

Where Maths Meet Cancer

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ITMO Cancer - Aviesan

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aviesan ITMO Cancer

French National Cancer Institute (INCa)

- ▶ INCa is a National Health and Scientific Specialist Agency dedicated to cancer control.
- ▶ INCa is established under the Public Health Act of 2004 & reports to the Ministries of Health and of Research.
- ▶ INCa is supported by an International Scientific Advisory Board, an Ethics Committee, an Audit Committee and a Committee of Patients & Health Professionals.
- ▶ INCa has an annual budget of €100 million, half of which is allocated to research funding.
- ▶ INCa employs 150 people.
- ▶ INCa develops an integrated approach across the whole cancer control continuum : Surveillance, prevention, screening, care, research & information.

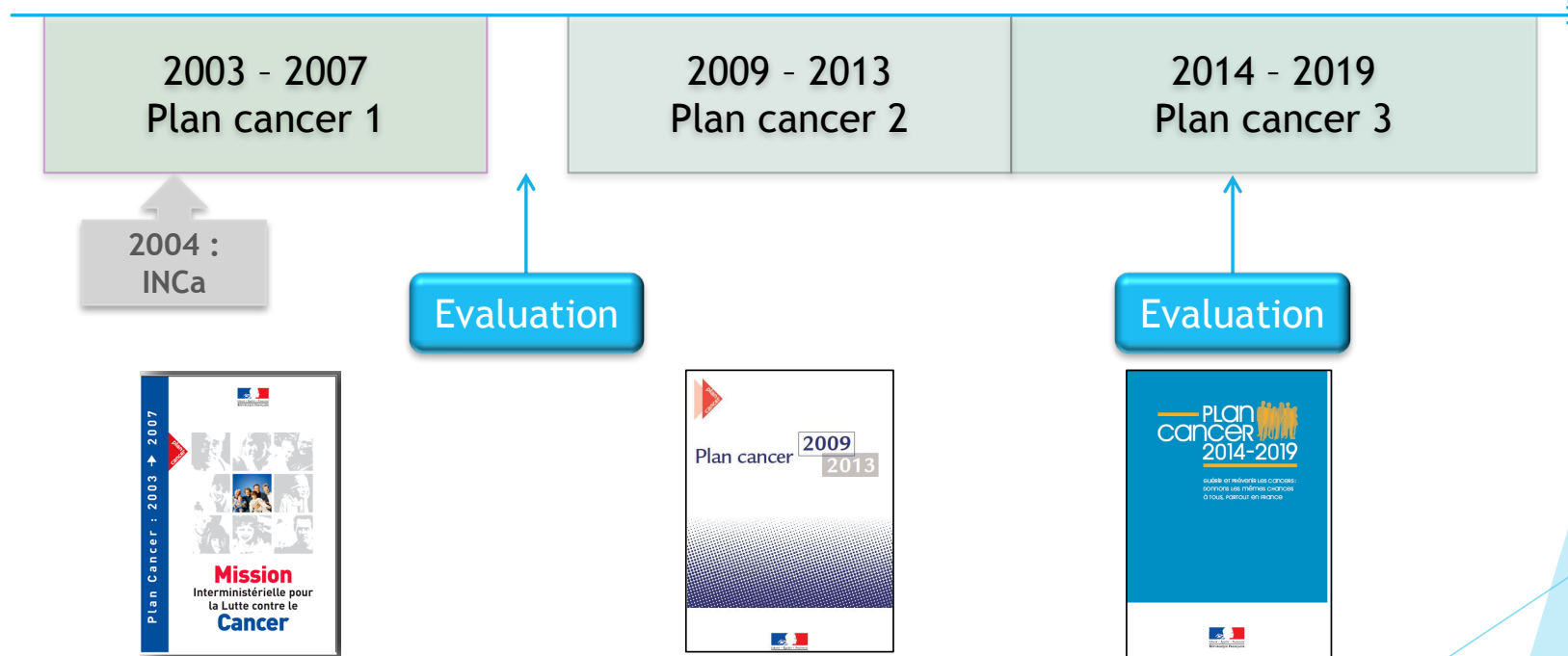


Aviesan

- ▶ Set up in 2009, the **French National Alliance for Life Sciences and Health (Aviesan)** groups the main stakeholders of life and health sciences in France to:
 - ▶ increase cross-disciplinarity by opening biology and medicine up to contributions from mathematics, physics, chemistry, information technology, engineering sciences, human and social sciences;
 - ▶ ensure that projects are consistent in thematic and infrastructure terms;
 - ▶ carry out clinical, economic and social promotion of knowledge, particularly by facilitating industrial partnerships;
 - ▶ define shared standpoints in terms of European research and international cooperation;
- ▶ These objectives is performed within 10 thematic multi-organization institutes (**ITMOs**) whose primary role will be to chair the strategic debates within their own scientific community

Governmental support in Cancer

An ongoing governmental commitment for over 10 years



The major missions in the framework of the National cancer control plan

Emerging and promoting the access

► to the scientific, technological innovations

Recurrent calls for proposals

Specific calls for proposals

Access to innovation

Cancer research structuring

Competitive programmes
International Scientific Evaluation

In all the research fields:
biology, translational, clinical and human and
social sciences-epidemiology-public health

Leading and coordinating the actions and the stakeholders...

Cancer research structures

- ▶ Integrated cancer research sites-SIRICs (8)
- ▶ Early-phase clinical trials centres-CLIP² (16)

Tools to foster Cancer research

- ▶ Molecular genetics centres (28)
- ▶ Clinical trial registry
- ▶ Mobile clinical research teams (26)
- ▶ Cohorts
- ▶ Tumour biobanks and biological & clinical databases (7)

Coordination of cancer research stakeholders

- ▶ Regional cancer hubs-Cancéropôles (7)
- ▶ Cooperative intergroups (13)
- ▶ Rare cancer networks (18)
- ▶ Public-private partnerships
- ▶ International partnerships
- ▶ Patient associations

Cancer Control Plan Funding Research 2017



€115 MILLION

INVESTED IN CANCER RESEARCH,
MULTI-YEAR FUNDING
(INCa, Ministry of Health, ITMO Cancer)



INCa HAS LAUNCHED AND OPERATED
11 CALLS FOR RESEARCH
PROPOSALS

899 SUBMITTED/ **192** PROJECTS FUNDED
12 PATIENTS REPRESENTATIVES INVOLVED IN
THE EVALUATION COMMITTEES

ITMO Cancer

- ▶ ITMO Cancer, is part of Aviesan, the French National Alliance for Life Sciences and Health, which gathers the main stakeholders of life and health sciences in France.
- ▶ ITMO, the theme-based multi-organization institute for Cancer, aims to
 - ▶ Federate all research teams working on cancer diseases regardless of their parent research organisation
 - ▶ Submit concrete actions to improve the performance and competitiveness of French research
 - ▶ Ensure proper coordination between all bodies and institutions involved in cancer research
 - ▶ Lead consultation
 - ▶ Facilitate interdisciplinary exchanges in the cancer community

ITMO Cancer

800 RESEARCH TEAMS



6,000 RESEARCHERS,
LECTURERS, ENGINEERS AND
TECHNICIANS FROM
UNIVERSITIES, HOSPITALS,
EPST AND INSTITUTES



€30 MILLION
INVESTED IN CANCER RESEARCH
PROGRAMMING
Cancer Plan Annual Funding

4 CALLS FOR
PROPOSALS

40,196 ARTICLES DURING
2011 TO 2015 PERIOD
(Source Cellule Mesures,
indicateurs, bibliométrie,
Inserm 2016)



7th WORLD RANK OF
PUBLICATIONS IN THE FIELD
(Source Cellule Mesures, indicateurs,
bibliométrie - Inserm 2016)

4th WORLD RANK OF TOP 1%
HIGHLY CITED PAPERS
(Source Cellule Mesures, indicateurs,
bibliométrie Inserm 2016)

“Physics, Mathematics and Engineering Science Applied to Cancer” (PMSI) Call (1)

Aims:

- ▶ attract physicists, mathematicians and engineers to the question of cancer
- ▶ support multidisciplinary research to help the understanding, diagnosis or treatment of cancer
- ▶ 108 projects funded and led by 247 teams (2011 and 2017)
- ▶ Close to half of the coordinators with no or little experience of cancer
- ▶ Mathematicians partners in almost half of consortia

The two day report seminar in April 2018 demonstrated deep interactions between physicists, mathematicians and cancer biologist/clinicians to the question of cancer in this programme

“Physics, Mathematics and Engineering Science Applied to Cancer” (PMSI) Call (2)

Topics:

- ▶ Imaging (including signal treatment tools)
- ▶ Radio- or Hadron-therapies (including dosimetry, Monte Carlo simulations)
- ▶ Modelling and biophysics (including models of tumour growth and responses to irradiation or nanoparticles)
- ▶ Nanotechnologies
- ▶ Innovative therapies

Led to insights on tumour growth, tumour cells stiffness, effects of irradiation, nanoparticle behaviour...
Production of tools, devices, new algorithms

“Systems Biology” Call

Aims:

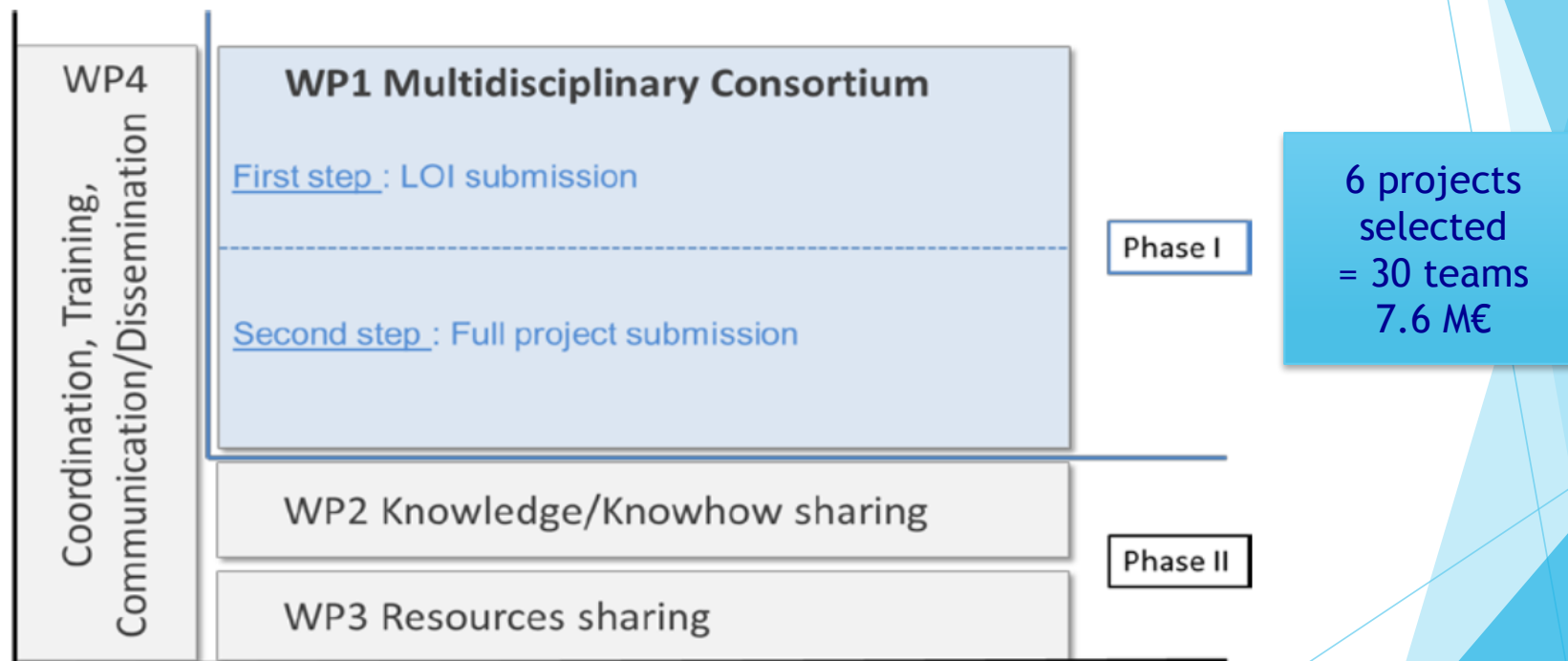
- ▶ support research using integrative approaches and modelling related to cancer biology questions
- ▶ 26 projects led by 80 teams funded between 2012 and 2017

Topics:

- ▶ Models of regulatory pathways, mitotic spindles...
- ▶ Tumour/metastases growth models
- ▶ Data analysis pipelines (integration of mass spec data and protein-protein interactions data, RNAseq)
- ▶ Software for automatic mitotic event detection in microscopy

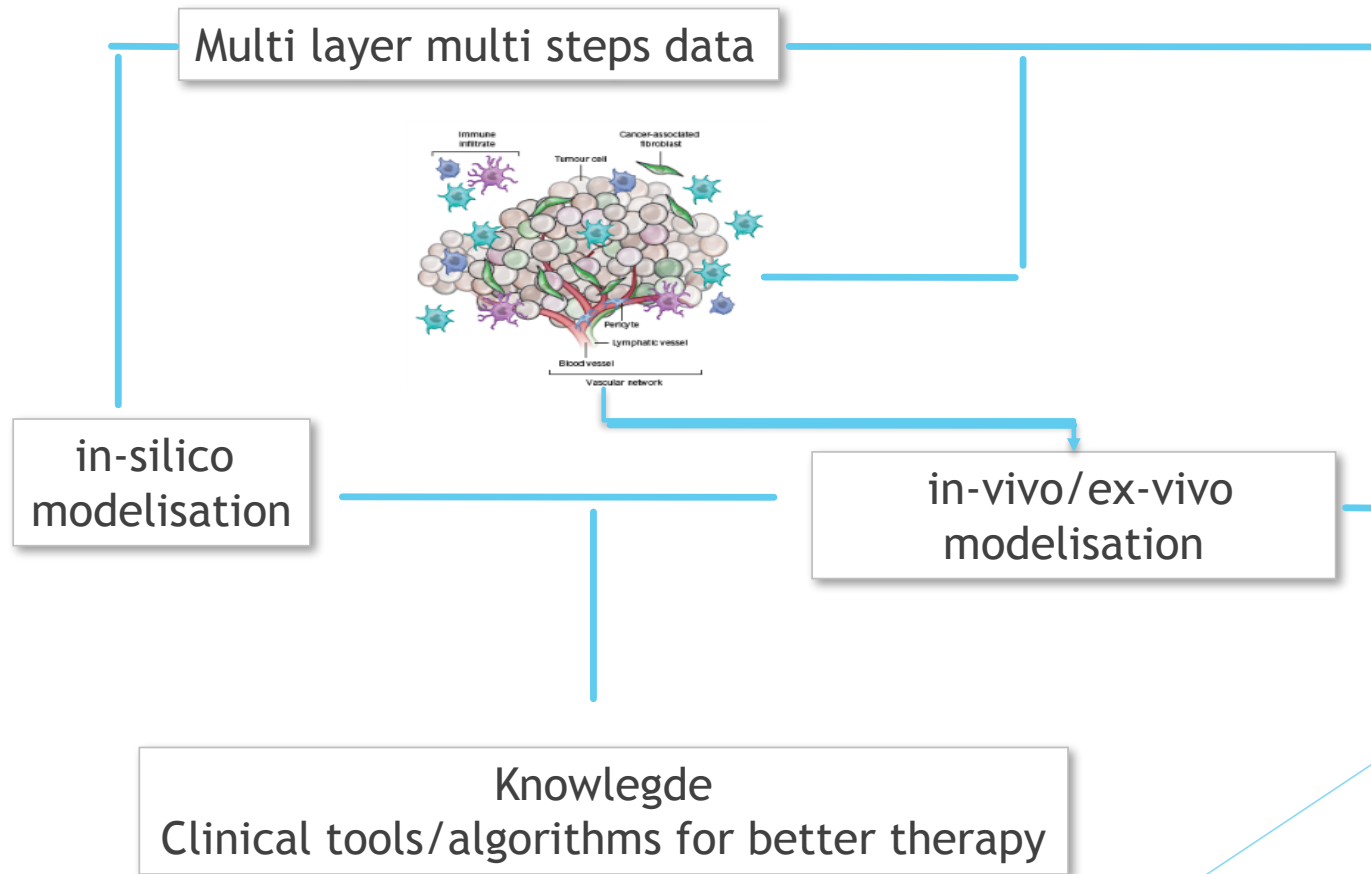
Allowed the identification of potential metabolic pathways, driver mutations, splicing variants, biomarkers or therapeutic targets...

« Tumor Heterogeneity and its ecosystem » « THE » call and consortia

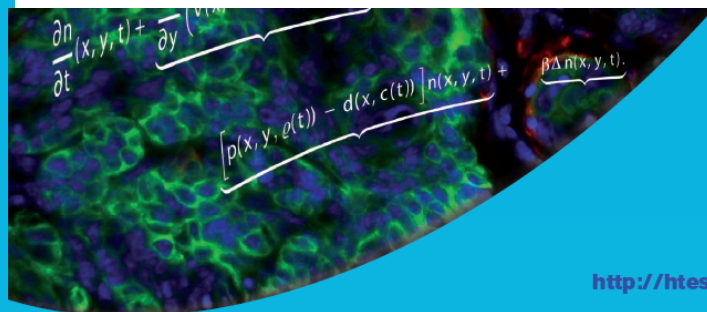


Programme HTE

« THE Program »



First workshop Mathematical modelling



February 28, 2017

INTS auditorium
6, rue Alexandre Cabanel
Paris 15^e

<http://htesymposium.sciencesconf.org>

First THE workshop

MATHEMATICAL MODELLING OF TUMOUR HETEROGENEITY IN TUMORAL ENVIRONMENTS, AND ITS IMPACT ON THERAPIES

Organizers: Jean CLAIRAMBAULT, Irène BUVAT, Christine CHOMIENNE

Speakers:

Helen BYRNE, Oxford (UK)
Trevor GRAHAM, Queen Mary University of London (UK)
Roeland MERKS, CWI (NL)
Gregory NUEL, CNRS, LPMA, UPMC, Sorbonne Universités, Paris (FR)
Benoît PERTHAME, LJLL, UPMC, Sorbonne Universités, Paris (FR)



Maths meet Cancer in 2020 and beyond....

Towards a new dimension of understanding of oncogenesis (1)

Massive data era
one of the most impressive technological revolutions accompanying scientific achievements

Variety of data constantly growing

capitalise on
massive data
resources

Abundant methods, data contribute to the growing knowledge on cancer

.....but still very few genes have been
annotated (molecular network, location,
function, etc.),
new hypotheses should to be tested

Maths meet Cancer in 2020 and beyond....

. Towards a new dimension of understanding of oncogenesis (2)

- ✓ Use and improve reference methodologies for **database production**,
- ✓ Require **reproducible and good quality data**
- ✓ Encourage the **sharing of data**
- ✓ Contribute to an international collective effort in building data banks
- ✓ Support and develop research into biomedical **data mining methods**.

Vast heterogeneous data banks
constitute new experimental
material

prioritise
information quality
and
representativeness
over quantity

Maths meet Cancer in 2020 and beyond....

Data should be adequately formatted
clinical annotations need to be stated in a comprehensive
reliable, precise and, if possible, standard manner.

Software to explore sequences, **particularly non-coding sequences**, not previously studied
needs to be developed.

Dialogue with researchers is
also required, before
embarking on data
collection.

Maths meet Cancer in 2020 and beyond....

Towards a new dimension of understanding of oncogenesis (3)

- Cell proliferation- Cell deaths- Differentiation-Plasticity
- Evolution of cancerous and non cancerous cell populations
- Interaction of cancerous and non cancerous clones
- Subcellular representation of molecular complexes
- Representation of tumour/stroma interactions (competitive or mutualistic),
- Representation and control of molecular targets at single-cell level.

New Concepts

New
pathways

New
mathematical
approaches

Maths meet Cancer in 2020 and beyond....

Towards a new classification of cancers

- At the molecular level, large-scale, high-throughput and cell imaging techniques allow a very large number of variables to be analysed simultaneously at different times applied to a growing number of tumour types
- Stratification of cancer by means of “omic” technologies (genomics, epigenomics, transcriptomics, proteomics, metabolomics, etc.)
- The ability to identify and validate new parameters among the vast data has become indispensable.

**New
dimension
to shed light
on
complexity**

In-depth characterisation of the biosignature of each tumour in space (its environment) and time (throughout its evolution, from initiation to possible relapse)

Maths meet Cancer in 2020 and beyond....

Translational research: from precision to personalized medicine (1)

- optimisation of **biomarker panels** that include several parameters (comprising genetic, epigenetic, proteomic factors) for a given patient
- Universal high-performance companion diagnostic tests
- **Validation platforms** on a national scale,
- construction of **robust databases**
- **biobanks** meeting standard quality criteria for the preparation, storage and annotation of samples,

Successful
large-scale
harmonisation
of methods

Capitalise
on massive
data
resources

Mathematical
approaches and new
algorithms to
integrate these
multiple parameters
need to be developed

Maths meet Cancer in 2020 and beyond....

Translational research: from precision to personalized medicine (2)

◆ Novel basis for multidisciplinary drug design research:

- comparison of new genomic and, particularly, proteomic and biochemical data and existing chemical libraries)

◆ Develop chemobiology

◆ Integrate data from in vitro- in vivo-in silico experimental models

◆ Develop new predictive methods:

- Patient population studies using public health-type statistical studies, Collection of digital data banks (samples, images, clinical records, environmental, behavioural, nutritional and family data, or even data relating to physical exercise at various stages in life

Mathematical
modelling based
on adaptive
dynamic studies

Develop methods for
stratification of
responders and
prediction

avies

Concluding remarks

Multidisciplinary task forces are needed to rethink the way in which cancer research is tackled

- Take into account the evolution of digital technologies
- Use dedicated exploratory methods
- Lean on artificial intelligence, statistical learning and semantic enrichment
- Require validation by experts

- ✓ to elucidate the complexity of cancer
- ✓ to enable the emergence of original knowledge
- ✓ to effectively prevent and treat cancer

Final wish

Multidisciplinary expertise and interaction between researchers, molecular biologists, clinical practitioners, pathologists, imagers and bioinformaticians, mathematicians ...

Place each cancer research team in contact with different disciplinary research laboratories to develop explanatory and predictive models

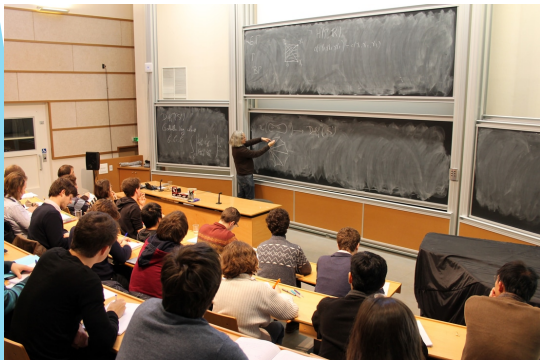
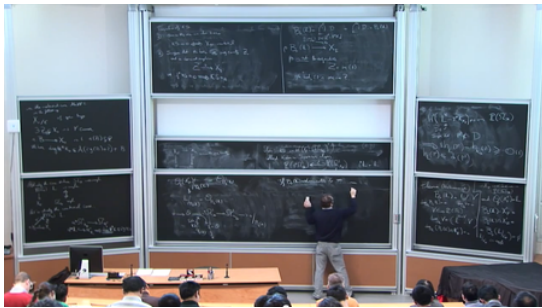
Second conference CIRM

CIRM's aim is to give researchers in mathematical sciences the opportunity to present recent research results and to initiate future collaborative research projects.

Interdisciplinarity is also important and conferences should have the highest quality leadership and attract international participation

Share latest discoveries in mathematical sciences
To progress on core questions in this discipline
Prepare ambitious projects in collaboration with other sciences

Ensure transfer of knowledge towards **young researchers**



ITMO Cancer

ITMO CANCER DIRECTION

- ▶ Christine Chomienne: Director
- ▶ Alain Eychenne: Deputy Director
- ▶ Muriel Altabef: Associate Director
- ▶ Laurent Delva (INSERM Councillor)
- ▶ François Castagner (ExPost Project Manager)
- ▶ Kehlia Sendeyo (New Programs- Project Manager)
- ▶ Diana Keremian

ITMO CANCER EXPERTS

- ▶ *François Berger*
- ▶ *Jean-Paul Borg*
- ▶ *Irène Buvat-Guillemet*
- ▶ *Salem Chouaib*
- ▶ *Jean Clairambault*
- ▶ *Jacqueline Clavel*
- ▶ *Yvan De Launoit*
- ▶ *Olivier Delattre*
- ▶ *Annick Harel-Bellan*
- ▶ *Claude Leclerc*
- ▶ *Fabrice Pierre*
- ▶ *Ariel Savina*
- ▶ *Eric Solary*

<https://itcancer.aviesan.fr>