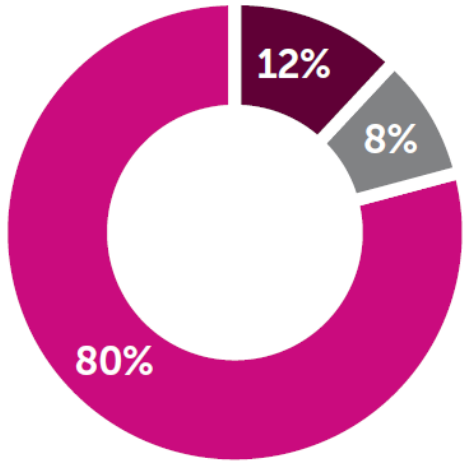
4
ASSOCIATED LABORATORIES AT NECKER-ENFANTS MALADES HOSPITAL

862
SCIENTIFIC PUBLICATIONS (IHU PERIMETER)

37
NATIONAL

31
OF PHD S
AND STUD

37
NATIONALITIES



- French
- European Union
- Outside the European Union

MORE THAN
30,000
CONSULTATIONS ON SITE

6
INTEGRATED CARE AND RESEARCH PROGRAMS (ICARPS)

25
AFFILIATED REFERENCE CENTERS FOR RARE DISEASES

6
AFFILIATED HOSPITAL UNITS

2
CLINICAL INVESTIGATION CENTERS

544
ONGOING CLINICAL STUDIES IN THE IHU PERIMETER

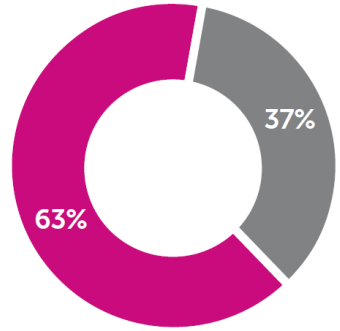
NEARLY
140,000
SAMPLES (BIOLOGICAL RESOURCE CENTER)

On 12/31/2019

537 PERSONS

472,07 FULL-TIME EQUIVALENT (FTE)

Breakdown of employees by gender on 12/31/2019



Female

Male

Publica-Private

A **Scientific Cooperation Foundation**

→ Public-private partnerships

A **labelled Institute**

→ University-Hospital Institute (UHI) since 2011

→ Institut Carnot – ANR Label since 2020

An **Inserm-Université de Paris** research unit (UMR)

Scientific Advisory Board (SAB)

Elizabeth Blackburn, Présidente
2009 Nobel Prize in Medicine
Department of Biochemistry and Biophysics, University of California, San Fransisco, USA

Iain Drummond
MDI Biological Laboratory, Bar Harbor, USA

Bernard Malissen
Center for Immunophenomics Marseille-Luminy, France

Antoine Triller
Institute of Biology of the Ecole Normale Supérieure, Paris, France

Stylianos Antonarakis
Department of Medical Genetics, University of Geneva, Faculty of Medicine, Switzerland

Denis Duboule
Laboratory of Developmental Genomics, Lausanne, Switzerland

Anthony Monaco
Tufts University, Medford/Sommerville, USA

Aravinda Chakravarti
NYU Grossman School of Medicine, New-York, USA

Douglas Higgs
MRC Weatherall Institute of Molecular Medicine, Oxford University, United Kingdom

Fiona Powrie
Kennedy Institute of Rheumatology, University of Oxford, United Kingdom

External evaluation

IMAGINE'S ADDED VALUE

A unique location

Support Team

Fundraising, development, communication, regulatory, technology transfer, administration

Conference space

Congresses
Education programs

Research labs

24 research teams

Research labs

24 research teams

Core facilities

Biobank

>150,000 samples

Physicians

31 Reference Centres
8 Clinical Units
3 Clinical Facilities (CIC, Database)

Statistics
Data-Science Center

Clinicla Invest. Centre

Patients

Families, patient's organizations
>35,000 consultations each year

Merge care and research

Integrated care and research programs (iCARPs)

Immunology Infectiology	Neuro-development	Development & cardiology	Nephrology	Hematology	Translational bioinformatics & computer decision support systems
Research laboratories					
Clinical research Rare disease center(s)					
Clinical services and labs					

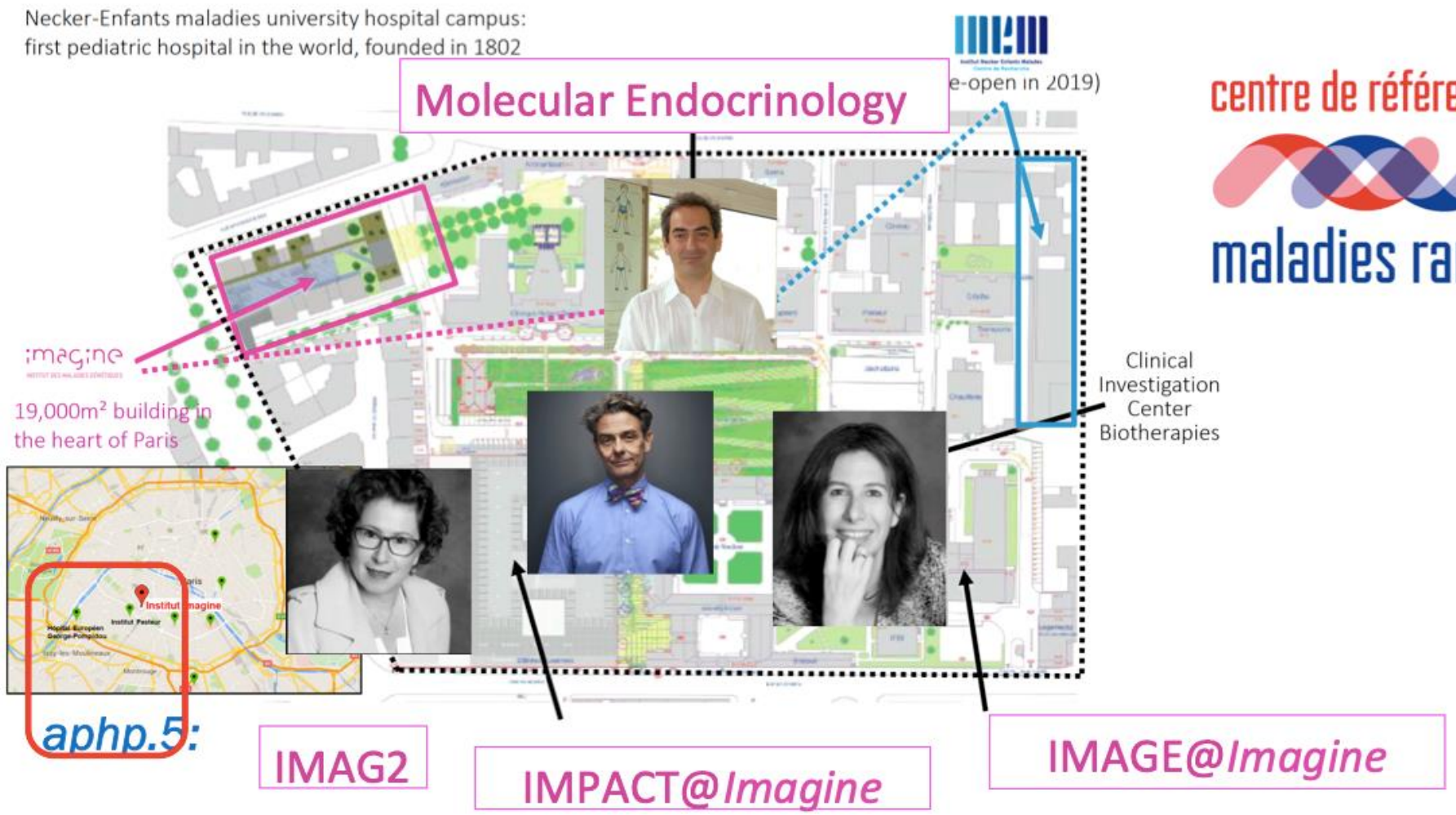
Imagine and SFR platforms

WP 1 Cohorts	WP 2 Genomics & Bioinformatics	WP 3 Patho-physiology	WP 4 Clinical research	WP 5 Scientific sourcing	WP 6 Training & education	WP 7 HSS & societal role	WP 8 Management organization development	WP 9 Hosted contracts	WP 10 Real estate

OPEN TO THE CAMPUS

To open to our Campus

Opening to new affiliated stakeholders



centre de référence maladies rares

Core Facilities

Preclinical platforms

Animal facilities (mice, zebrafish, drosophila)
Transgenesis CRISPR-Cas9
iPS Cells
Histology
Cell sorting
Cell imaging
Proteomics

Inserm

Translational platforms

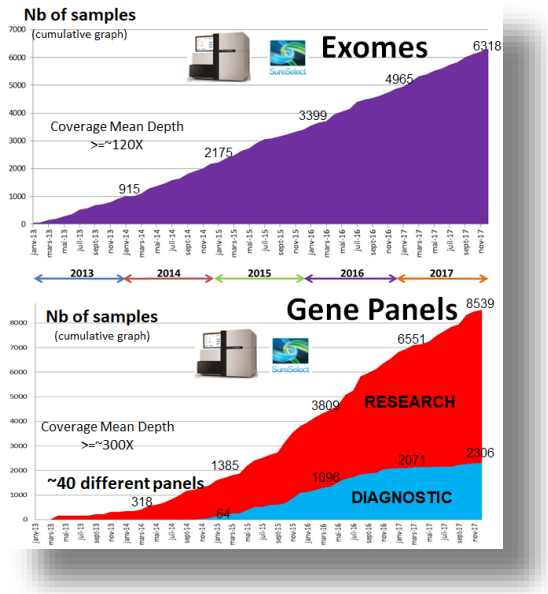
Genomics
Bioinformatics
DNA biobank
Clinical bioinformatics lab
Clinical databases & Warehouse

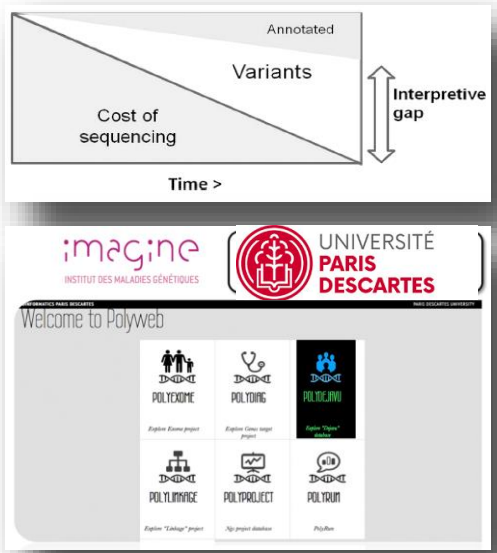
UNIVERSITÉ PARIS DESCARTES

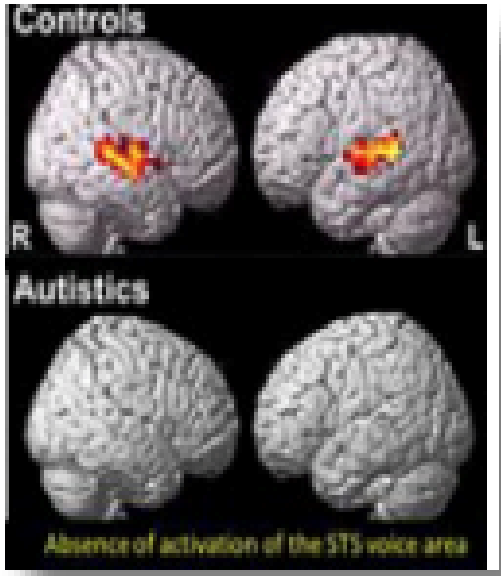
Clinical units

Biotherapy-CIC
Clinical Investigation Centers
Department of laboratory medicine
Innovative service of gene therapy
Image@*Imagine*

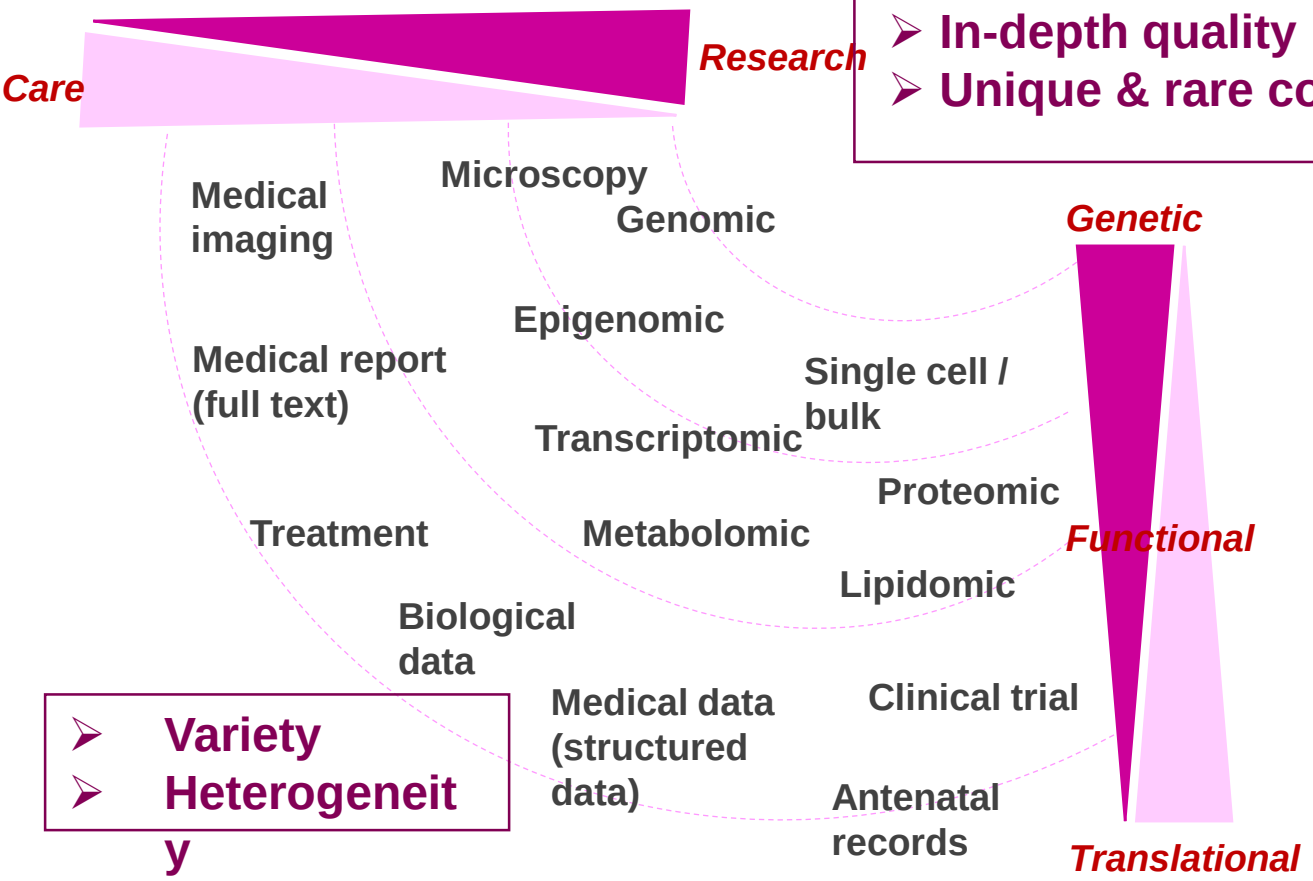
Necker ENFANTS MALADES
ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS







A Data-Centered Project



- In-depth quality
- Unique & rare cohorts

- Variety
- Heterogeneity

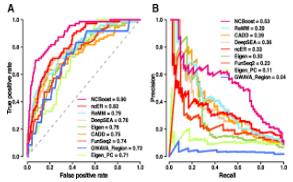
- High Throughput

770 000 Patients
8 M Medical Reports
53 M Structured Data

23 500 Exomes or Genomes
50 000 Panels
3 000 RNA-Seq
5 M single-cell librairies (#800 exp.)

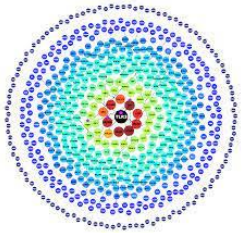
- Tools and achievements to date

Ncboost
CNV XPlorer
Cell-ID

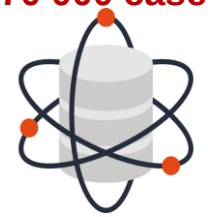


Clinical and Research Databases (125)

Human gene connectome



Biomedical Data Warehouse
Dr Warehouse
(770 000 cases)



Polyweb
(23500 WESWGS
3 000 RNA-seq)

Omics
Single cell
(5M lib. 800 Exp.)

Dr Warehouse

IMAGINE's added value

Partner with **industry**

Scientific results

DIVA
Business devt
Clinical reearch
Grant office

TTO@Imagine

Innogrant

Accelerator
2019-2020

Lab-in-labs
2019-2020

Crosslab

Imagine network
France Biotech
Medicen
Findmed
HHSF

Bioentrepreneurs

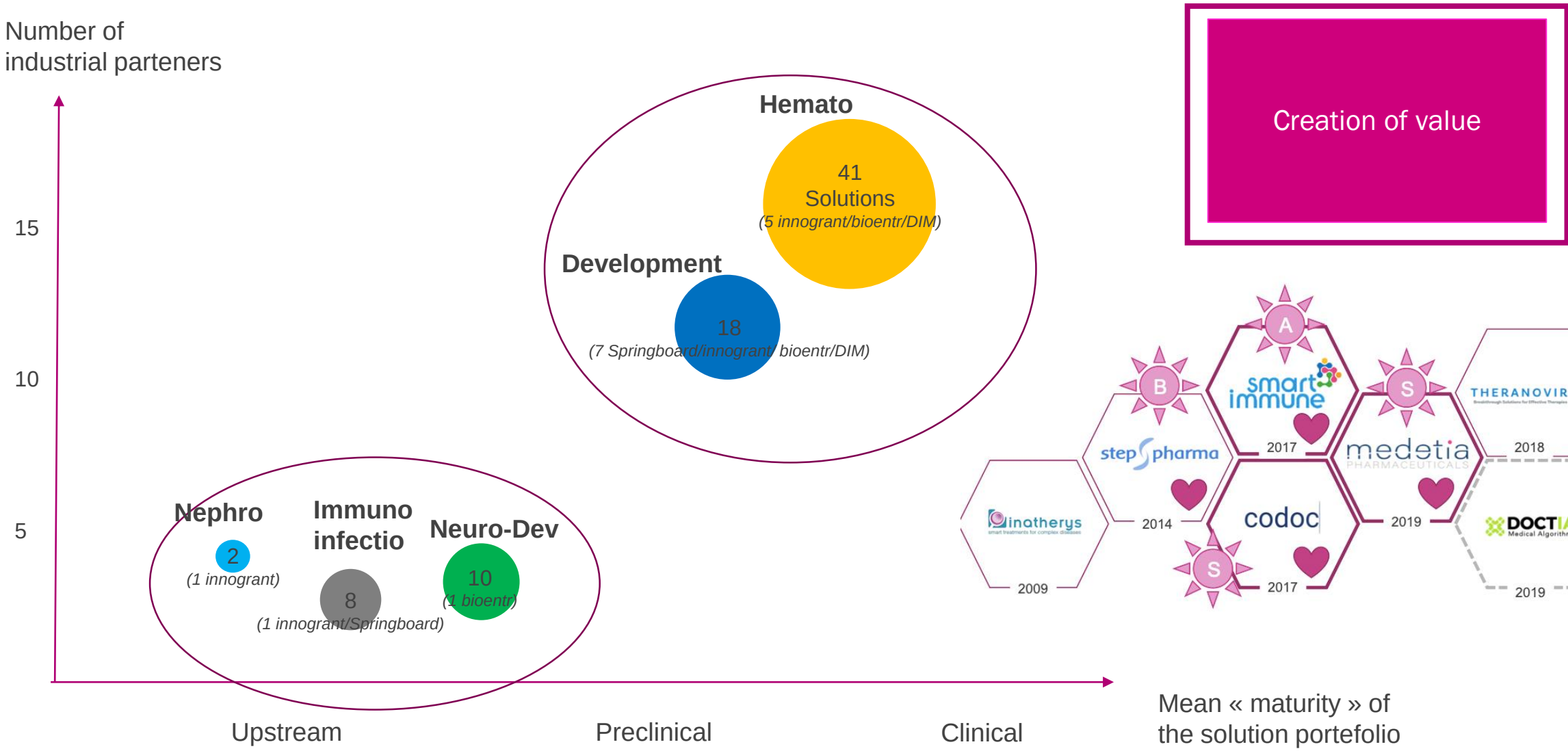
Innovation available to the patient

Sourcing **Funding** **Gathering**

Integration in clusters:

Medicen Paris, FinMed, France Biotech, Human Health Start-up Factory (HHSF)

Imagine Therapeutic Pipeline, Partnership and Start-ups



Creation of value

Fundraising

Tailored Medicine by Dior
2017-2020

La plus grande maison de haute-couture
invente la médecine sur-mesure à l'Institut *Imagine*

Exploring heterogeneity of T cells and HSPC in gene therapy trials for better safety and improved blood cell reconstitution

Pr Marina Cavazzana

Dior

IMAGINE's added value

Contribute to **national plans**

NATIONAL AND INTERNATIONAL STRATEGIC PARTNERSHIPS

Plan France Médecine Génomique 2025
SEQUOIA platform

Plan Maladies Rares 2018

EJP Rare Diseases

PRAIRIE: PaRis Artificial Intelligence Research Institute
French national program on Artificial Intelligence (3IA)

Imagine's Added Value (1): Prominent Figures

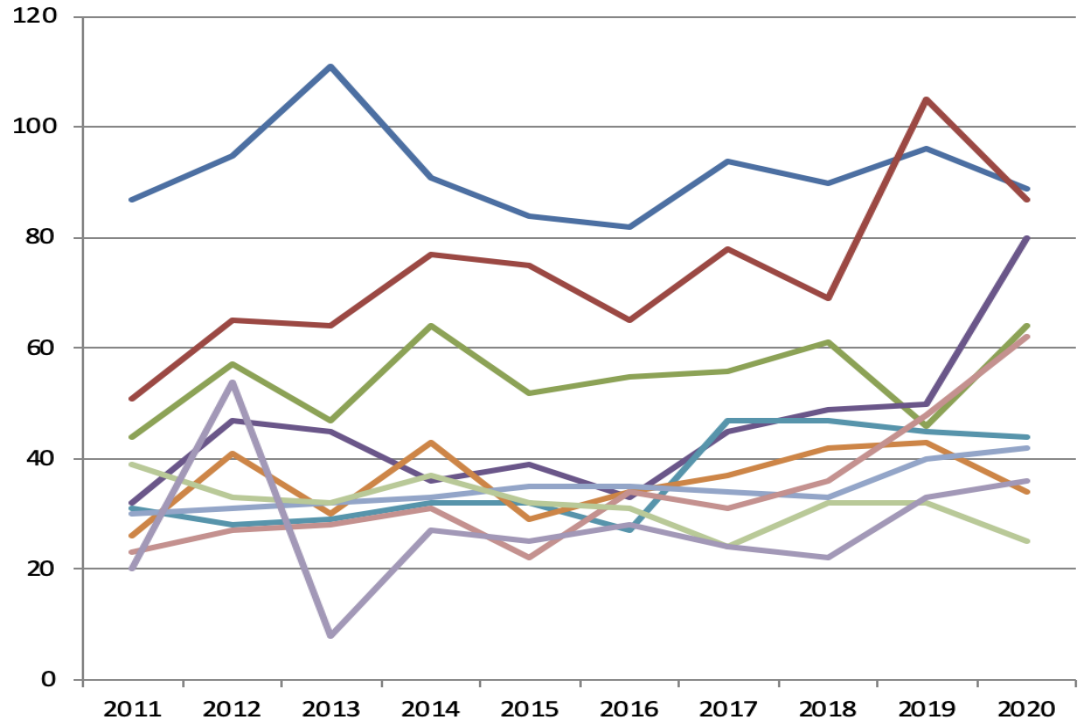
Major advances since the creation of *Imagine:*

- Identification of **250 disease genes**
- **35 clinical diagnostic tests** for more than 3,000 diseases,
- **World therapeutic « premières »** for sickle cell disease, beta-thalassemia, achondroplasia, interferonopathies…
- **61 potential treatments** under development
- More than **7,500 patients** included in clinical trials.

Imagine's Added Value (2): Scientific Publications 2011-2020

Web of Science Category	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	Total
Baseline for All Items	434	554	508	551	492	522	591	619	676	706	5653

Web of Science Category	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	Total	%
GENETICS & HEREDITY	87	95	111	91	84	82	94	90	96	89	919	16,3%
IMMUNOLOGY	51	65	64	77	75	65	78	69	105	87	736	13,0%
PEDIATRICS	44	57	47	64	52	55	56	61	46	64	546	9,7%
HEMATOLOGY	32	47	45	36	39	33	45	49	50	80	456	8,1%
MEDICINE, RESEARCH & EXPERIMENTAL	31	28	29	32	32	27	47	47	45	44	362	6,4%
INFECTIOUS DISEASES	26	41	30	43	29	34	37	42	43	34	359	6,4%
SURGERY	30	31	32	33	35	35	34	33	40	42	345	6,1%
CLINICAL NEUROLOGY	23	27	28	31	22	34	31	36	48	62	342	6,0%
BIOCHEMISTRY & MOLECULAR BIOLOGY	39	33	32	37	32	31	24	32	32	25	317	5,6%
DERMATOLOGY	20	54	8	27	25	28	24	22	33	36	277	4,9%



Imagine's Added Value (3): Attractivity

SAB recruitement

2014

Yanick Crow
Laboratory of neurogenetics and neuroinflammation

Découvrir la fiche de présentation du laboratoire

erc 2018

2014

Annarita Miccio
Chromatin and gene regulation during development

Découvrir la fiche de présentation du laboratoire

erc 2020

2014

Matias Simons
Epithelial biology and disease - Liliane Bettencourt Chair of Developmental Biology

Découvrir la fiche de présentation du laboratoire

erc 2020

2015

Sigolène Meilhac
Heart morphogenesis

Découvrir la fiche de présentation du laboratoire

2016

Antonio Rausell
The Clinical Bioinformatics lab

See the lab presentation

2017

A. Pierani

2017

M. Ménager

2018

E. Kabashi

erc 2015

erc

European Research Council

2022 CALL FOR

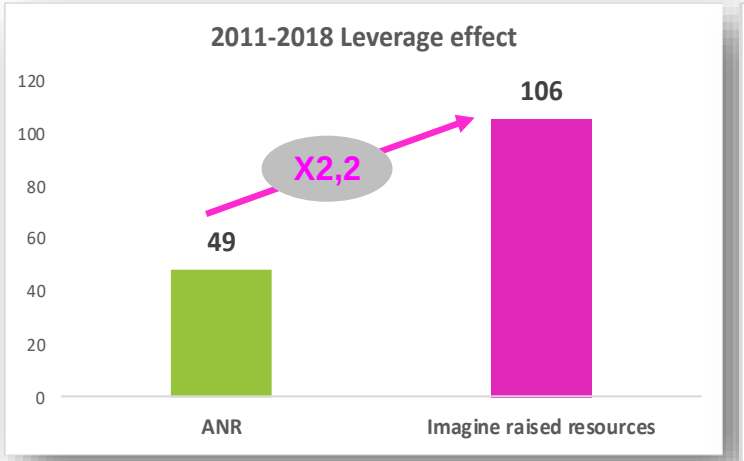
***IMAGINE* DIRECTOR ELECT**

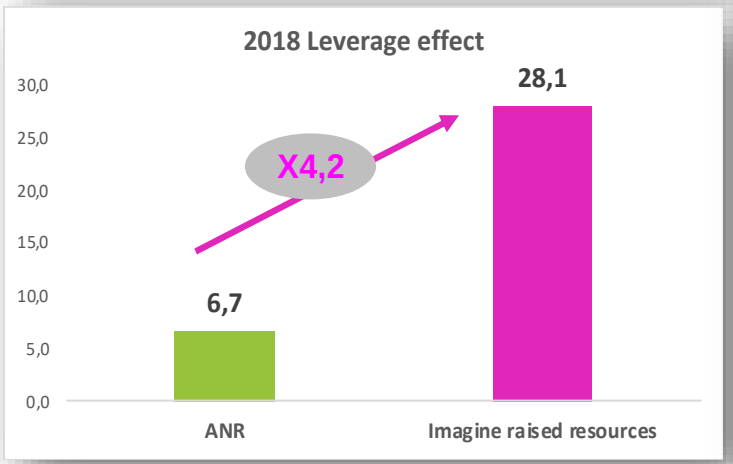
imagine
INSTITUT DES MALADIES GÉNÉTIQUES

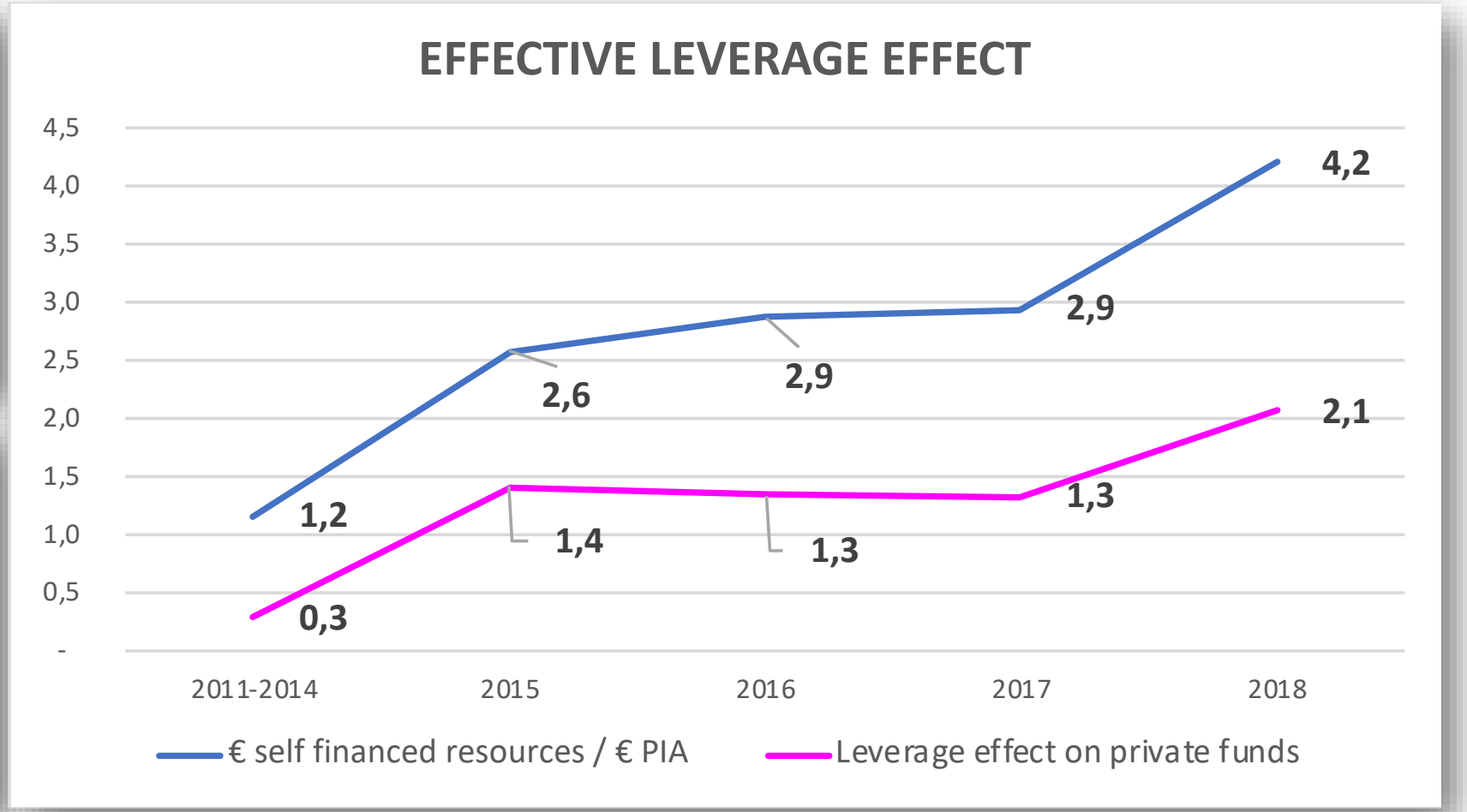
Group leader positions at *Imagine,* Institute for Genetic Diseases

INVESTIR L'AVENIR

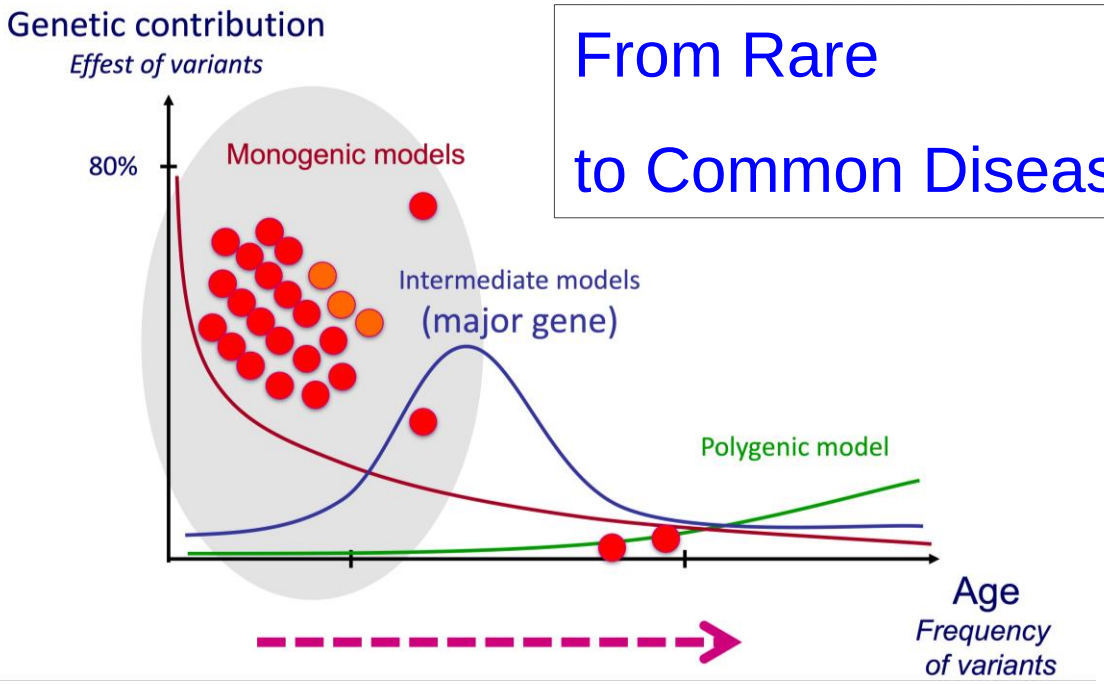
Imagine's Added Value (4): Leverage Effect







« Leverage effect»



From Rare to Common Diseases

Type 1 Interferon Deficiency: A Blood based Signature for Detecting Patients at Risk of Severe Covid-19 for a therapeutic approach

Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients.
Hadjadj J, Yatim N, Barnabei L, Corneau A, … , …, ……., Rozenberg F, Fischer A, Duffy D, Rieux-Laucat F, Kernéis S, Terrier B.

Covid-19: 15% of severe forms of the disease are due to genetic and immunological abnormalities.

Inborn errors of type I IFN immunity in patients with life-threatening COVID-19
Qian Zhang et al.

Auto-antibodies against type I IFNs in patients with life-threatening COVID-1
Paul Bastard et al.

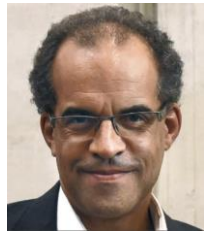
Science

JAMA Internal Medicine | Original Investigation

Effect of Tocilizumab vs Usual Care in Adults Hospitalized With COVID-19 and Moderate or Severe Pneumonia
A Randomized Clinical Trial

Olivier Hermine, MD, PhD; Xavier Mariette, MD, PhD; Pierre-Louis Tharaux, MD, Ph Philippe Ravaud, MD, PhD; for the CORIMUNO-19 Collaborative Group

JAMA Internal Medicine



From Child- to Adulthood

6 integrated care and research programs (iCARPs)

	Immunology Infectiology	Neuro-development	Development & cardiology	Nephrology	Hematology	Translational bioinformatics & computer decision support systems
Research laboratories						
Clinical research Rare disease center(s)						
Clinical services and labs						

Imagine and SFR platforms

imagine

INSTITUT DES MALADIES GÉNÉTIQUES

INVESTIR L'AVENIR

IHU FRANCE

Vielen Dank
Thank you

Integration

Genetics – Clinics

Basic– Translational

Children – Transition - Adults

Rare to Common

Innovation – Good practices

“ Public – Private ”