

# JIB | JOURNÉES DE L'INNOVATION EN BIOLOGIE

**MÉDECINE PERSONNALISÉE, MÉDECINE PRÉDICTIVE...  
LE BIOLOGISTE MÉDICAL HOSPITALIER OU DE VILLE A-T-IL SA PLACE PAR LA PRESTATION DE CONSEIL ?**

Capitaliser sur  
les expériences



pour enrichir  
le présent

en intégrant  
les scénarios  
long termes

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***Cancérologie Radiothérapie***  
***Institut de Cancérologie HARTMANN***  
***Institut RAFAEL***



Rafaël

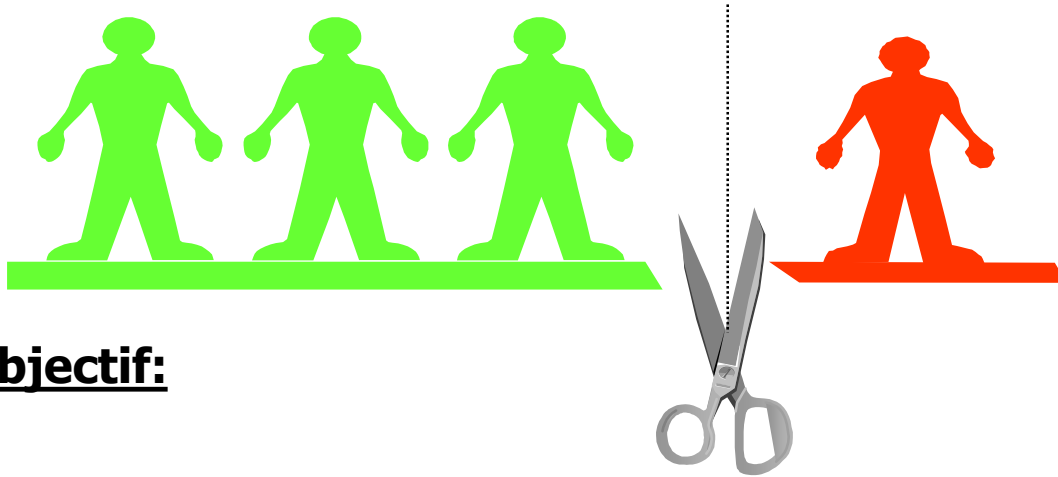
## 18<sup>e</sup> siècle

**« L'art de la Médecine consiste à distraire le malade,  
pendant que la Nature le guérit »**



**VOLTAIRE**

# La Statistique $\neq$ Médecine personnalisée



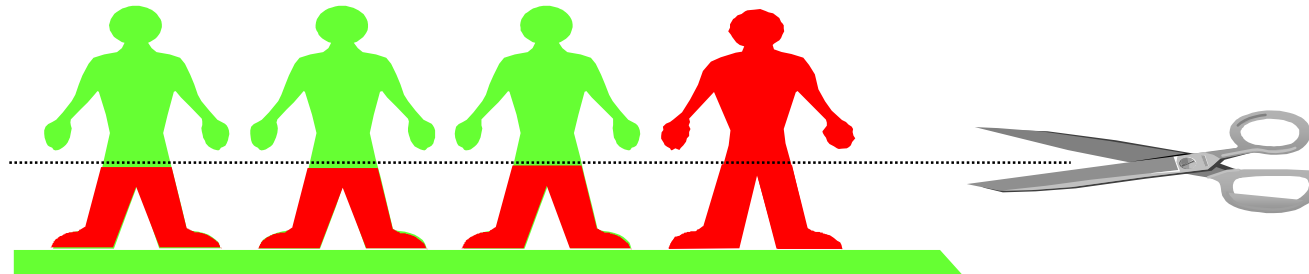
Un seul patient rechutera

$\Rightarrow$  Ce patient seul recevra un traitement maximal

**Objectif:**

**Réalité:**

please cut here



Statistiquement, chaque patient a un risque de rechute.

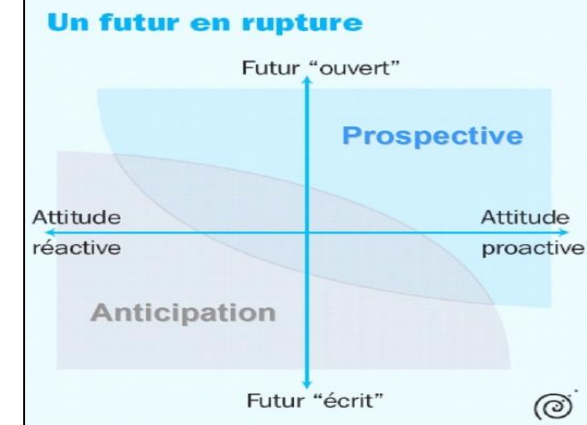
$\Rightarrow$  Chaque patient reçoit un traitement maximal, "probablement" efficace

# Prospective : comment traitera-t-on les tumeurs rénales et prostatiques et urothéliales dans 10 ans ?

*Prospective: How will renal, prostatic and urothelial tumours be treated in 10 years?*

Alain Toledano<sup>a,\*,b</sup>, Mayada Bourmech<sup>a</sup>, Hanah Lamallem<sup>a,b</sup>, Marc Bollet<sup>a,b</sup>, Olivier Bauduceau<sup>a,b</sup>, Pascal Pujol<sup>a,b,c</sup>, Patrick Bloch<sup>b</sup>, David Khayat<sup>a,b</sup>

*A. Toledano et al. / Néphrologie & Thérapeutique 13S (2017) S115-S125*



Génétique

Nanomédecine

Imagerie Moléculaire

Bioinformatique

Théranostique



NBIC

Impression 3D

Médecine Digitale

Santé connectée

Robotisation

Nouveaux Modèles de Recherche

Xéno patients- Avatars

## Le Futur :

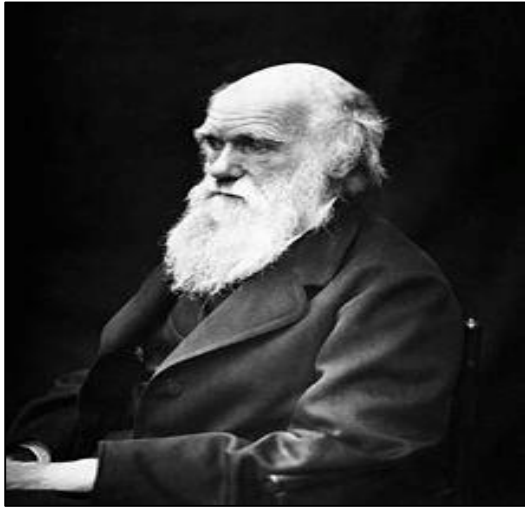
- En rupture ou en continuité ?
- Changement immédiat ou différé ?
  - Ouvert ou fermé ?

## PROSPECTIVE A 10 ANS ...

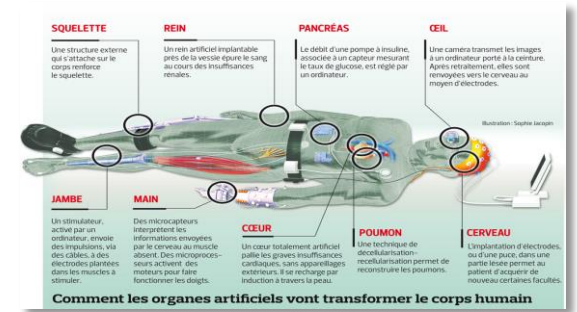
La **prospective** n'a pas pour objet de **prédire** l'avenir, de nous le dévoiler comme s'il s'agissait d'une chose déjà faite, mais de nous aider à le **construire**



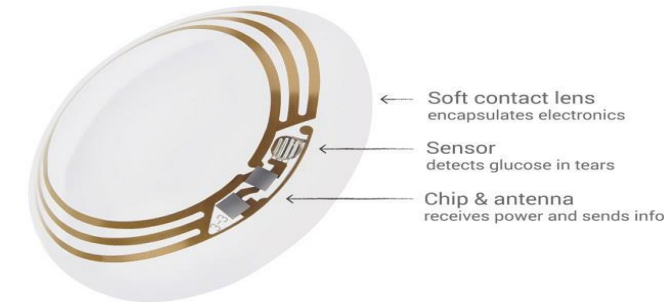
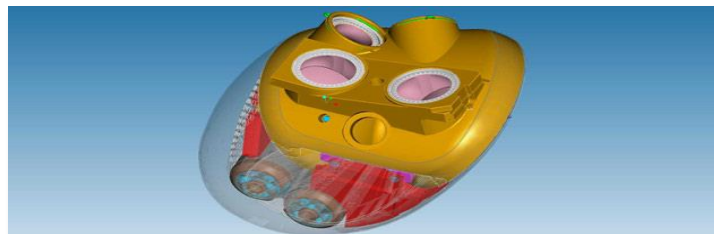
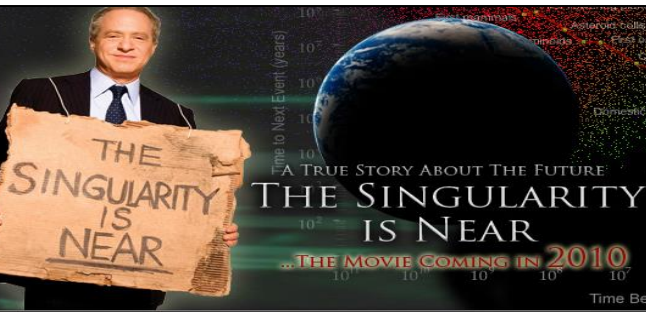
# Modification Culturelle

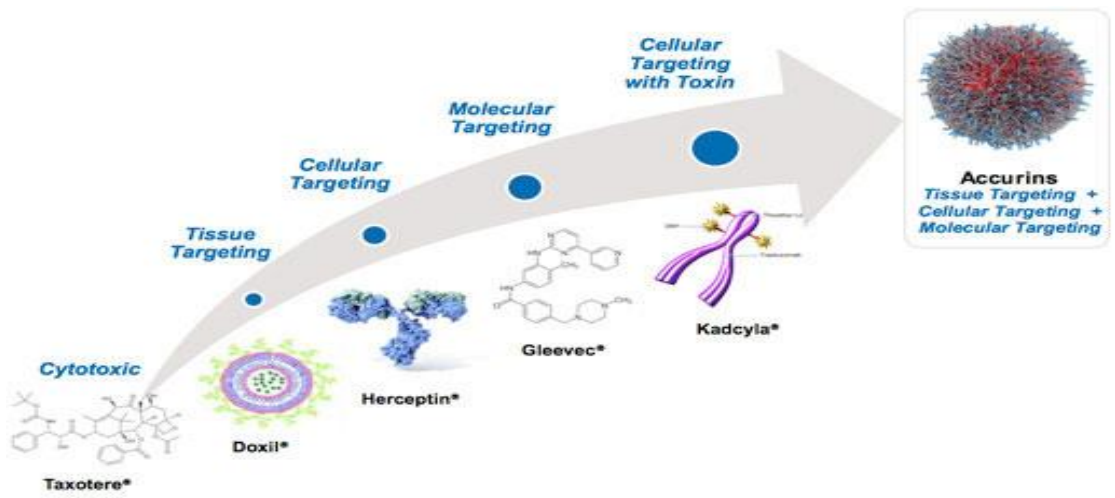


Charles Darwin, 1869

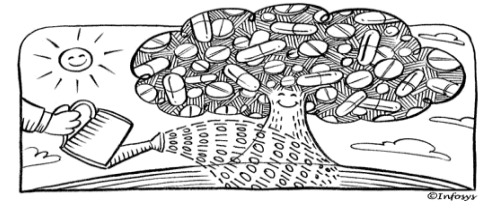


Ray Kurzweill, 2013





# NEW DRUGS



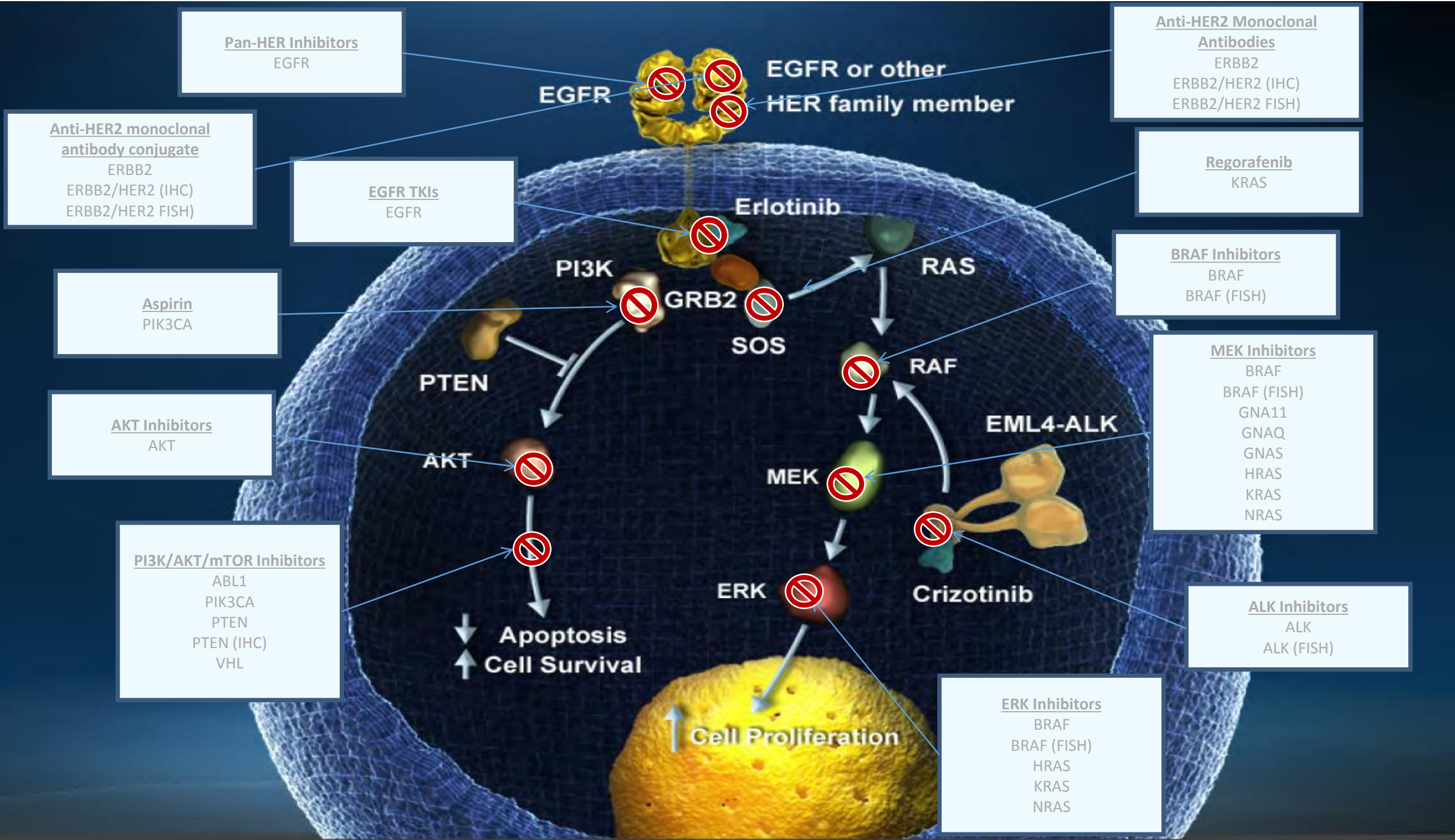
*« Les médecins administrent des médicaments dont ils savent très peu, à des malades dont ils savent moins, pour guérir des maladies dont ils ne savent rien.. »*



VOLTAIRE

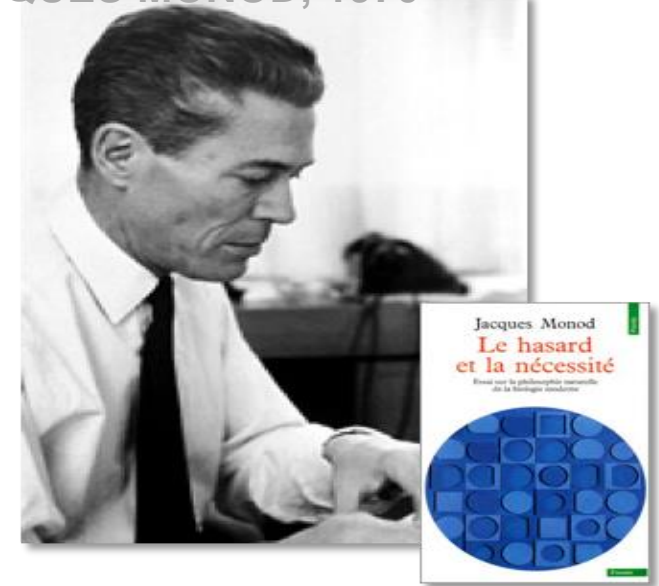






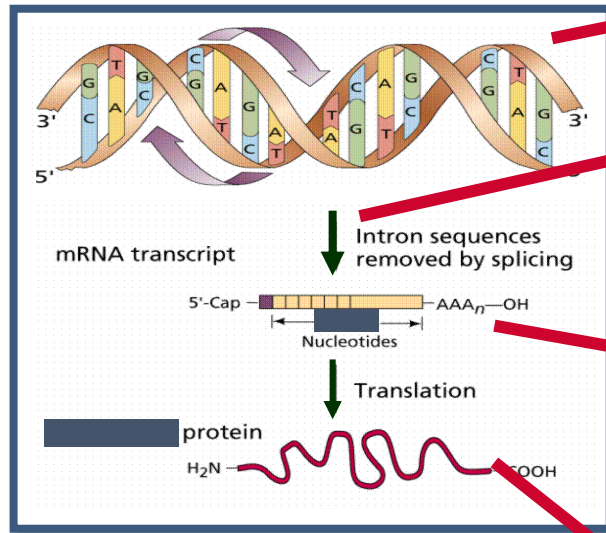
# LA REVOLUTION GENETIQUE

JACQUES MONOD, 1970



« La taille moléculaire de l'ADN interdit, sans doute à tout jamais de modifier le génome »

Continuum

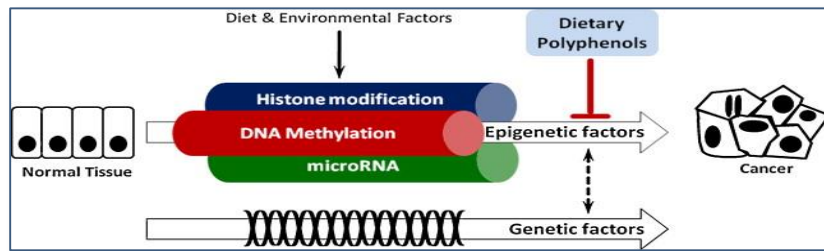


Genomics

Epigenomics

Transcriptomics

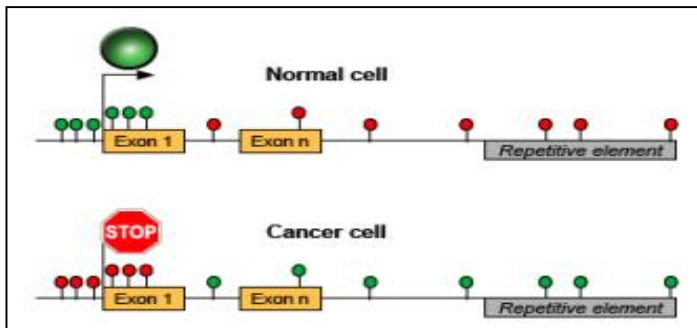
Proteomics



< 10 000 bases DNA during a whole life



50 milliards per hour

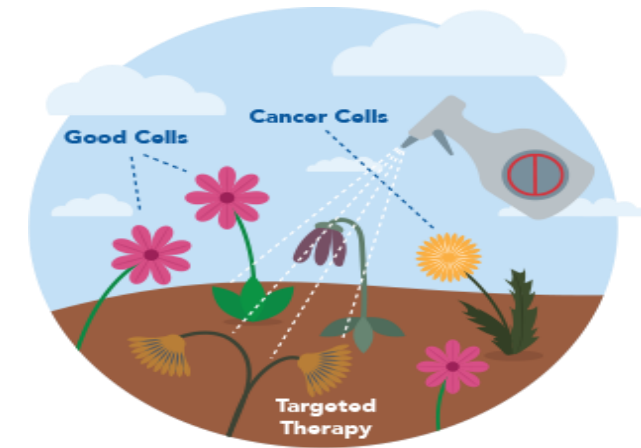
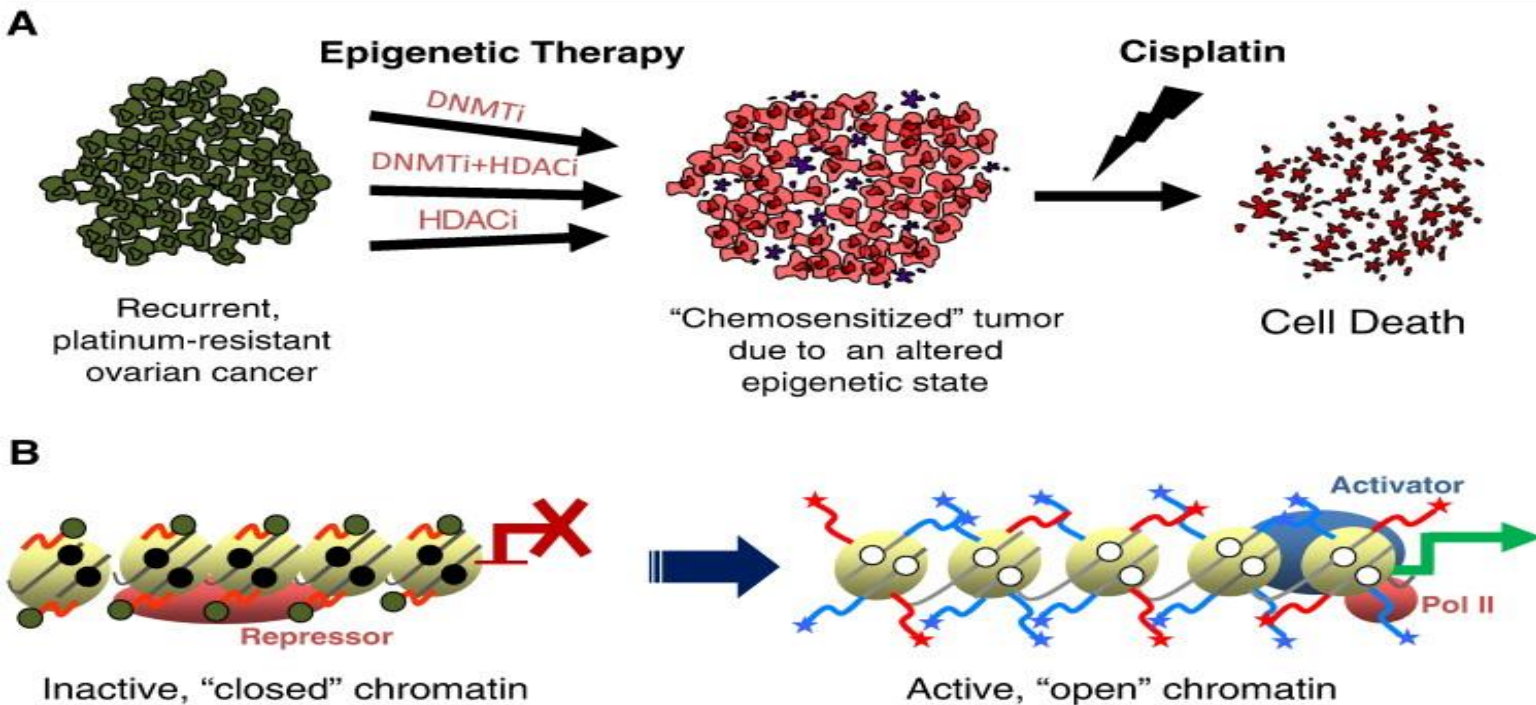
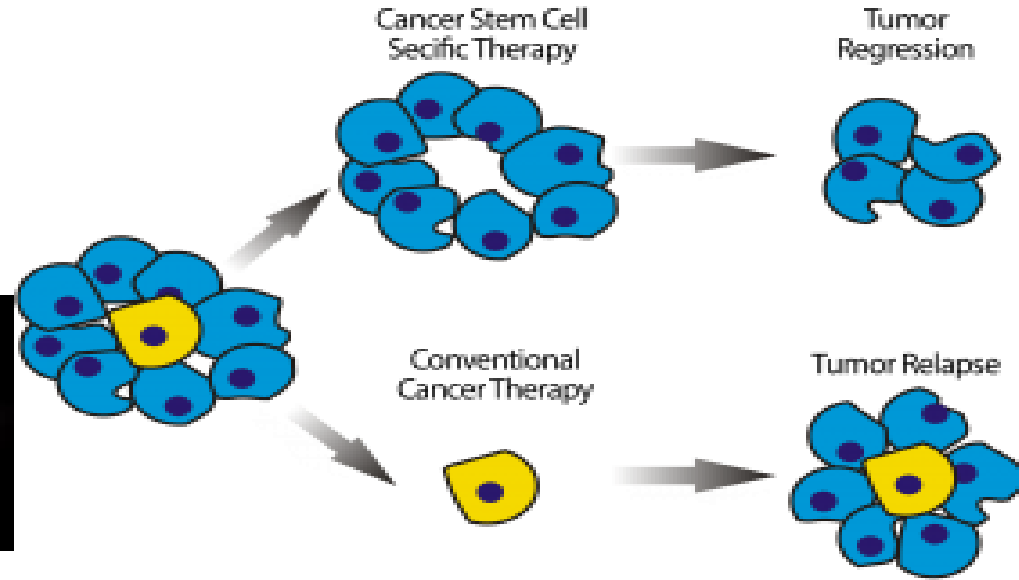


Next Generation Sequencing





# EPIDRUGS



**Détruire les cellules souches tumorales**

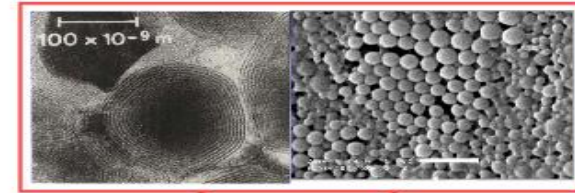
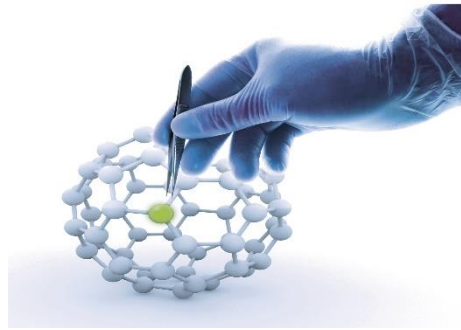
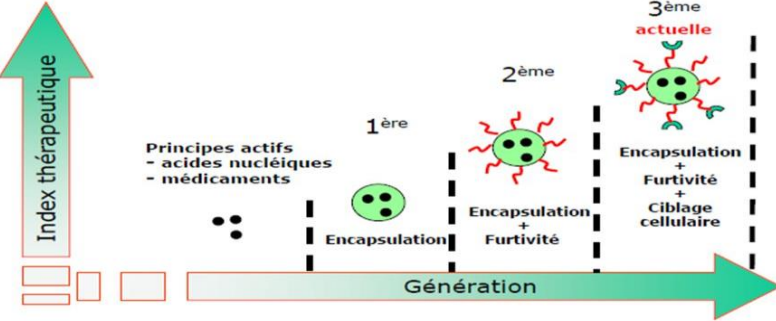


CURRENT CONCEPTS

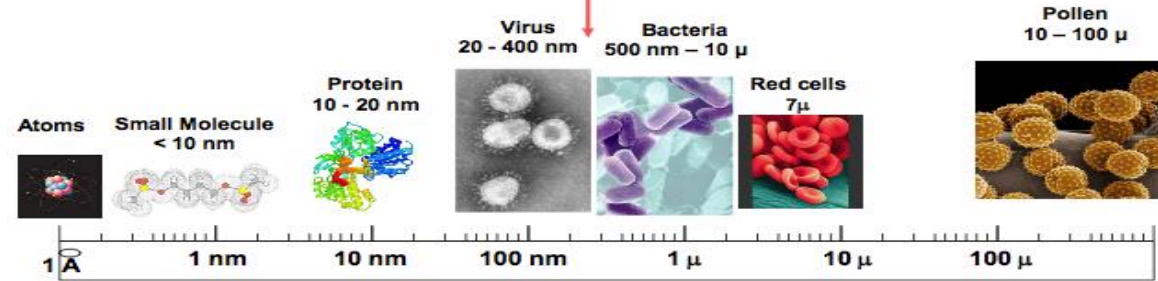
# Nanomedicine

Betty Y.S. Kim, M.D., Ph.D., James T. Rutka, M.D., Ph.D.,  
and Warren C.W. Chan, Ph.D.

## La Vectorisation et nanovecteurs



Ils ressemblent aux particules naturelles

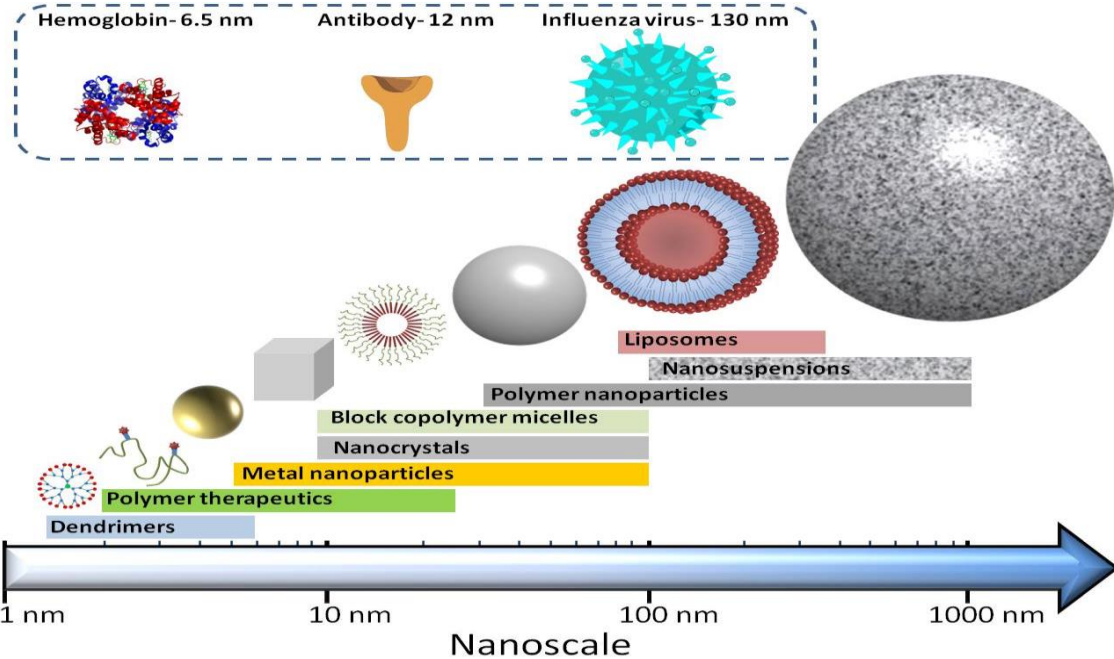


## Double défi des nanomédicaments:

PROTÉGER la molécule active de la dégradation par les enzymes de l'organisme

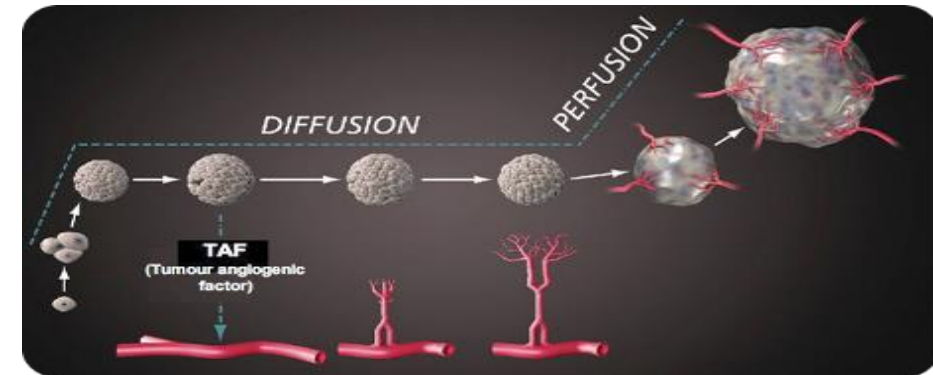
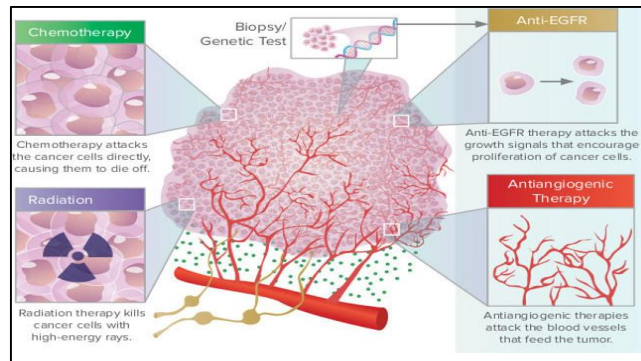
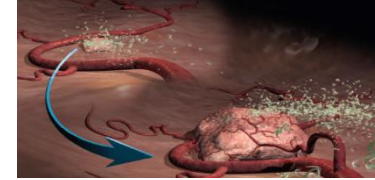


ADRESSER sélectivement vers le tissu ou cellule cible, et d'en contrôler la libération.



# ANGIOGENESE TUMORALE

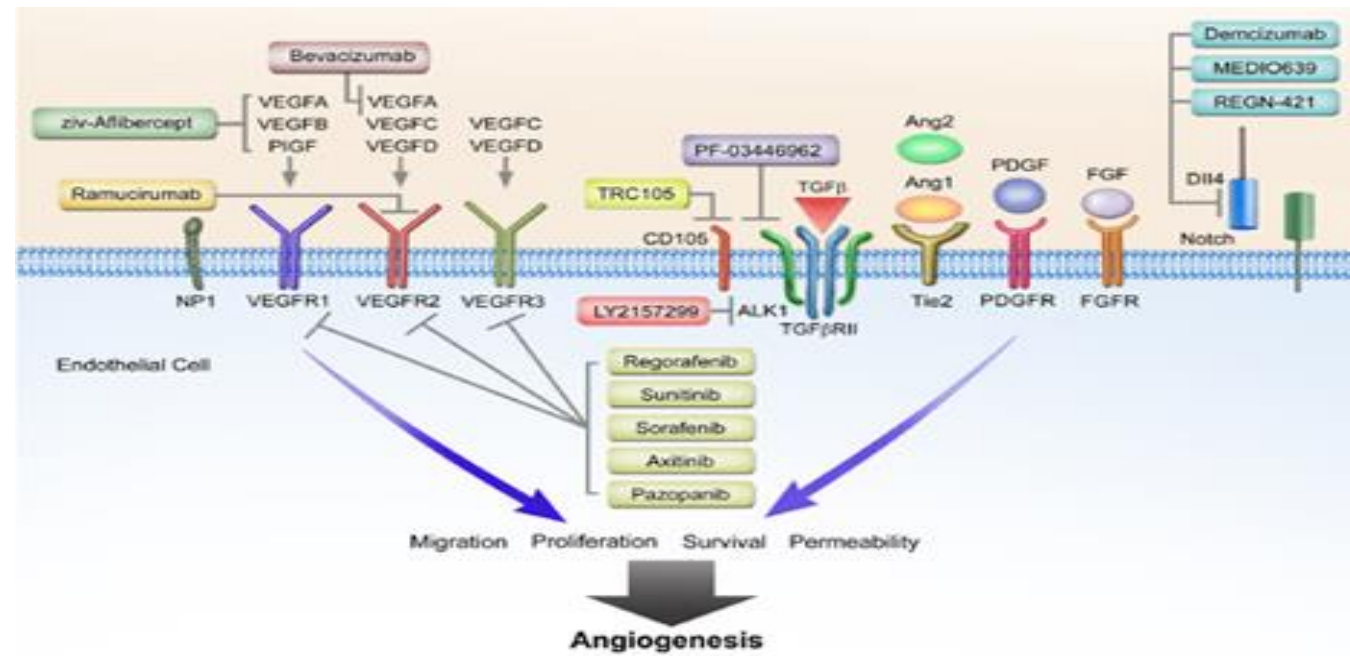
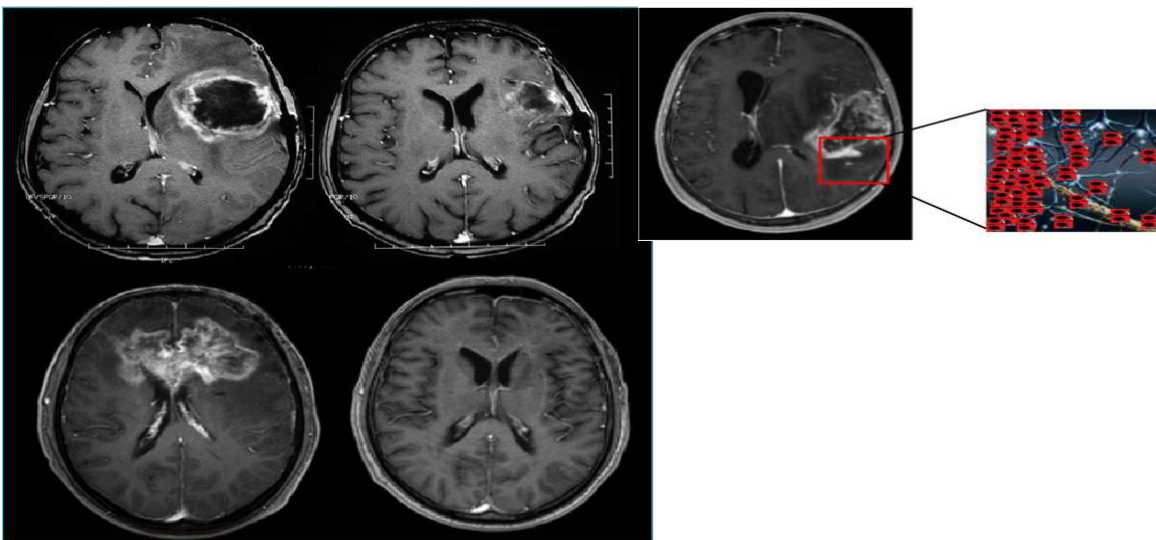
Judah Folkman, père fondateur de l'angiogénèse, NEJM 1971



La croissance, l'invasion tissulaire et la dissémination des cancers dépendent de la capacité des cellules tumorales à développer un réseau vasculaire

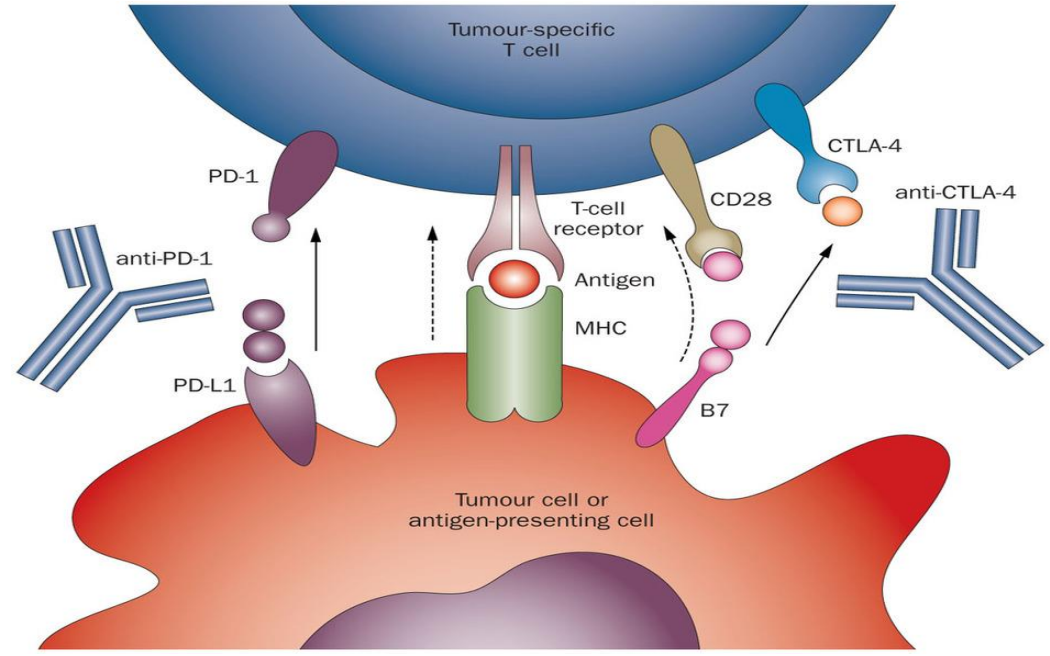
Décédé le 14 Janvier 2008

A affronté pendant 30 ans le scepticisme de la communauté médicale

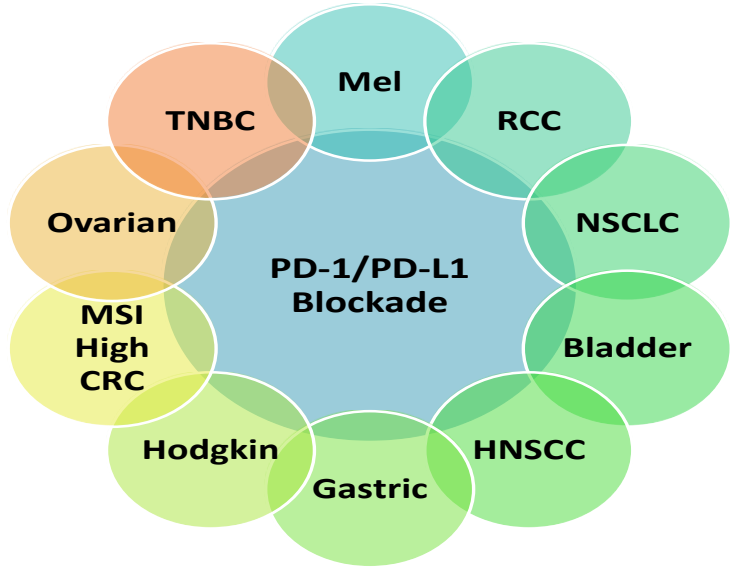




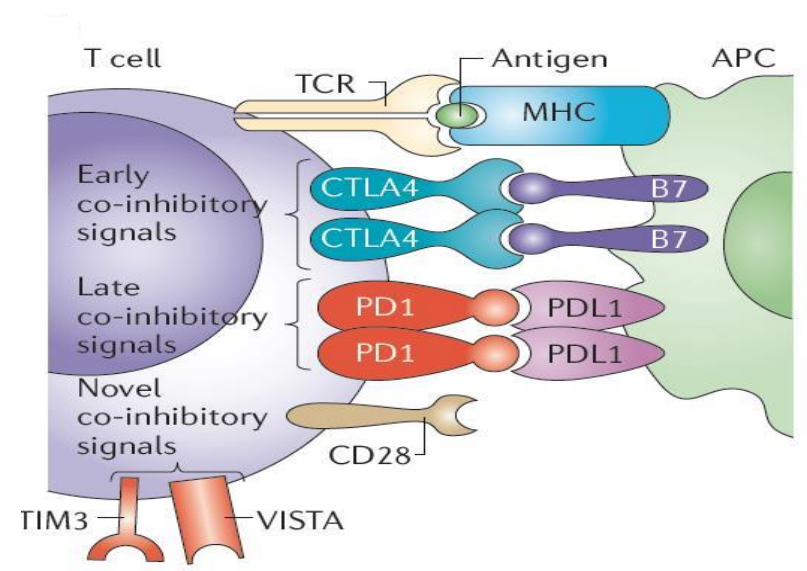
# 2015 FDA Approved Immunotherapies



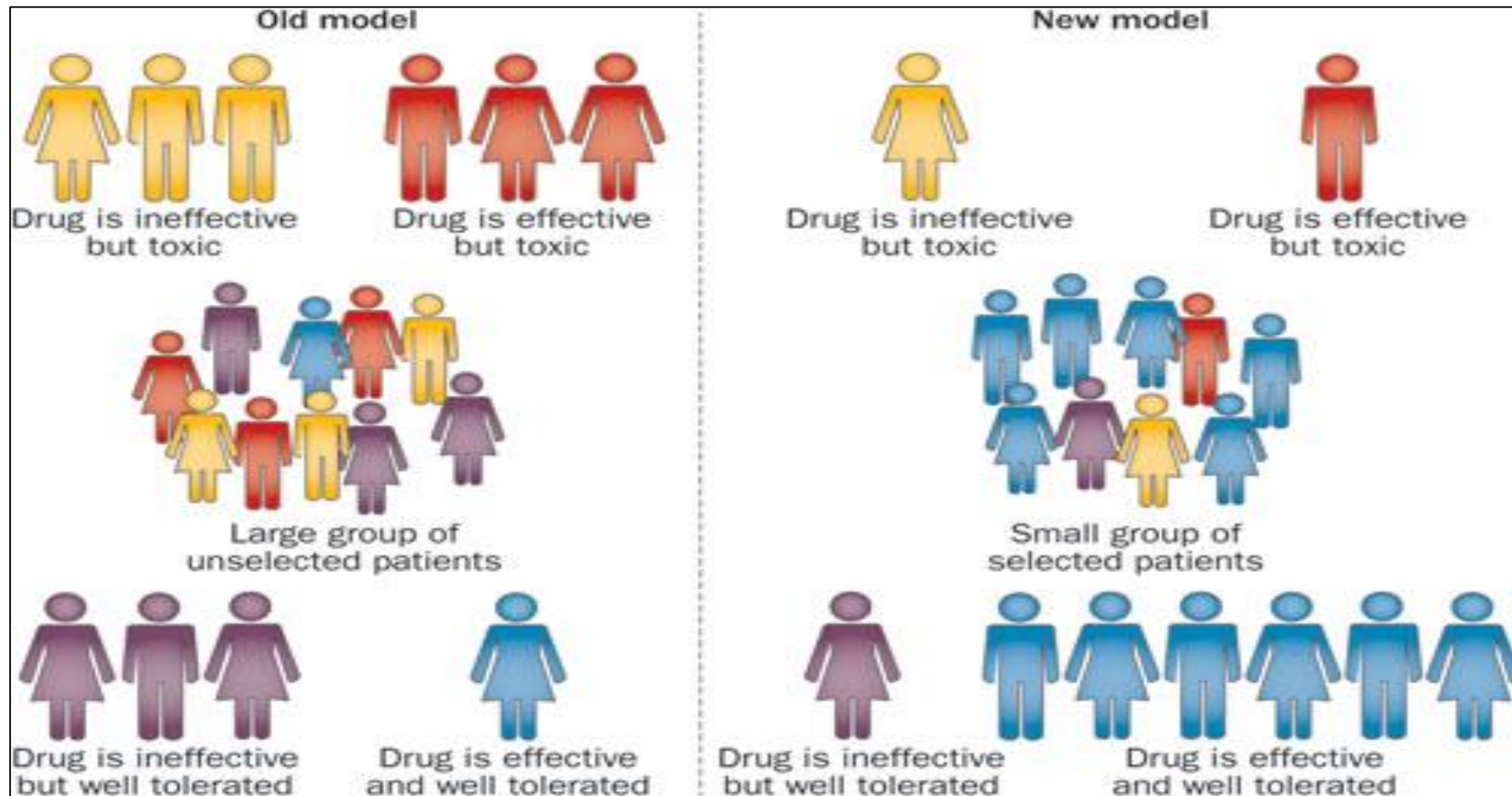
Immunomodulation as a new weapon in our armamentarium to fight cancer



## Lymphocyte Inhibition



# PHARMACOGÉNOMIQUE



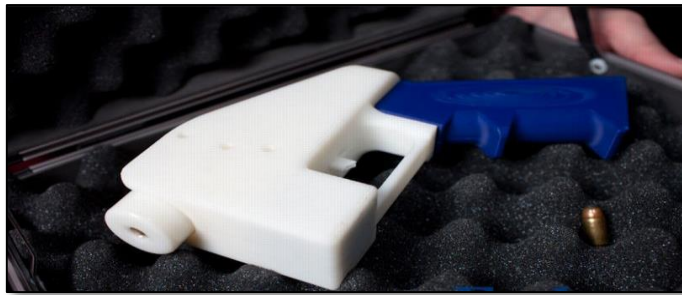


# 3D-PRINTED- DRUG

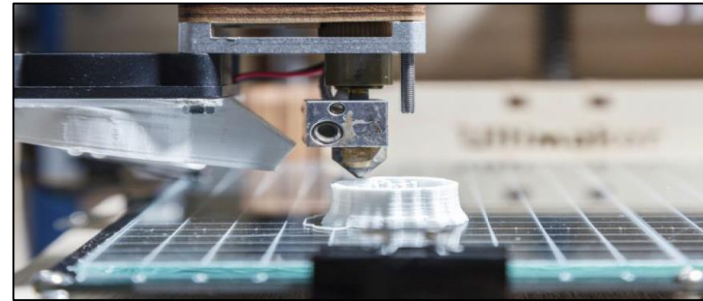
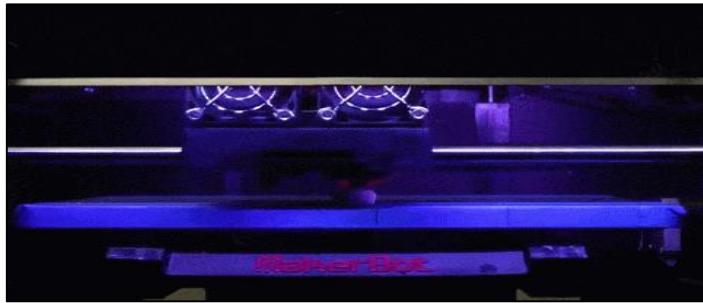


Lee Cronin, Chimiste écossais

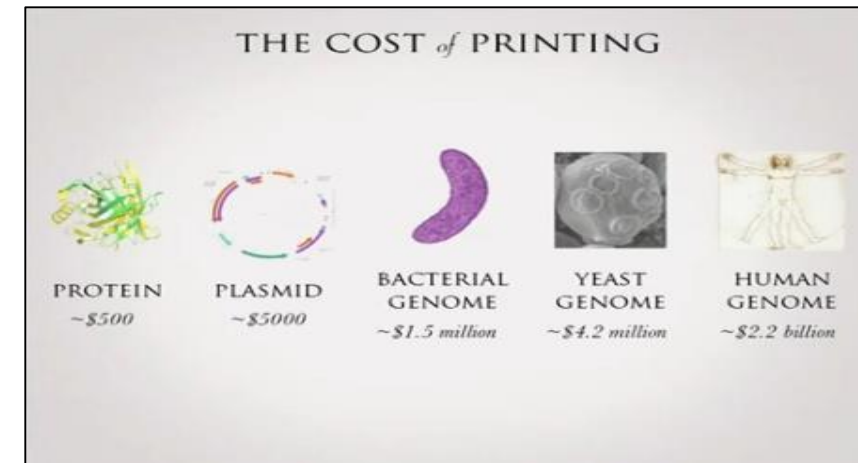
*Ultimately, Cronin says, "For me the cool bit, going into the future, is the idea of taking your own stem cells with your own genes and environment and printing your own medicine."*



États-Unis : un pistolet créé avec une imprimante 3D

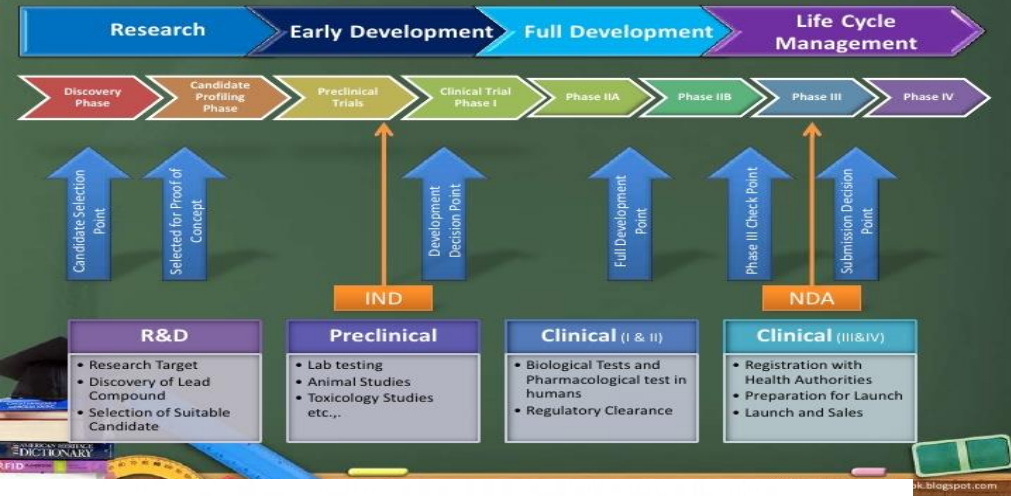


**SPRITAM : 1<sup>ER</sup> MÉDICAMENT 3D-FABRIQUE**  
Approuvé par FDA - 2016

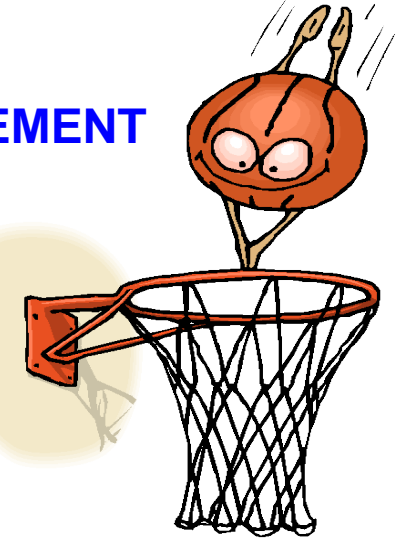




# New Drug Development Process



**MODIFIER LE PROCESSUS DE DEVELOPPEMENT DES MEDICAMENTS ?**



**ESSAI BASKET**

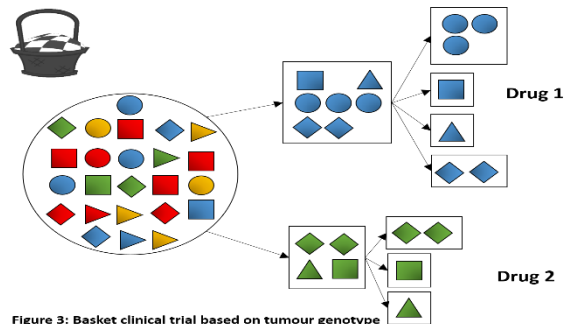
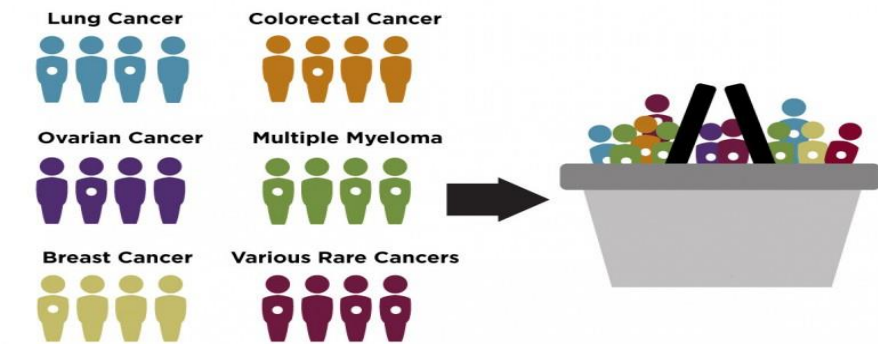
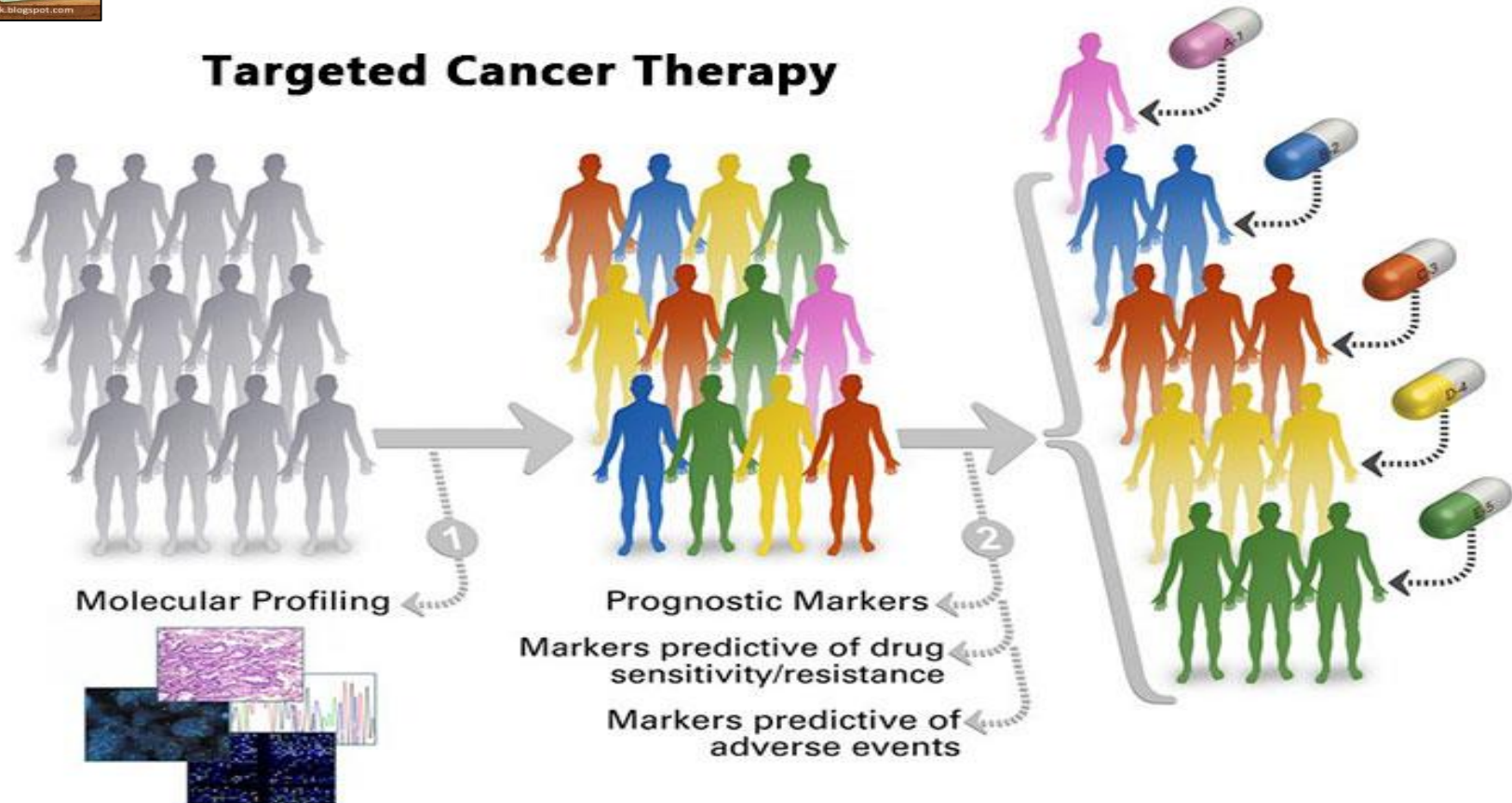
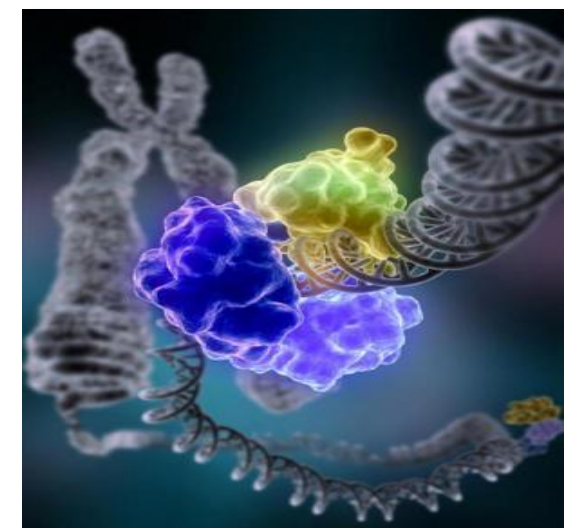
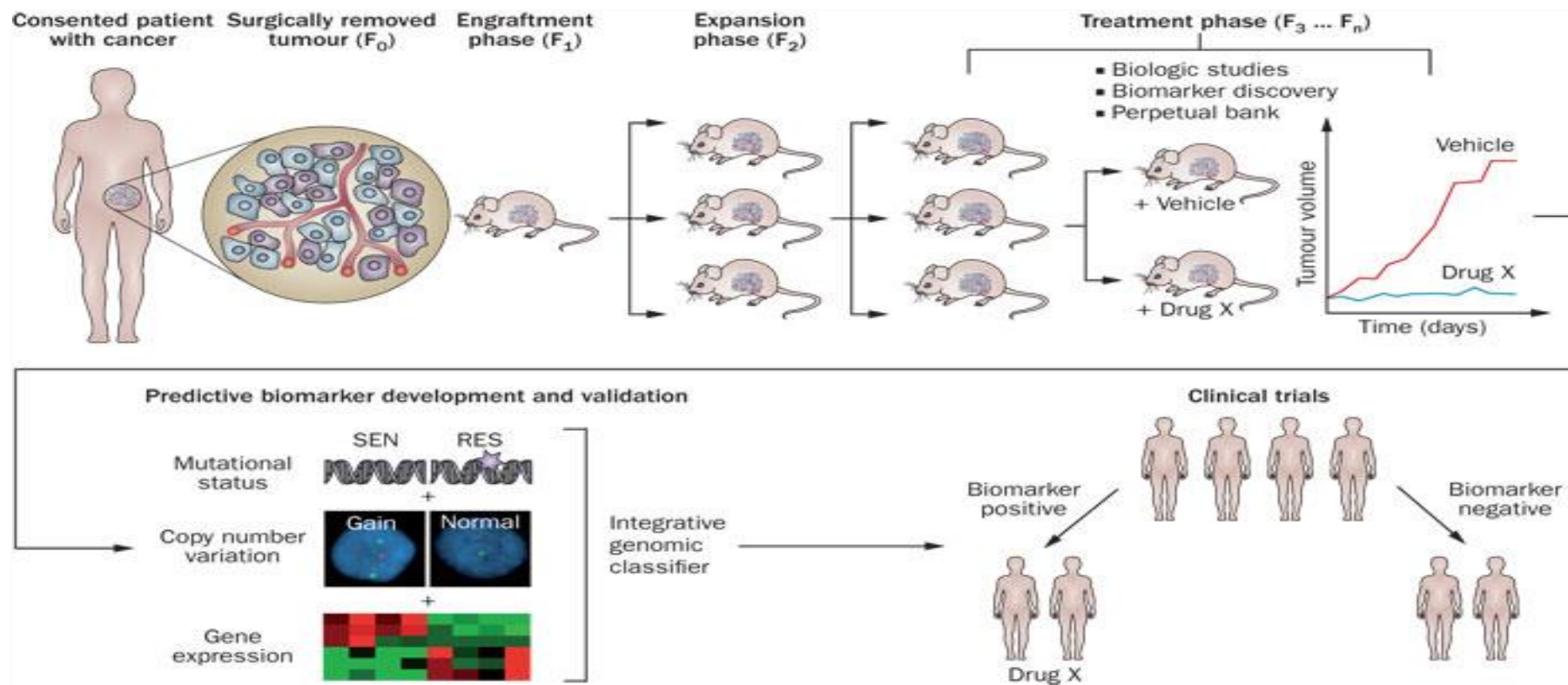


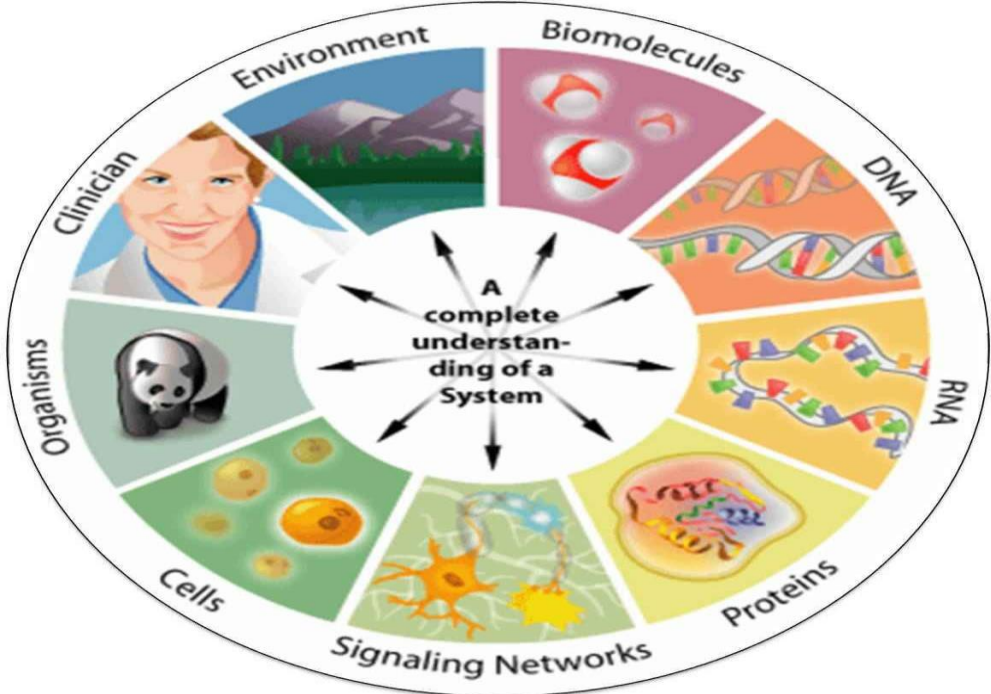
Figure 3: Basket clinical trial based on tumour genotype

# Targeted Cancer Therapy

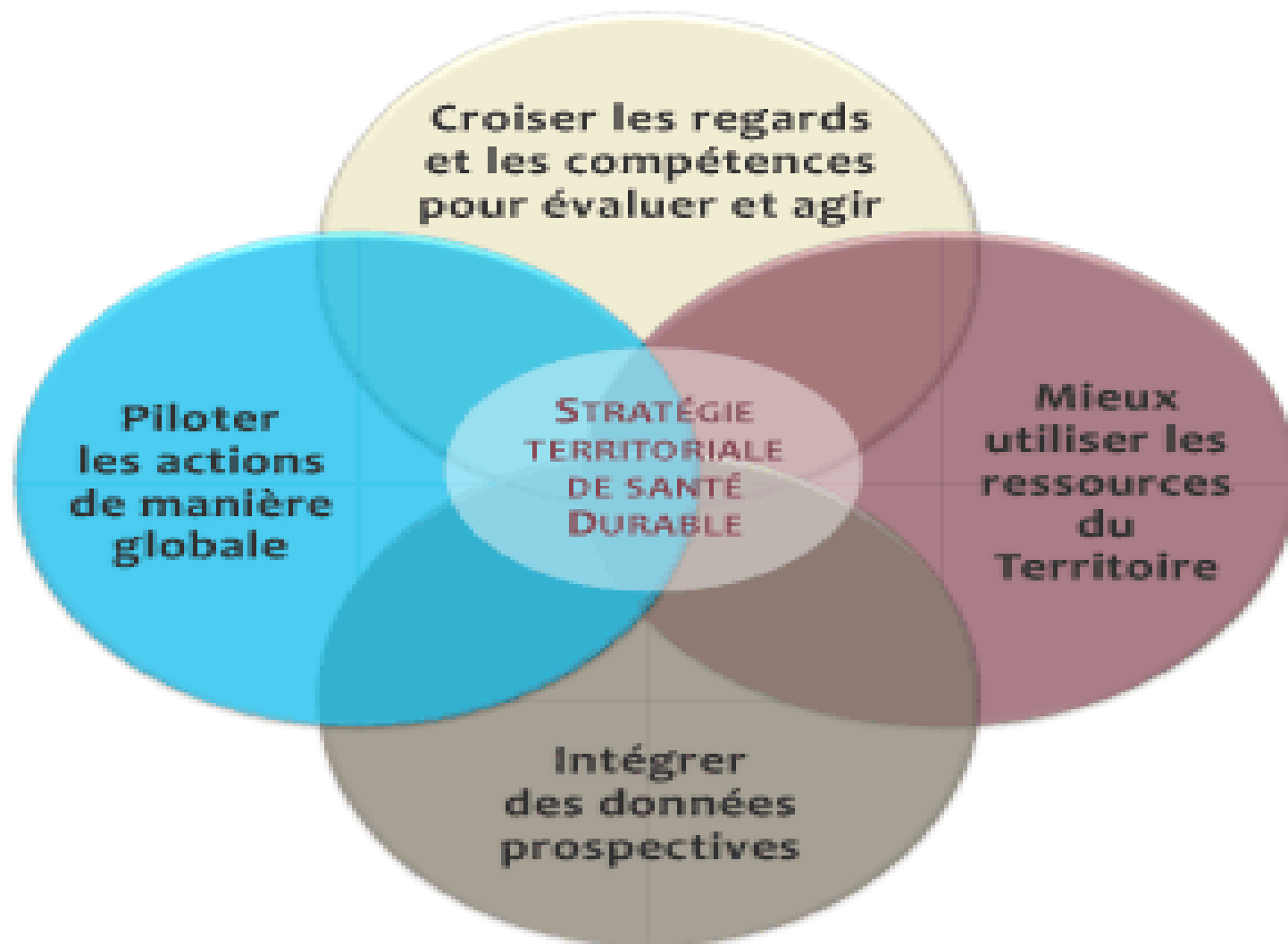


# XENOPATIENTS : REDÉFINIR LA RECHERCHE CLINIQUE





# SANTE ENVIRONNEMENTALE

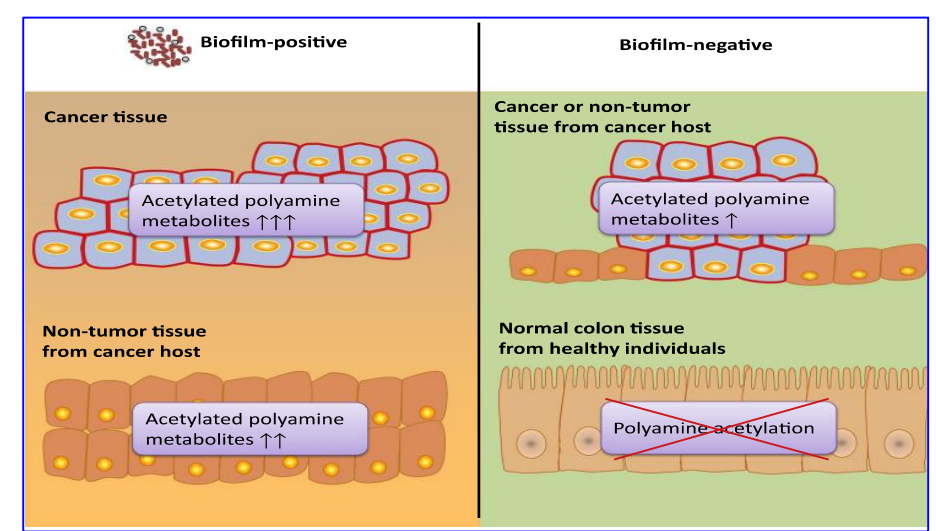




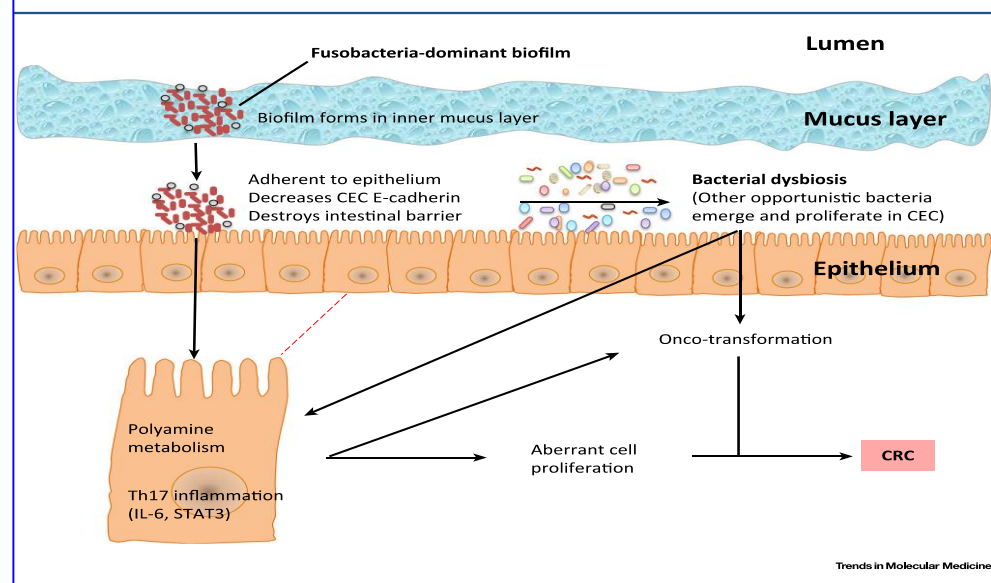
# Bacterial Biofilms in Colorectal Cancer Initiation and Progression

Shan Li,<sup>1</sup> Sergey R. Konstantinov,<sup>1</sup> Ron Smits,<sup>1</sup> and Maikel P. Peppelenbosch<sup>1,\*</sup>

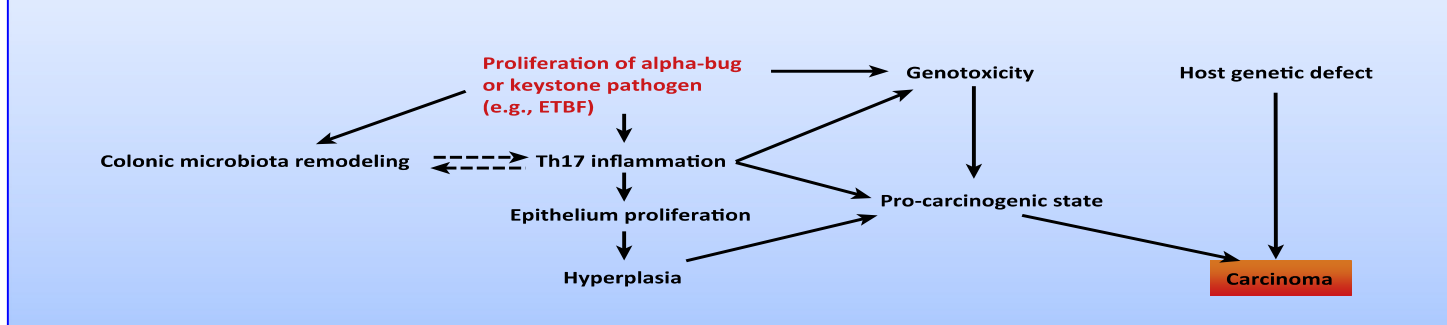
structures termed biofilms. We explore here the concept that a polymicrobial biofilm promotes pro-carcinogenic activities that may partially underlie progression along the adenoma-CRC axis.



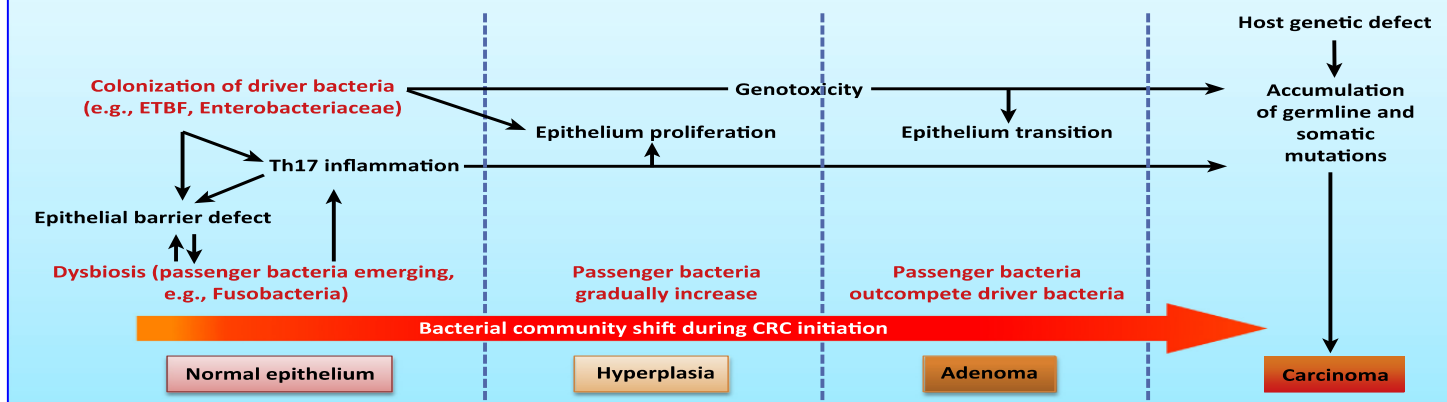
The Biofilm-Driven Colorectal Cancer (CRC) Carcinogenesis Model



(A) Alpha-bug (2011) and keystone pathogen (2012) models

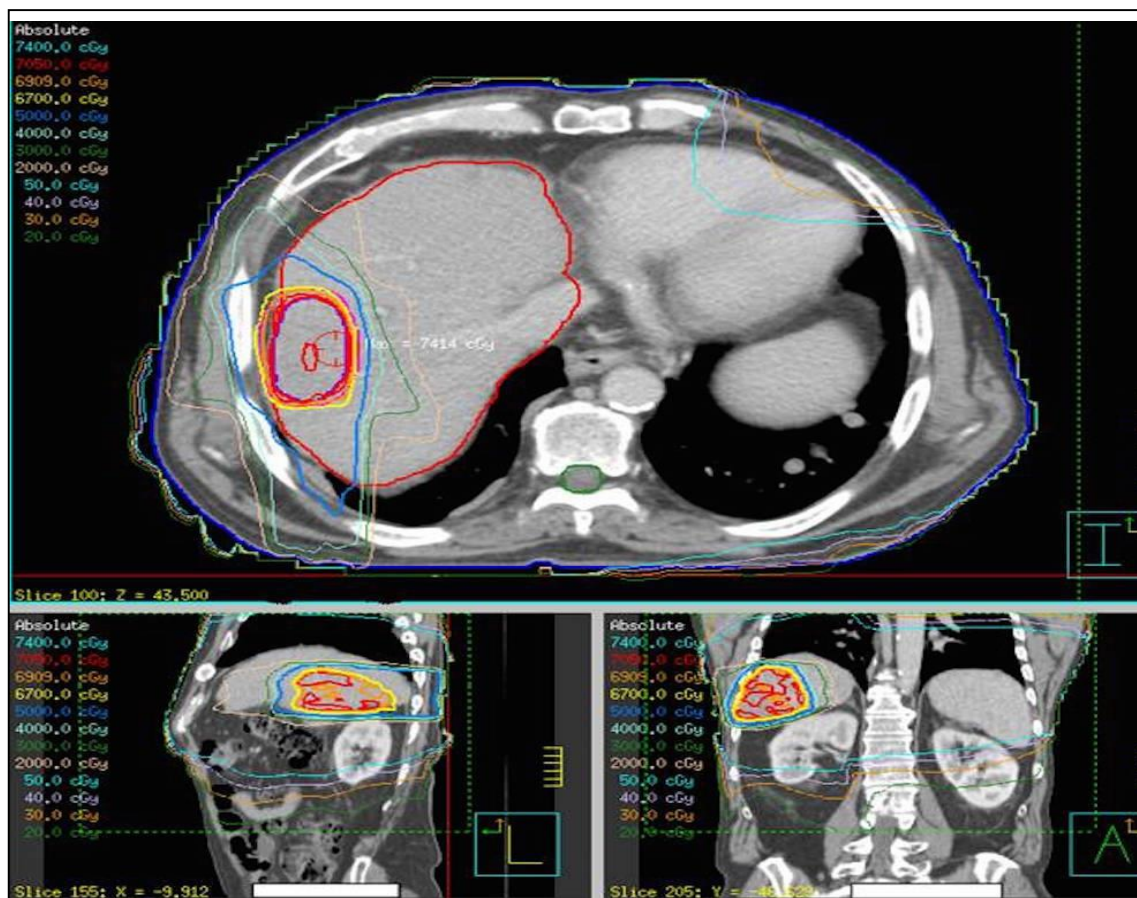


(B) Dysbiosis (passenger bacteria emerging, e.g., Fusobacteria)



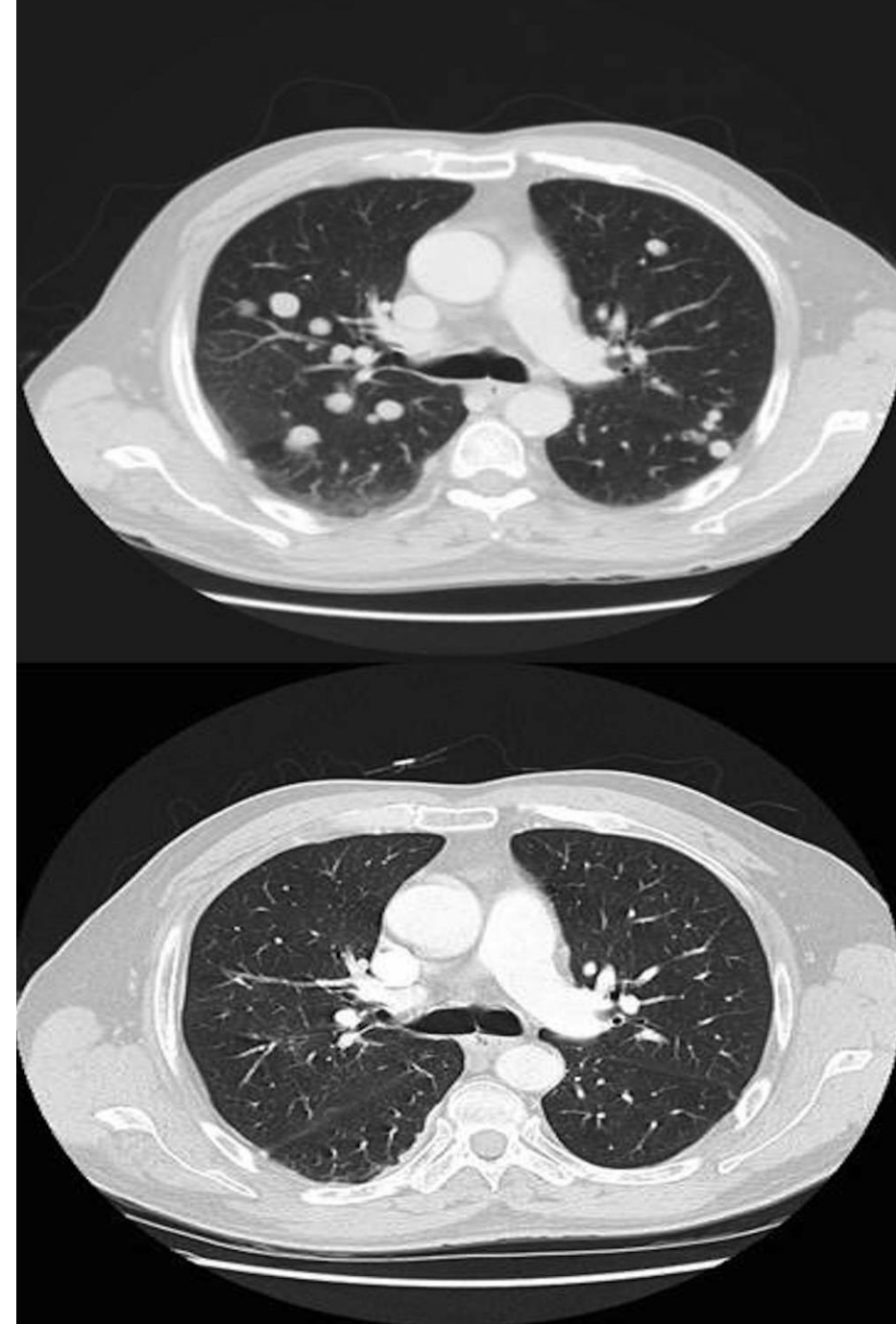
# Abscopal Effects: Case Report and Emerging Opportunities

Michael Lock<sup>1</sup>, Ahmad Muinuddin<sup>2</sup>, Walter I. Kocha<sup>3</sup>, Robert Dinniwell<sup>4</sup>, George Rodrigues<sup>5</sup>, David D'souza<sup>6</sup>



**FIGURE 2: Radiation dosimetry plan for liver treatment**

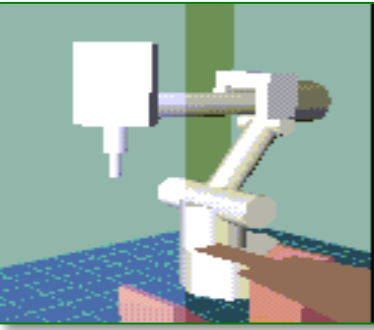
The patient underwent 70 Gy treatment in 15 fractions to the liver which was completed in April 2010.



**FIGURE 1: The axial CT scans of the thorax before and after**

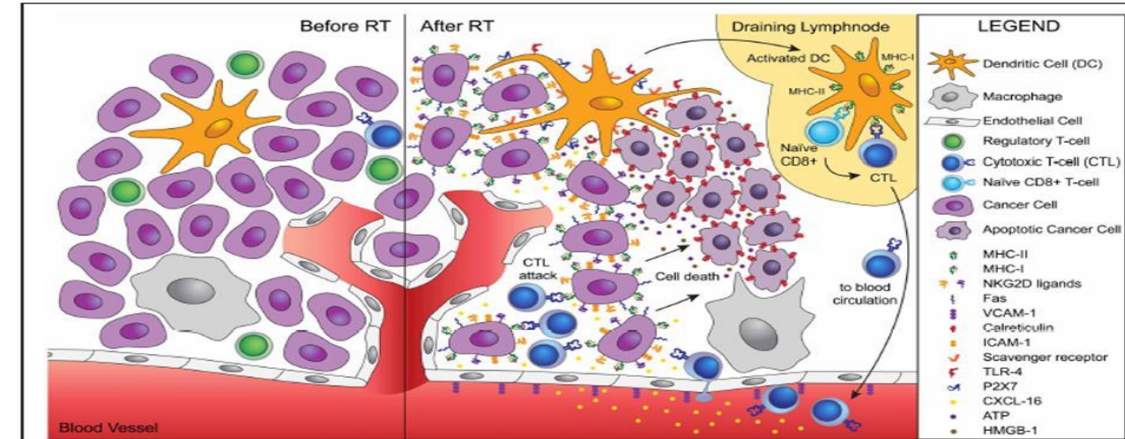
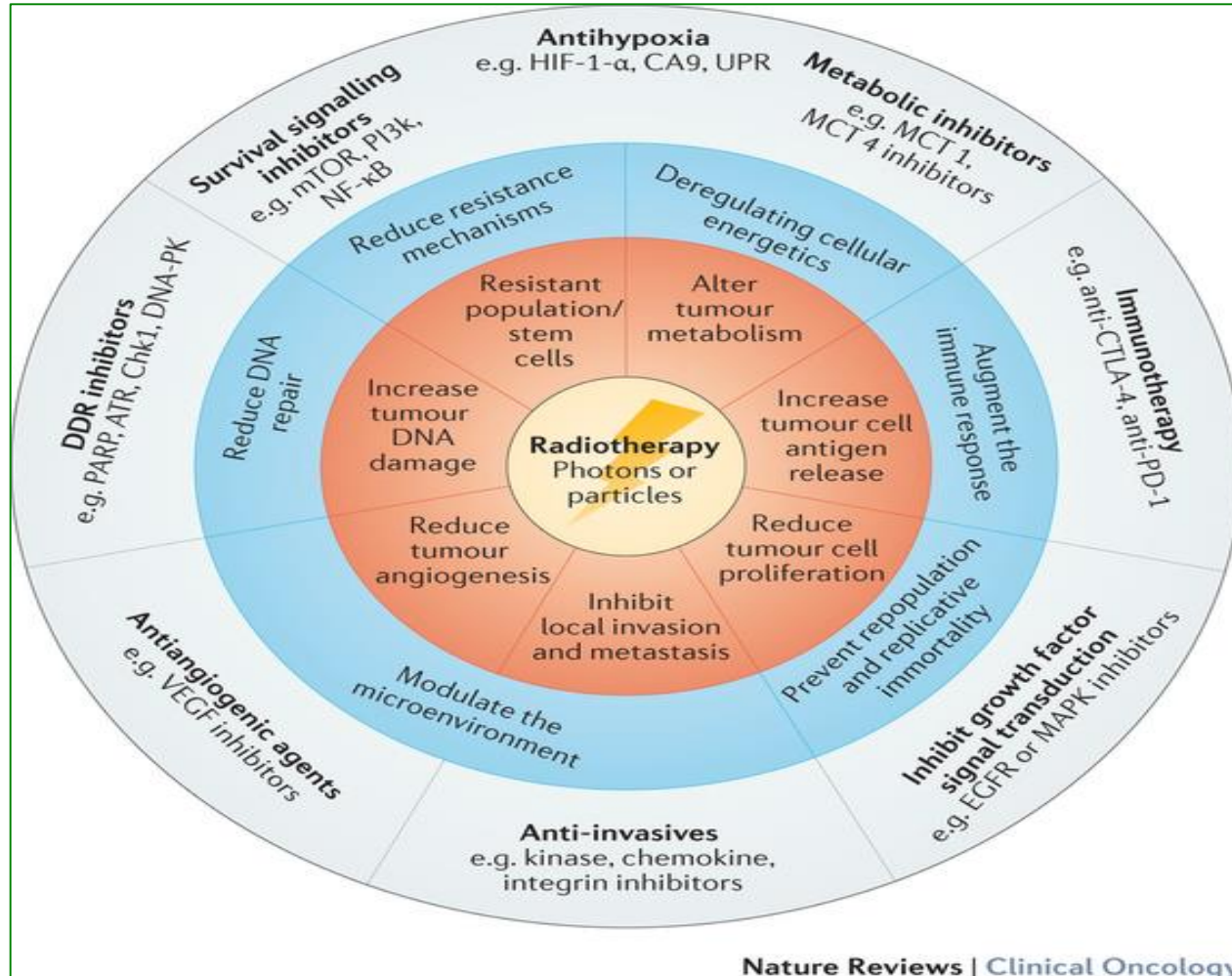


# MIEUX UTILISER LA RADIOTHERAPIE & LA RADIOIMMUNOTHERAPIE



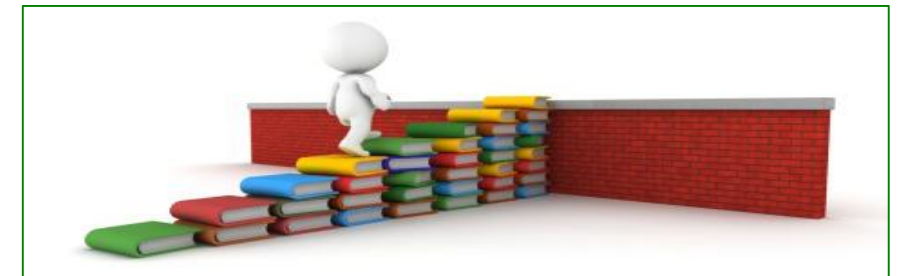
## Role of T Lymphocytes in tumor response to radiotherapy

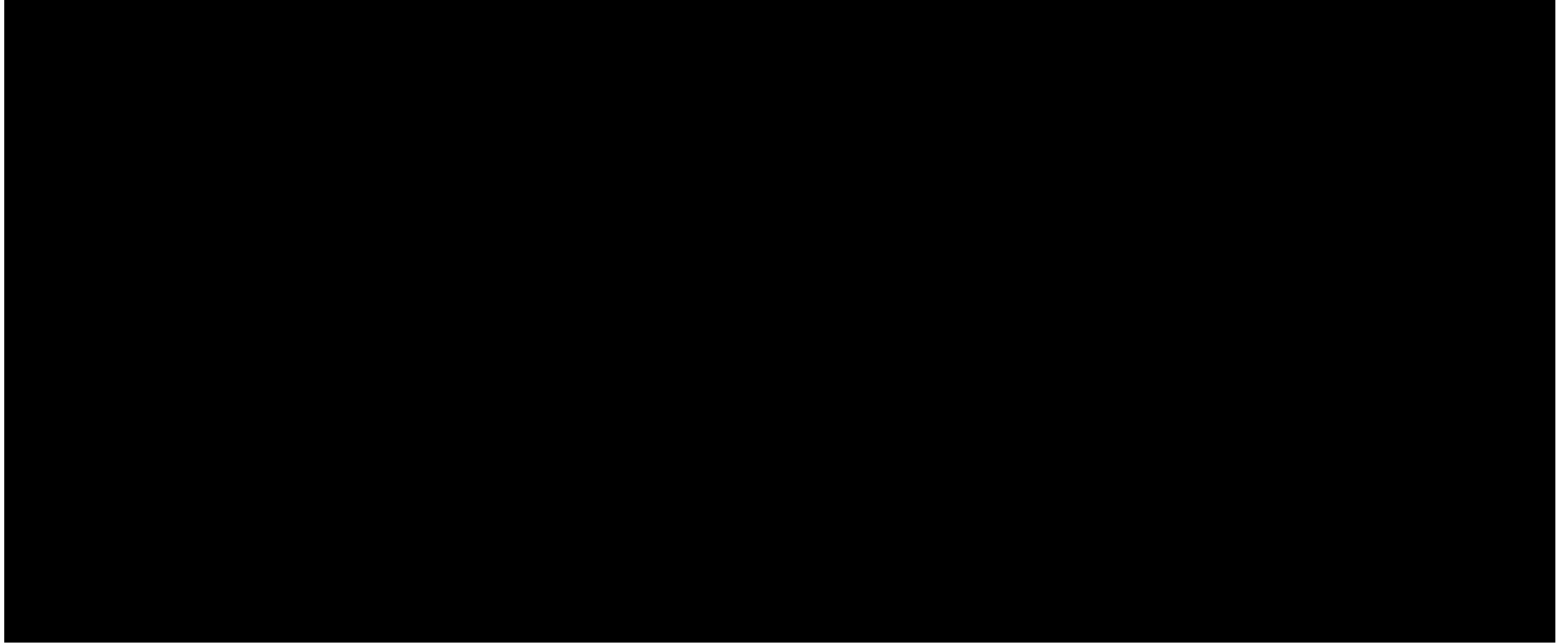
Sandra Demaria<sup>1\*</sup> and Silvia C. Formenti<sup>2</sup>



**FIGURE 1 | Ionizing radiation acts as a modifier of the tumor microenvironment converting the tumor into an *in situ* vaccine.** Radiation induces an immunogenic cell death of tumor cells characterized by calreticulin translocation to the surface of dying cells, and release of HMGB-1 and ATP. Calreticulin allows uptake of dying cells by dendritic cells via scavenger receptor(s). HMGB-1 binds to TLR4 and promotes the cross-presentation of tumor antigens, while ATP binds to P2X7 and triggers the activation of the inflammasome. Activated dendritic cells migrate to the draining lymph node, where they activate naive T cells specific for tumor

antigens. Activated CD8 T cells acquire effector functions and traffic to the tumor guided by radiation-induced chemokines. Tumor infiltration by CTLs is facilitated by radiation-induced upregulation of VCAM-1 on the vascular endothelium. Once in the tumor, CTLs interact efficiently with tumor cells expressing increased levels of MHC-I, ICAM-1, NKG2D ligands, and Fas that promote the formation of stable immunological synapses between targets and effectors and facilitate the killing of tumor cells by CTLs. Tumor cells killed by CTLs become a source of antigens for cross-presentation, thus fueling the process.







# The Concept of Hormesis in Cancer Therapy – Is Less More?

Andy Gaya<sup>1</sup>, Charles A. Akle<sup>2</sup>, Satvinder Mudan<sup>3</sup>, John Grange<sup>4</sup>

Clinical trial parameters	Induction regimen		Phase I			Phase II	
Site	Locally advanced SCCHN	Recurrent ovarian fallopian tube/peritoneal cancers	Locally advanced pancreatic or small bowel adenocarcinoma	Stage III/IV endometrial carcinoma	Recurrent/progressive GBM	Stage IIA/B-IIIa breast cancer	Recurrent NSCLC
Design	Paclitaxel (225 mg/m <sup>2</sup> ), carboplatin (area under the curve of 6), and four 80-cGy fractions of radiotherapy (two each on days 1 and 2). This sequence was repeated on days 22 and 23	One of three dose levels of docetaxel (20, 25, or 30 mg/m <sup>2</sup> ) concurrent LDFRT given as 60 cGy bid 2 days weekly for 6 weeks	Gemcitabine 1,250 mg/m <sup>2</sup> at 10 mg/m <sup>2</sup> /min on days 1 and 8 of a 3-week cycle. LDFRT at two dose levels: 60 cGy per fraction and 70 cGy per fraction on days 1, 2, 8, and 9 for 4 weeks	Six weekly cycles of FD-CDDP (40 mg/m <sup>2</sup> , maximum 70 mg IV) + LDFRT at 0.5 Gy/tx (total 3 Gy) and 0.75 Gy/tx (total 4.5 Gy)	LDFRT 0.3 Gy twice daily with cisplatin and fotemustine if progressing on temozolomide, or 0.4 Gy twice daily with temozolomide if recurrent	LDFRT 0.4 Gy/ per fraction, 2 fractions per day, for 2 days, every 21 days for 6-8 cycles) with non-pegylated liposomal doxorubicin and docetaxel	Pemetrexed (500 mg/m <sup>2</sup> IV) and concurrent LDFRT (40 cGy bid on days 1 and 2) was repeated fourfold every 21 days
Duration	5 years	2 years	37 months	27 months	20 months		2 years
Recruitment	40	13	10	12	26	10	19
References	Arnold <i>et al.</i> (34); Gleason Jr <i>et al.</i> (35)	Kunos <i>et al.</i> (36)	Regine <i>et al.</i> (37)	Wrenn <i>et al.</i> (38)	Balducci <i>et al.</i> (39)	Nardone <i>et al.</i> (40)	Mantini <i>et al.</i> (41)

LDFRT, Low Doses Fractionated Radiation Therapy.

« *Tout est poison, rien n'est poison, Il n'y a que le dose...* »

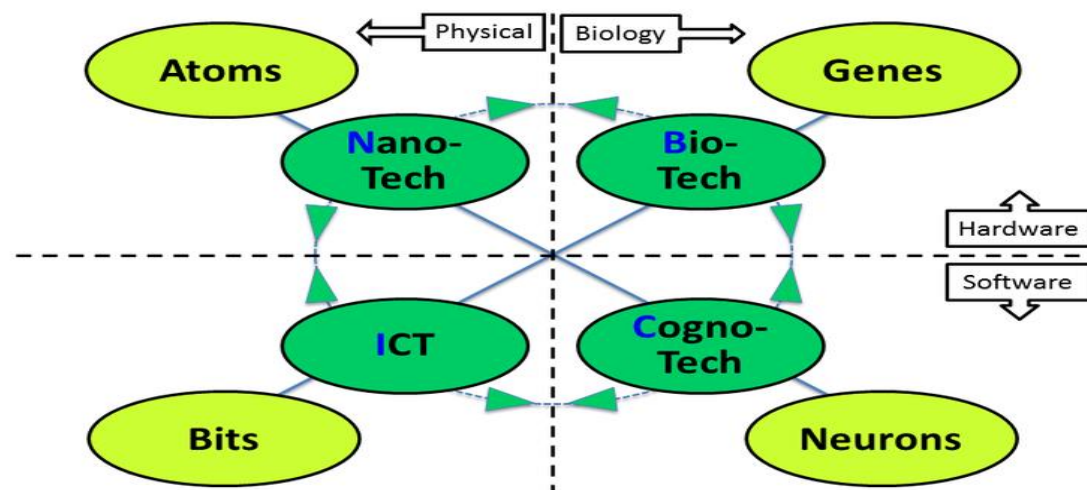
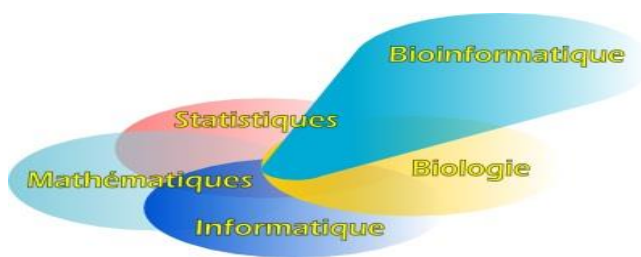
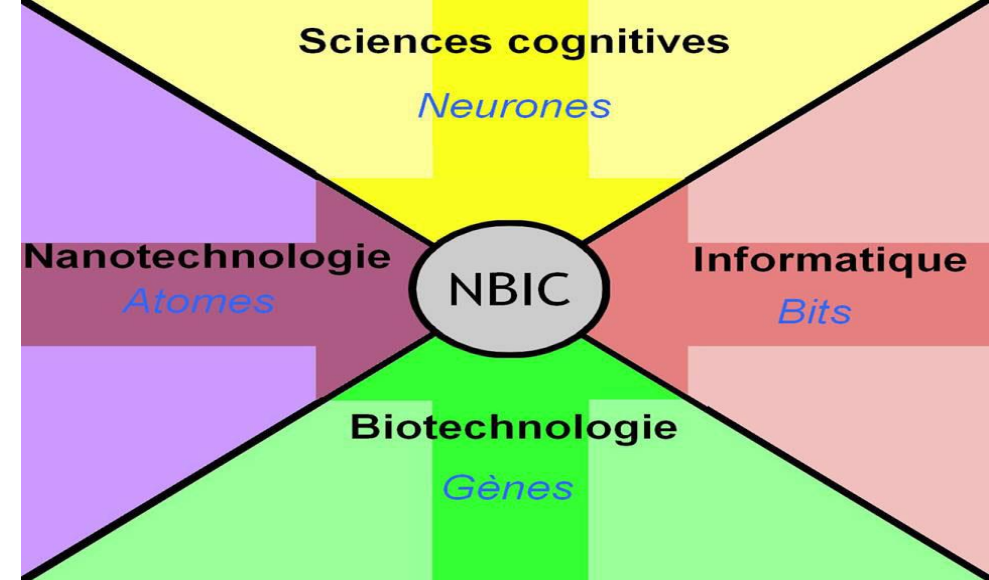


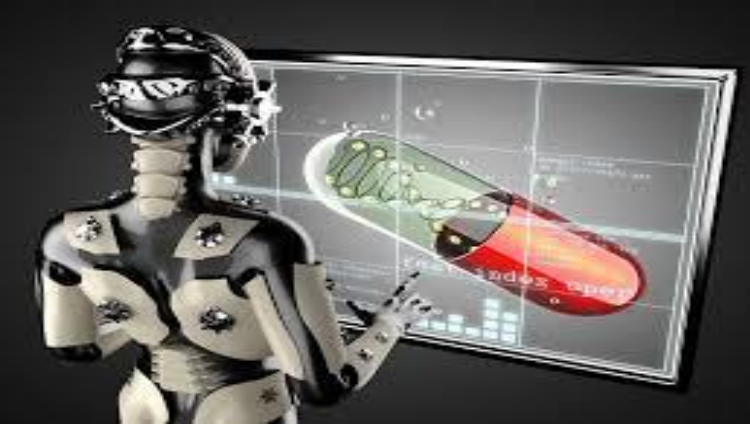
FIGURE 1: Paracelsus (Theophrastus Bombastus von Hohenheim) 1493-1541 Engraving from life by Augustin Hirschvogel in 1538.



**HORMESE**







# BIOPEN

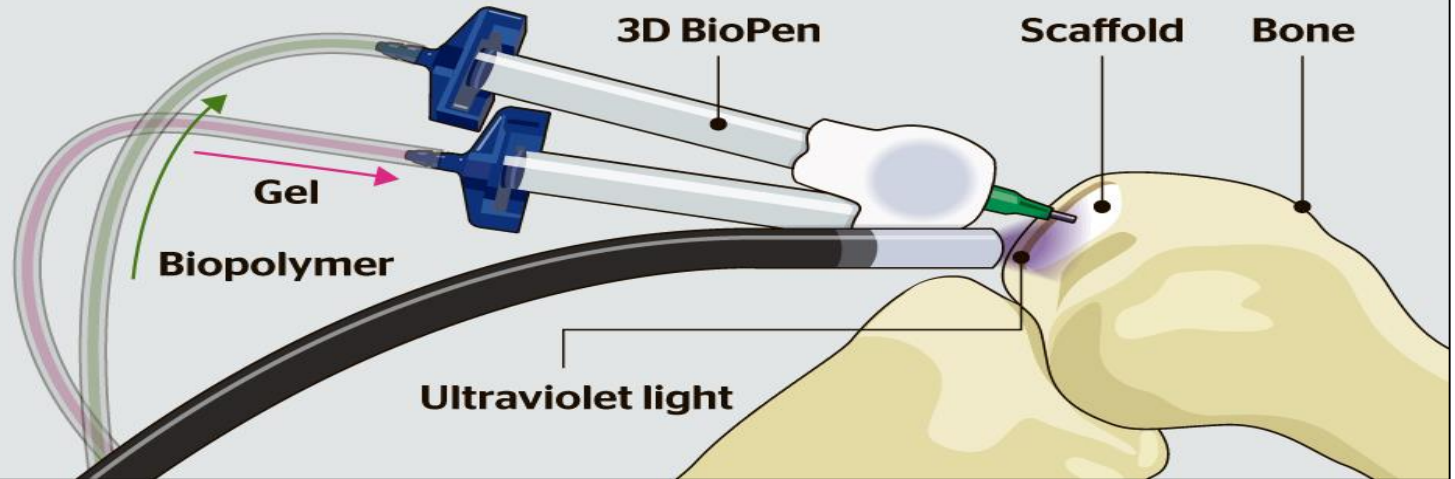


## How it works

**1** BioPen uses cell material inside a biopolymer such as alginate, which is in turn encased in a layer of gel

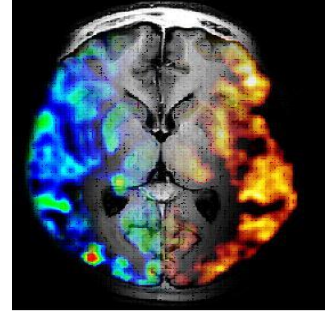
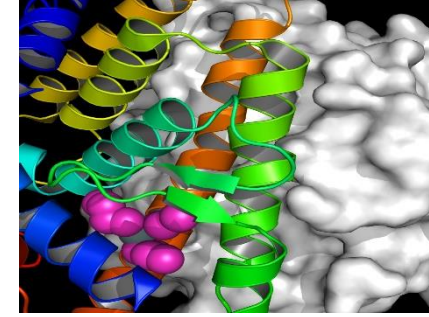
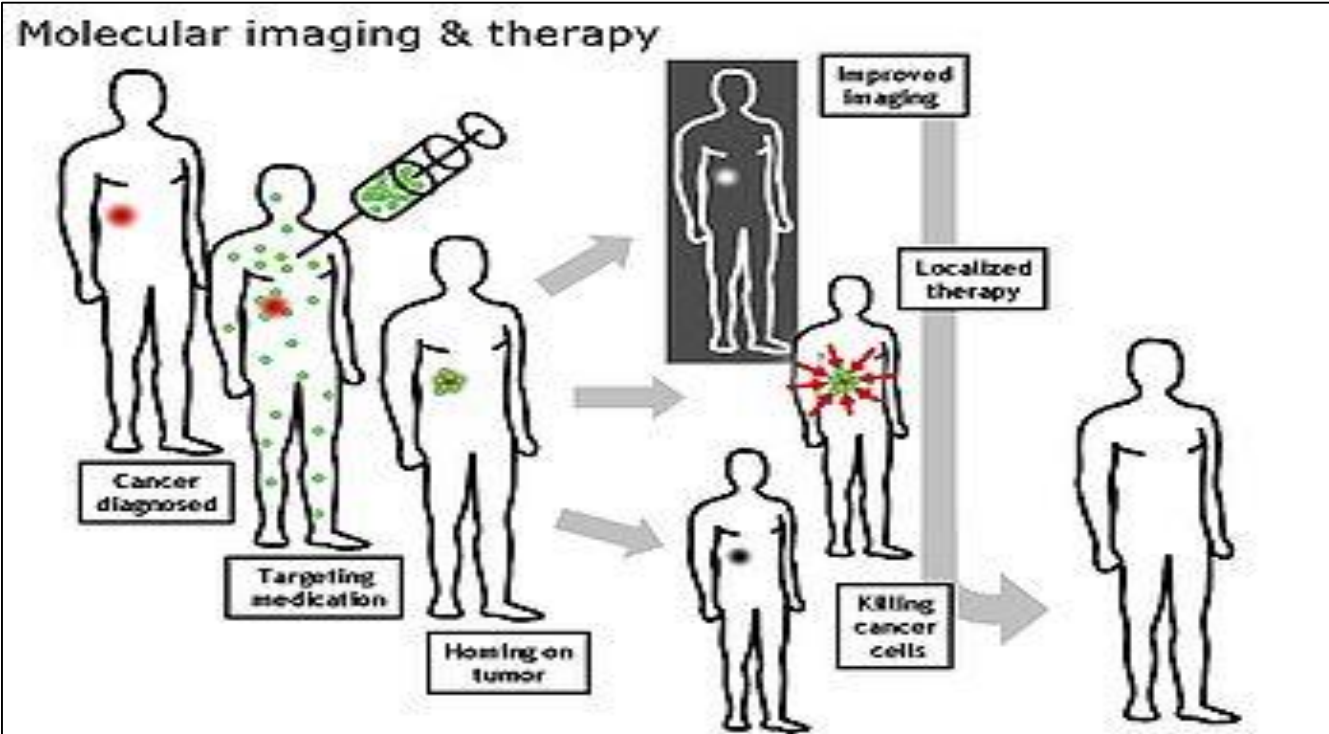
**2** As the surgeon “draws”, two layers of gel are combined in the pen head and extruded onto the bone surface

**3** Ultraviolet light hardens the gel and protects the cells that are built up to create a 3D scaffold on the wound site

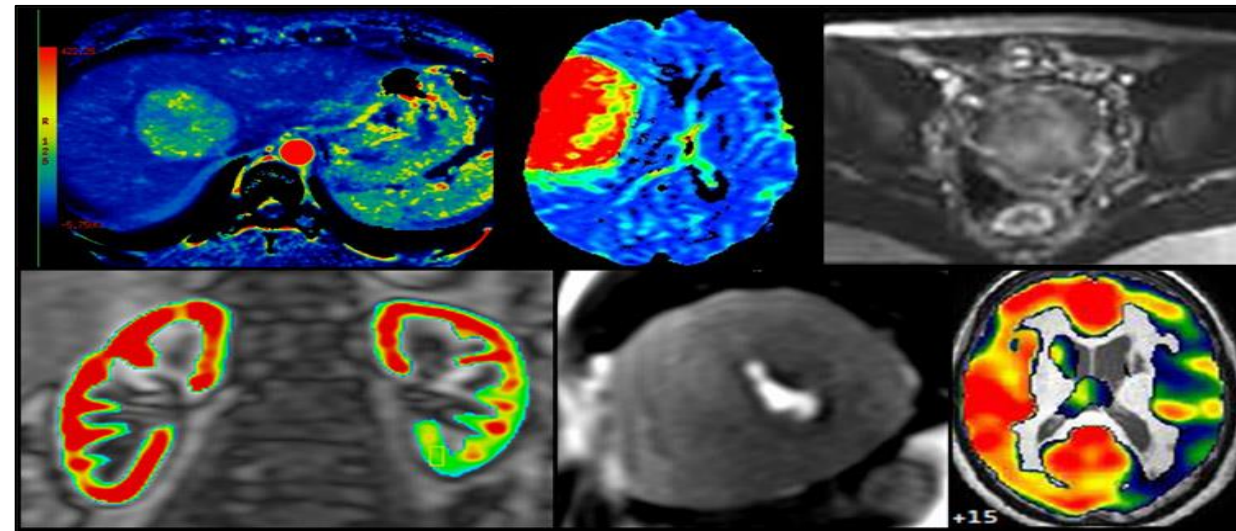
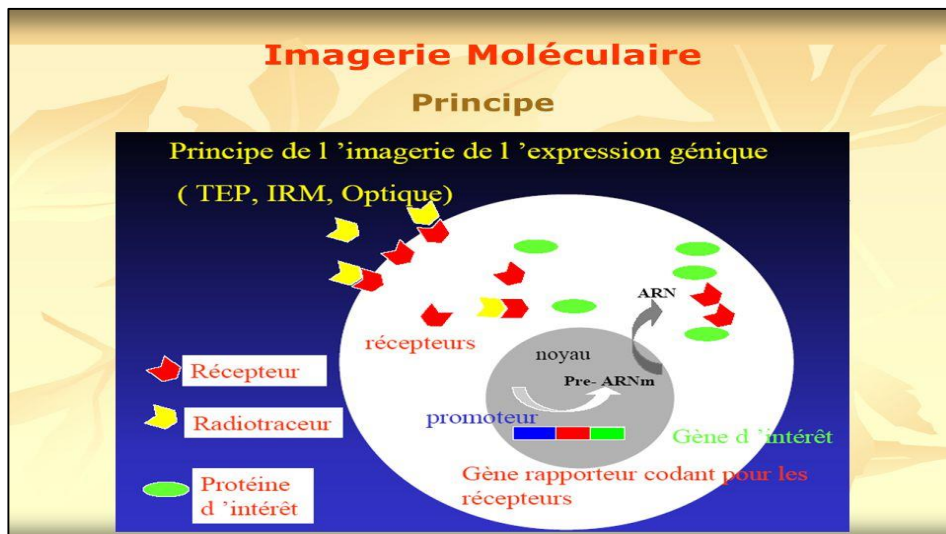




# THERANOSTIC

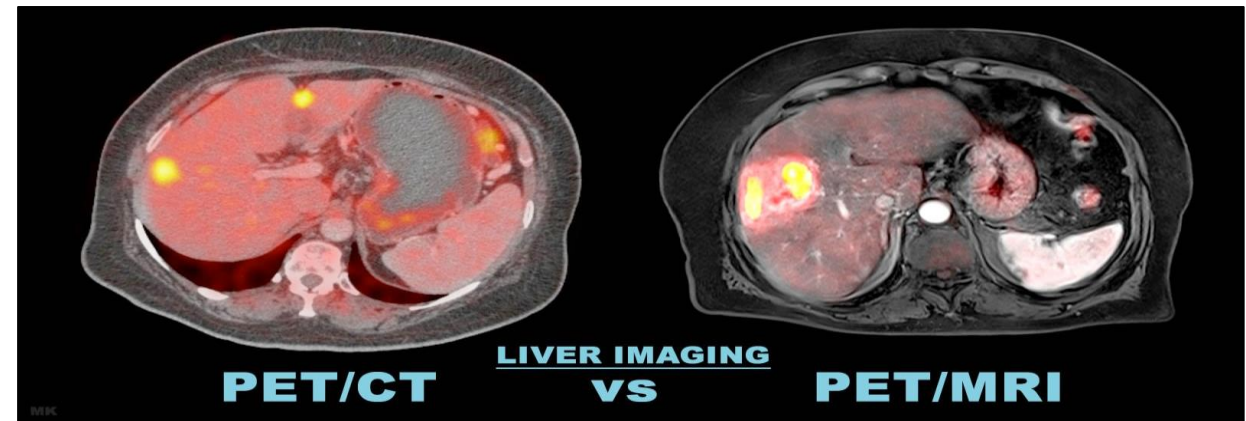
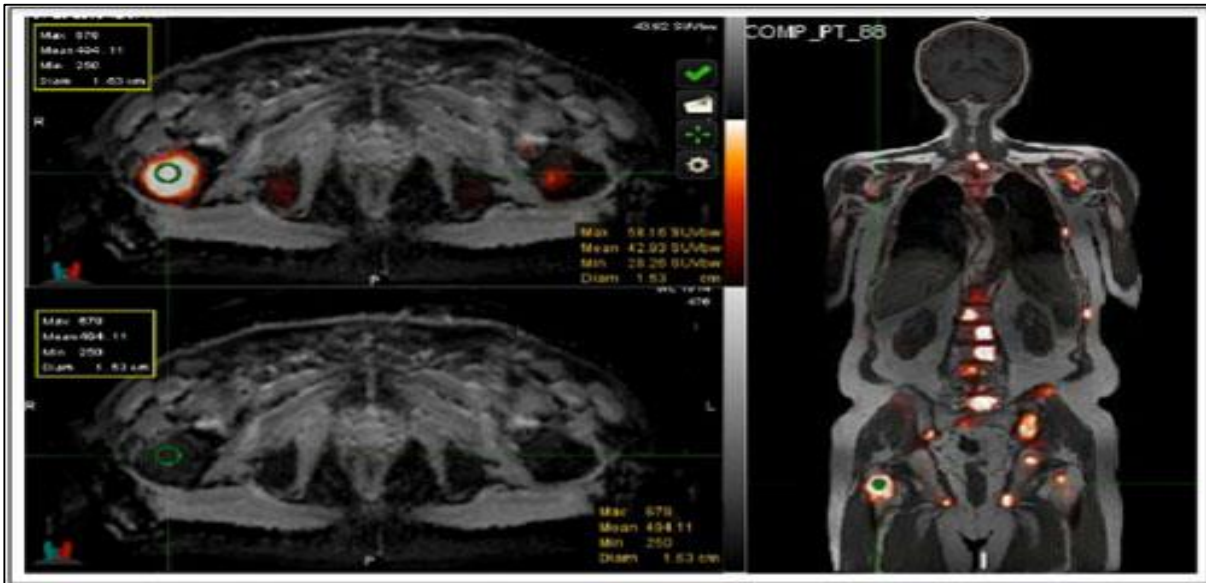
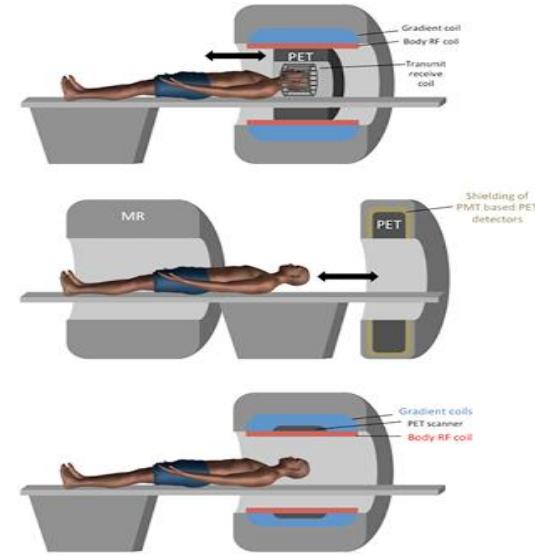
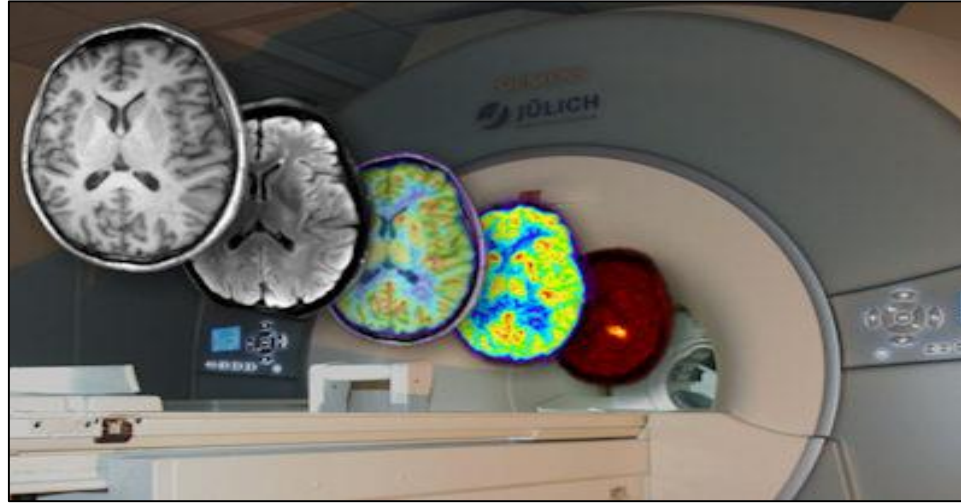
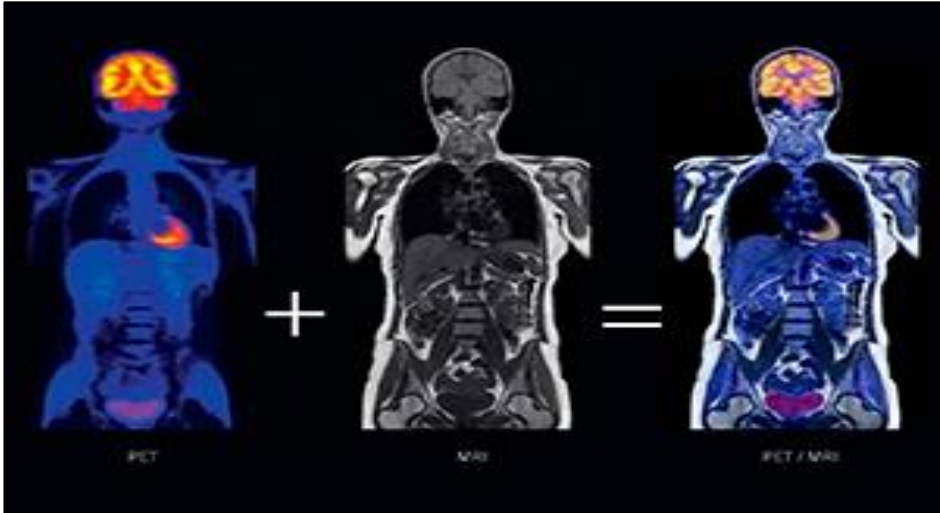


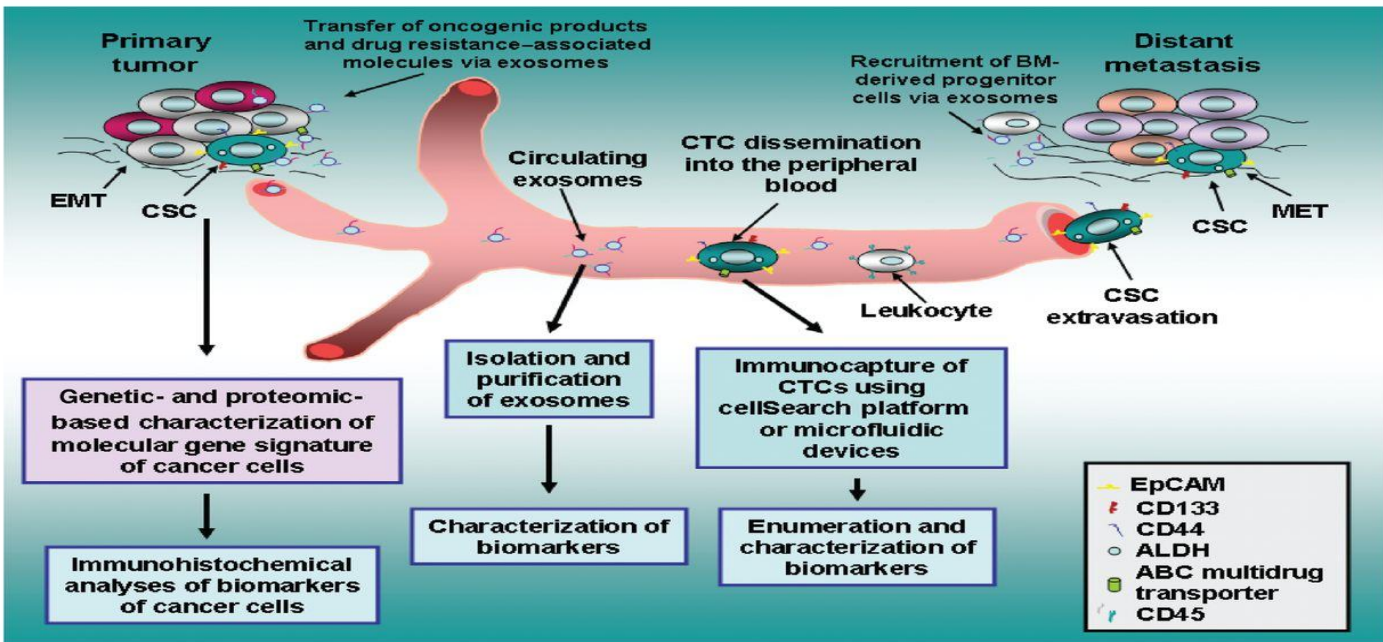
## IMAGERIE DE FLUORESCENCE



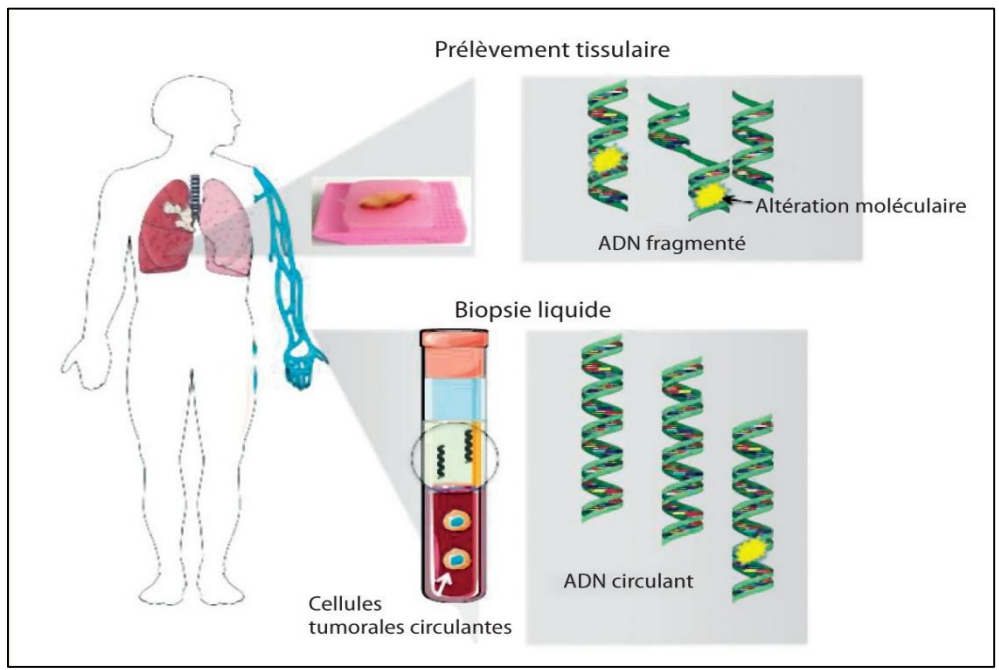


# TEP IRM



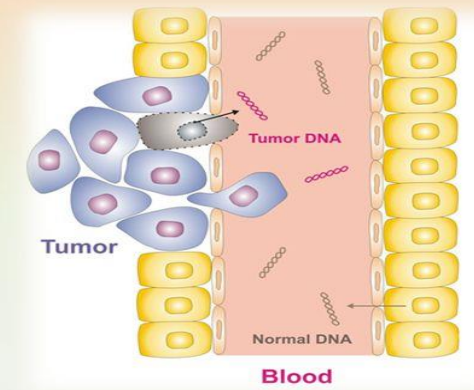


## CTC, ADN circulant : Biopsies liquides



## ADN tumoral circulant (ADNct)

- Surveiller la dynamique de la tumeur
- ADN tumoral circulant  $\approx$  0,01% ADN circulant total
- Proportionnel au développement de la tumeur
- Bio-marqueur spécifique (séquence dépendante)



<http://www.inostics.com>



# THEN AND NOW: BY THE NUMBERS



**THEN:**  
**Late-stage Diagnoses**

70% of men present with metastatic prostate cancer after experiencing symptoms such as bone pain.



**THEN:**  
**Risky Surgeries**

Prostatectomies take 4-6 hours, with 4-5 units of blood lost.



**THEN:**  
**Standard Options**

"One-size-fits-all" treatments are prescribed until they fail.

**NOW:**  
**Early Detection**

Most men are diagnosed through routine screening; only 5% present with incurable disease.



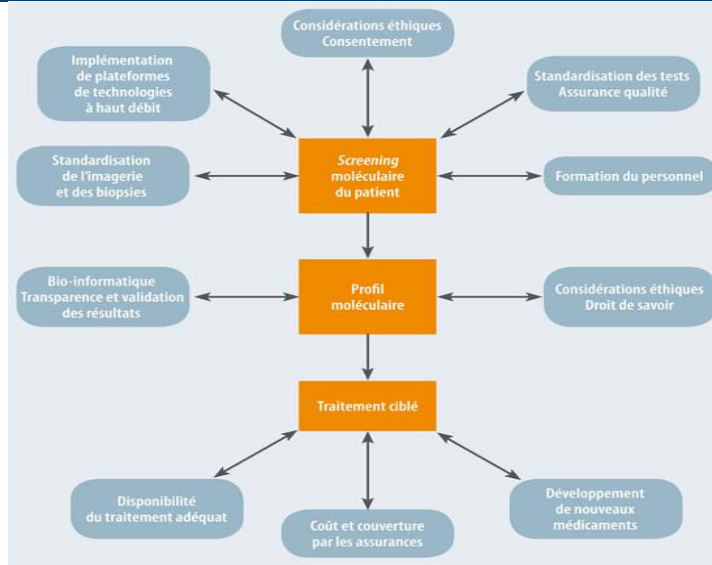
**NOW:**  
**Robotic Assistance**

2 hour procedures and minimal blood loss mean faster recoveries.



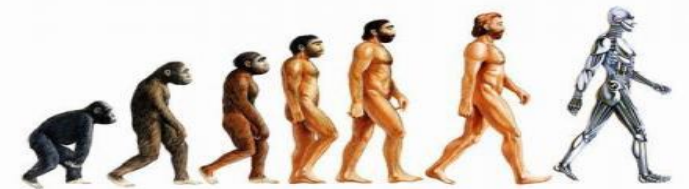
**SOON:**  
**Precision Medicine**

New studies show that 90% of tumors contain "actionable" mutations, allowing for individualized treatment plans.

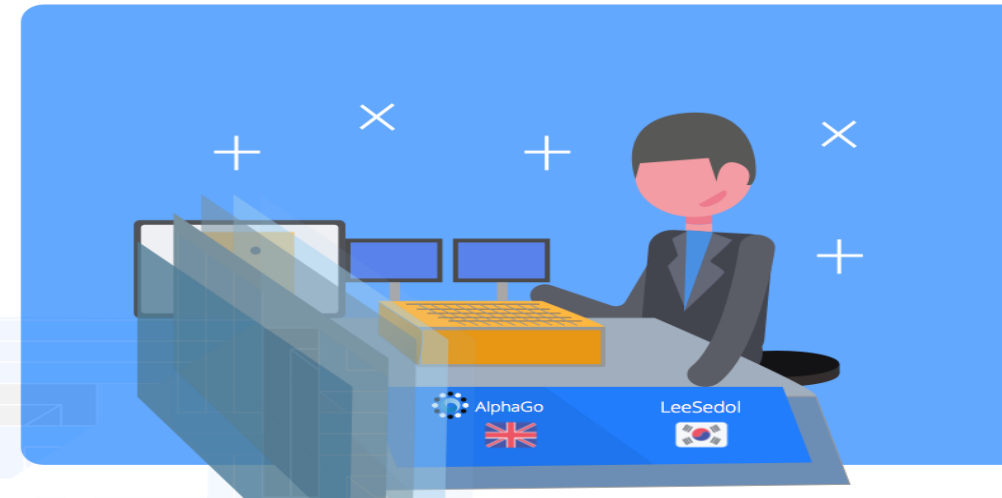


# INTELLIGENCE ARTIFICIELLE

Discipline scientifique recherchant des Méthodes de résolution de problèmes à forte complexité logique ou algorithmique



Google DeepMind







### MEDICAL ARTIFICIAL INTELLIGENCE

## Your virtual medical assistant

I'm being made with medical artificial intelligence.

I can assist you with medical questions & answers, your daily health & wellness, reminders and follow up.

I can also help doctors and nurses with personalized medical questions tied to patients EMRs and medical literature. We know doctors are really busy people and also need help.

My creators from Stanford University are also working on big data and personalized medicine.



Three screenshots of the Ask MedWhat app interface showing search results for "how to relieve from dysmenorrhea".

**Home** | how to relieve from dysmenorrhea

The following steps may allow you to avoid prescription medications:

- Apply a heating pad to your lower belly area, below your belly button. Never fall asleep with the heating pad on.
- Do light circular massage with your fingertips around your lower belly area.
- Drink warm beverages.
- Eat light but frequent meals.
- Follow a diet rich in complex carbohydrates such as whole grains, fruits, and vegetables, but low in salt, sugar, alcohol, and caffeine.

- Keep your legs raised while lying down, or lie on your side with your knees bent.
- Practice relaxation techniques such as meditation or yoga.
- Try over-the-counter anti-inflammatory medicine, such as ibuprofen. Start taking it the day before your period is expected to start, and continue taking it regularly for the first few days of your period.
- Try vitamin B6, calcium, and magnesium supplements, especially if your pain is from PMS.
- Take warm showers or baths.
- Walk or exercise regularly, including pelvic rocking exercises.

• Lose weight if you are overweight. Get regular, aerobic exercise.

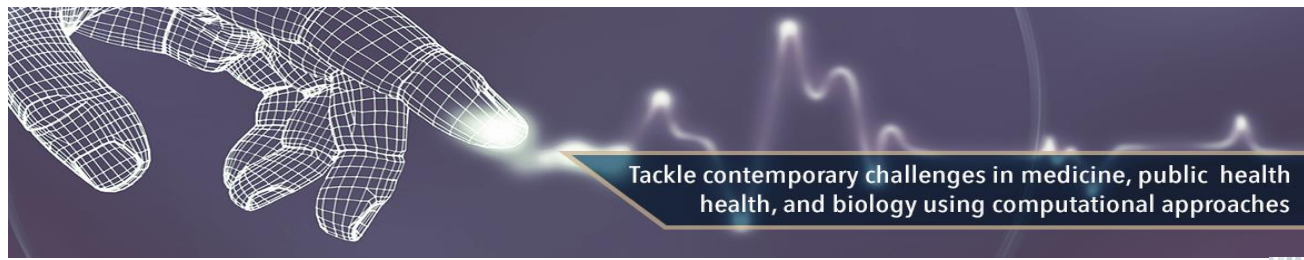
If these self-care measures do not work, your doctor may prescribe medications such as:

- Antibiotics
- Antidepressants
- Birth control pills
- Prescription anti-inflammatory medicines
- Prescription pain relievers (including narcotics, for brief periods)

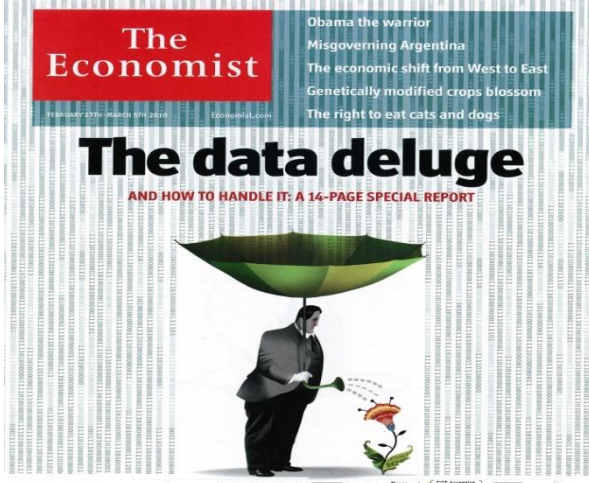
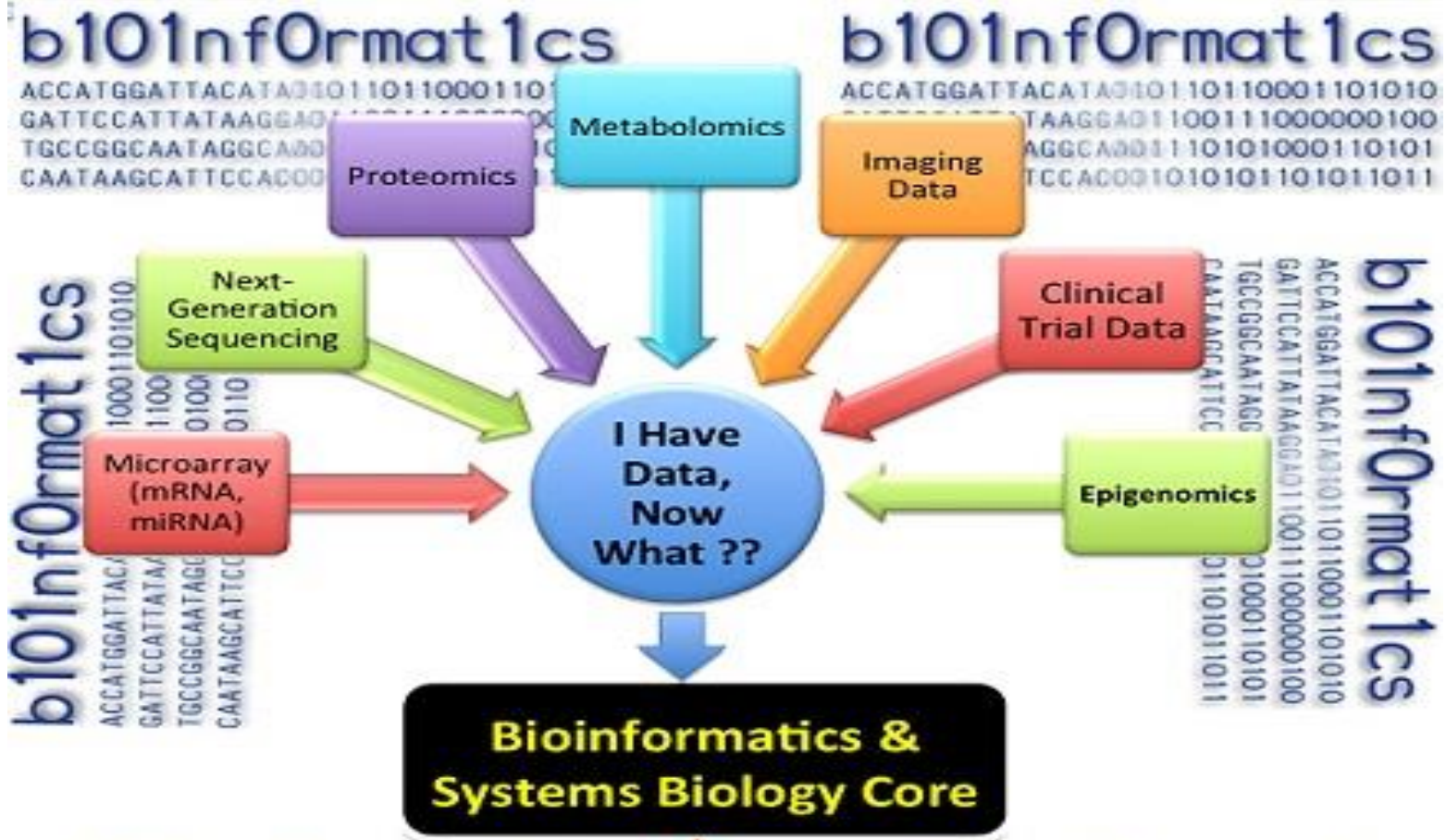
Did you like this answer?

LIKE DISLIKE



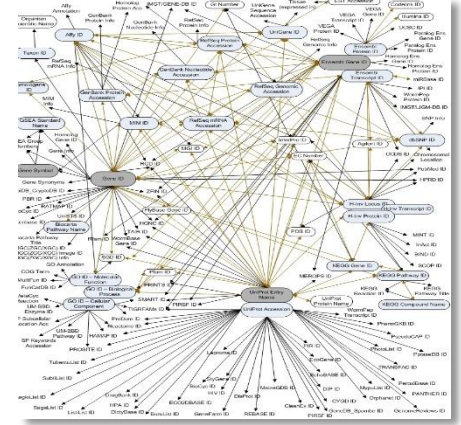


Tackle contemporary challenges in medicine, public health, and biology using computational approaches



**The Economist**  
 FEBRUARY 23RD - MARCH 5TH 2010  
 Obama the warrior  
 Misgoverning Argentina  
 The economic shift from West to East  
 Genetically modified crops blossom  
 The right to eat cats and dogs

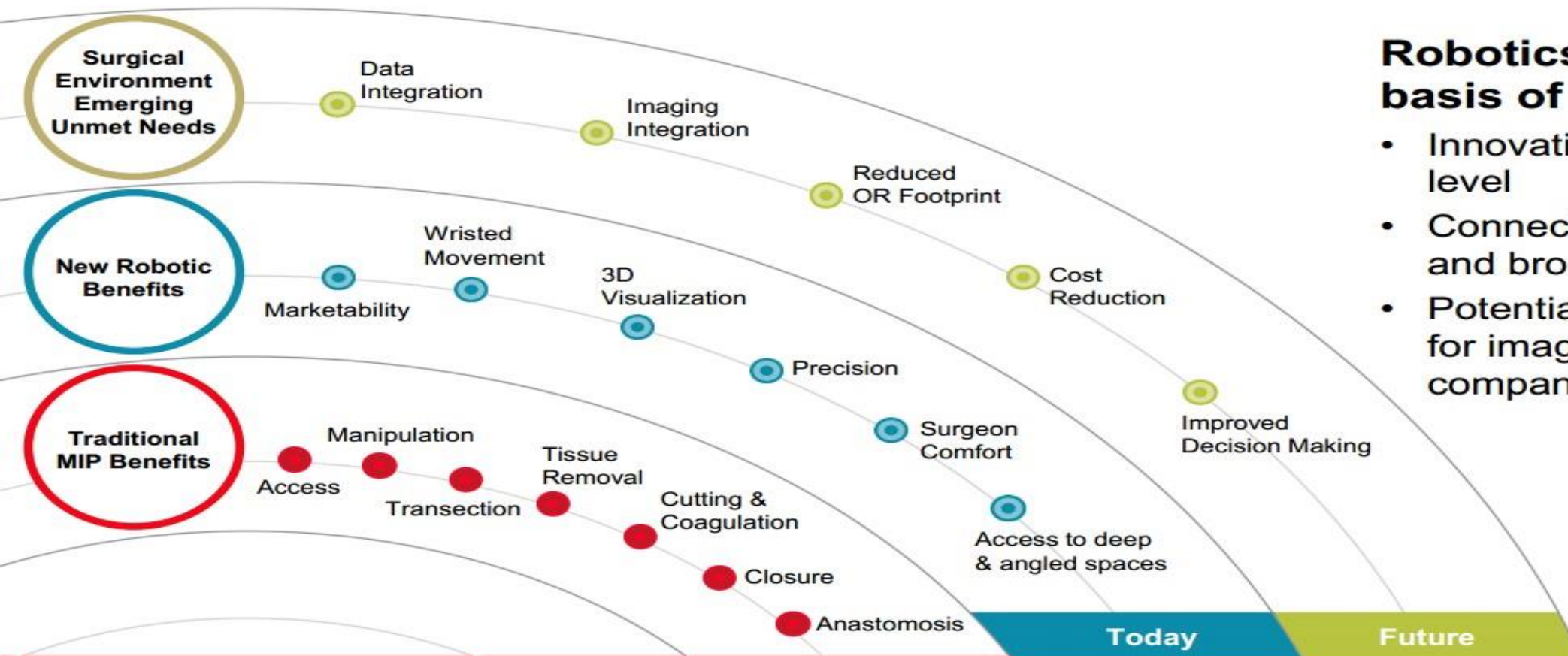
**The data deluge**  
 AND HOW TO HANDLE IT: A 14-PAGE SPECIAL REPORT







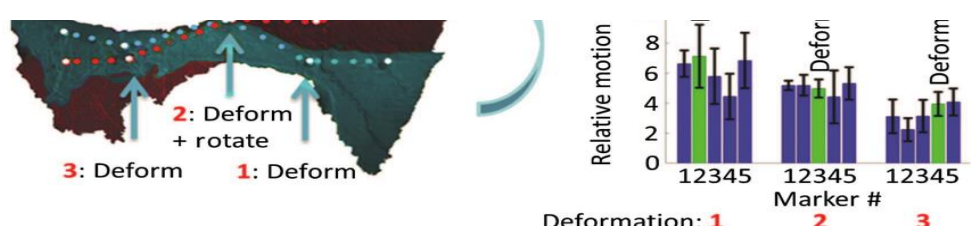
# Robotics Opportunities: Today and Future



## Robotics is shifting the basis of competition

- Innovation at the system level
- Connection between OR and broader environment
- Potential bridge to the OR for imaging & diagnostic companies

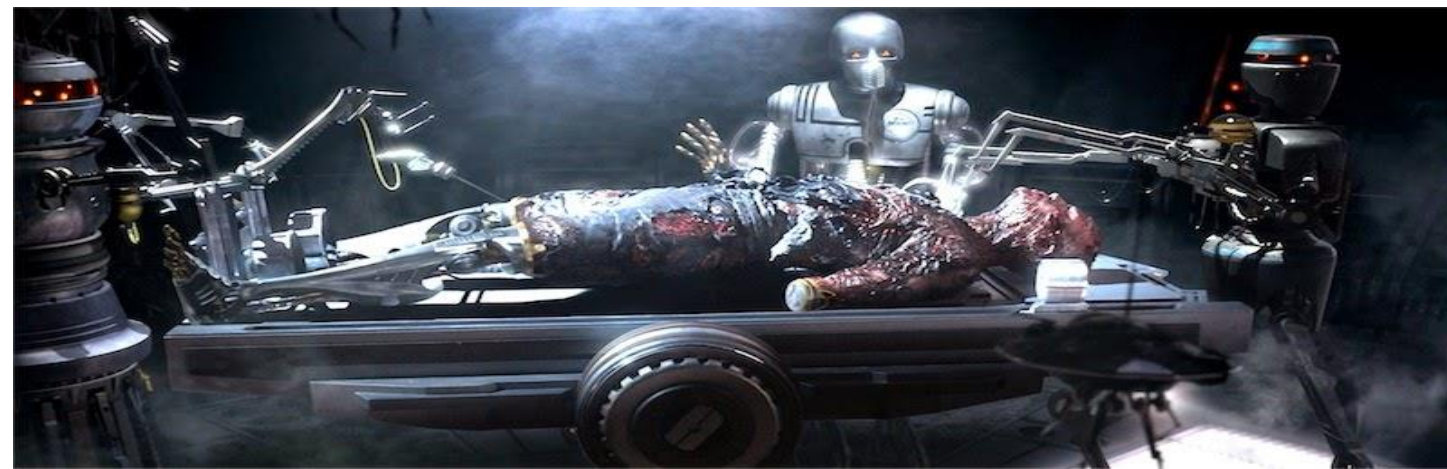
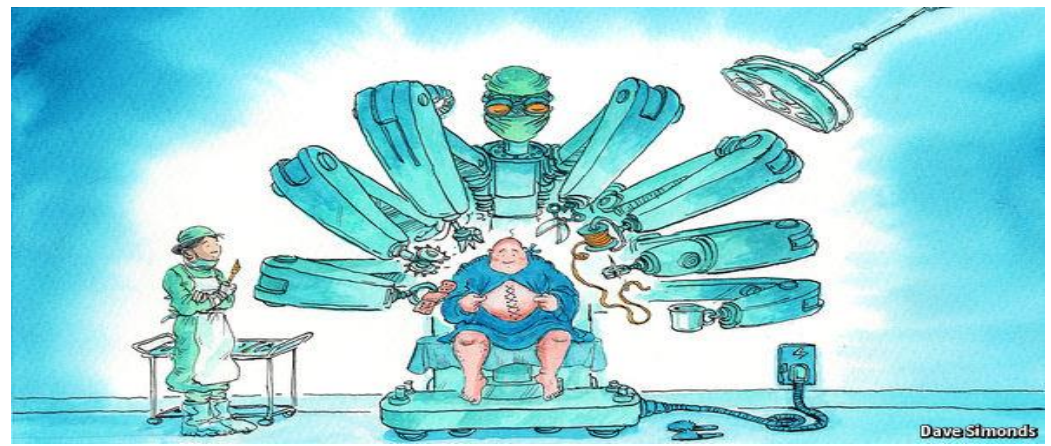
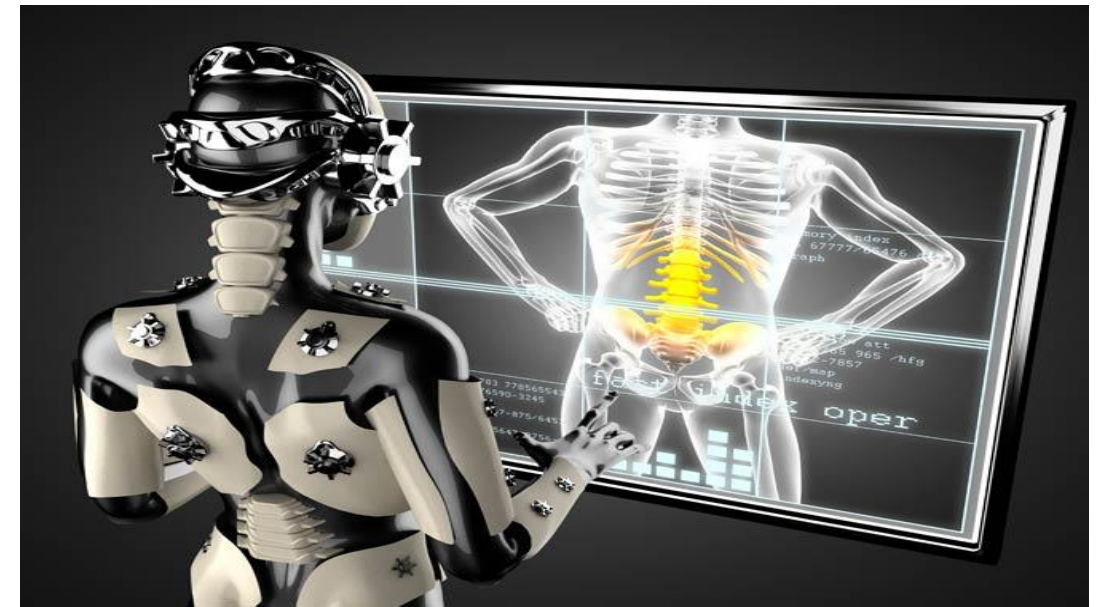
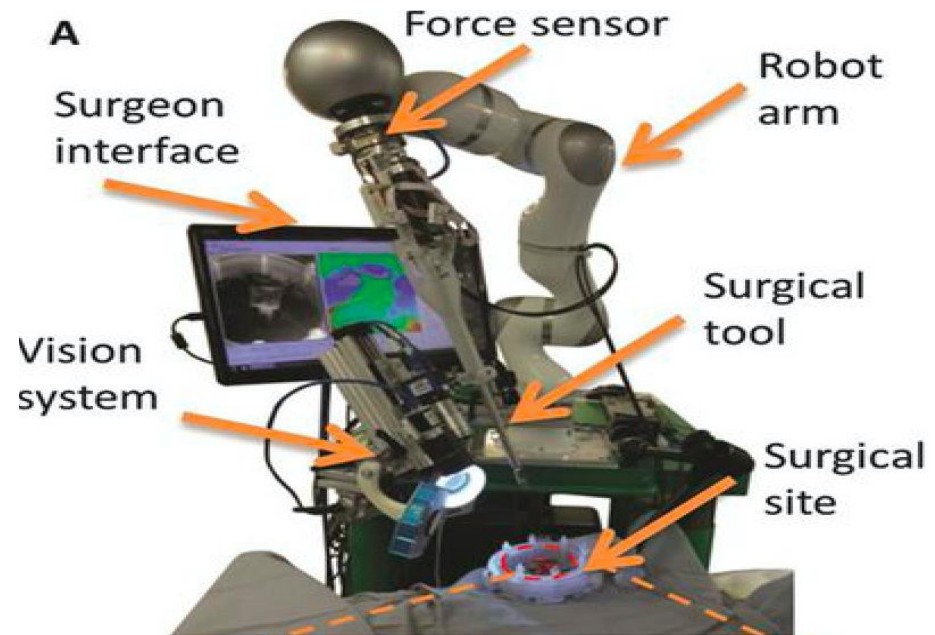




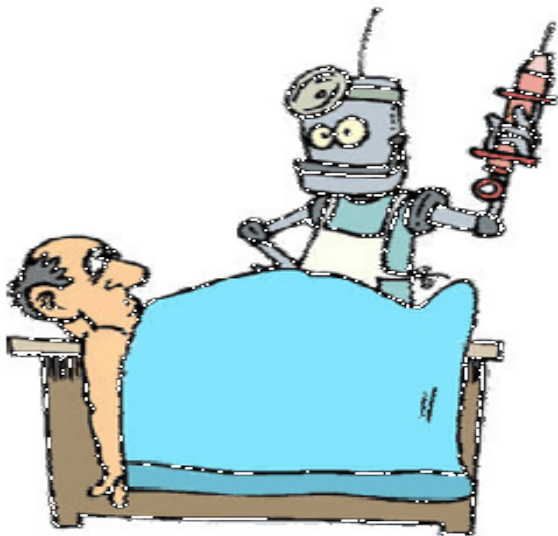
ENGINEERING

# Supervised autonomous robotic soft tissue surgery

Azad Shademan,<sup>1</sup> Ryan S. Decker,<sup>1</sup> Justin D. Opfermann,<sup>1</sup> Simon Leonard,<sup>2</sup>  
Axel Krieger,<sup>1</sup> Peter C. W. Kim<sup>1\*</sup>







© Photopress Belfast



### Notre mission

Inventer des technologies de robotique chirurgicale de dernière génération

### Une triple ambition

Augmenter le confort et la sécurité des patients

Assister et fiabiliser le geste des chirurgiens

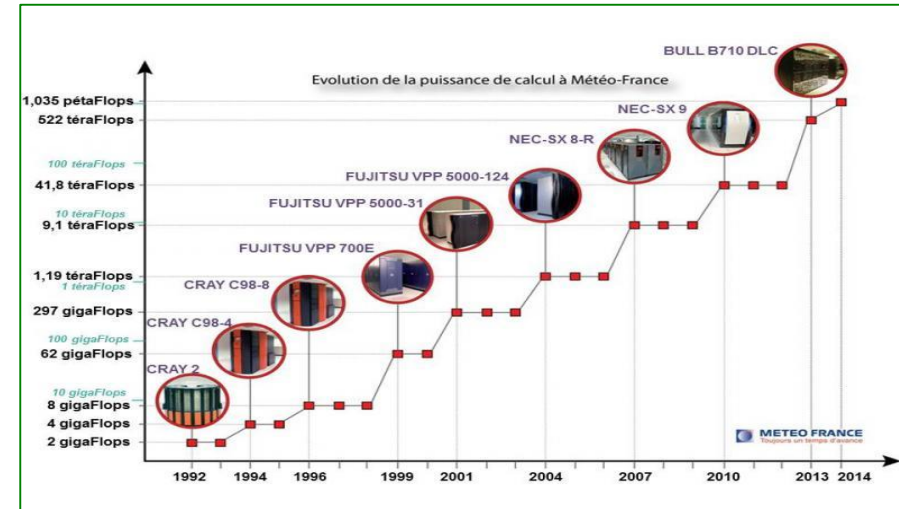
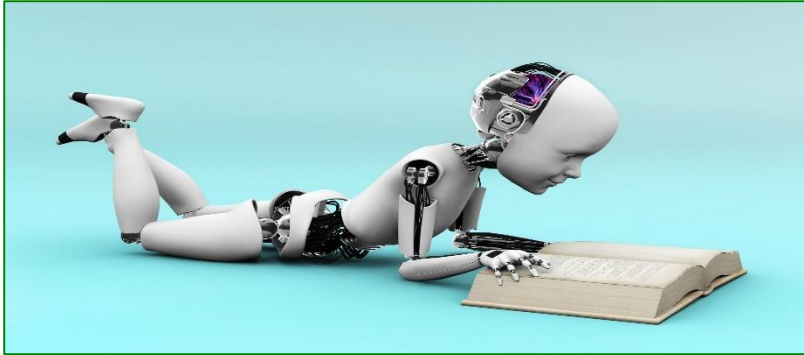
Contribuer à améliorer la performance des hôpitaux



## INTELLIGENCE si :

- Reproduction
- Curiosité

# INTELLIGENCE ARTIFICIELLE



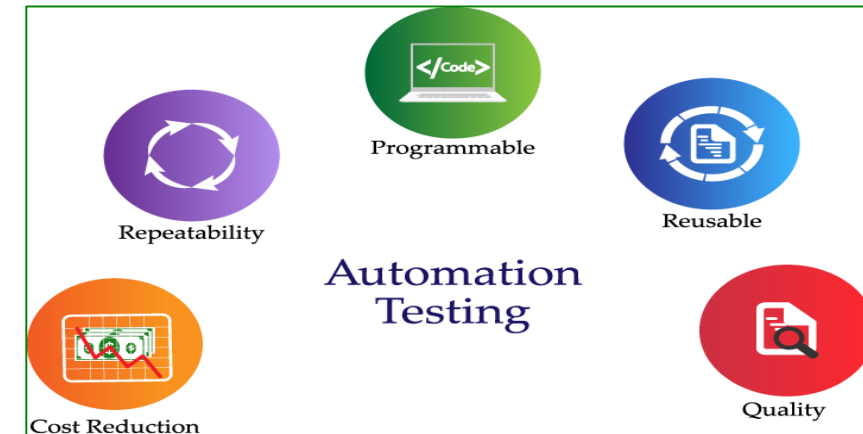
Une machine peut être programmée pour pouvoir réécrire, restructurer sa  
Connaissance initiale, à partir d'informations reçues ou perçues

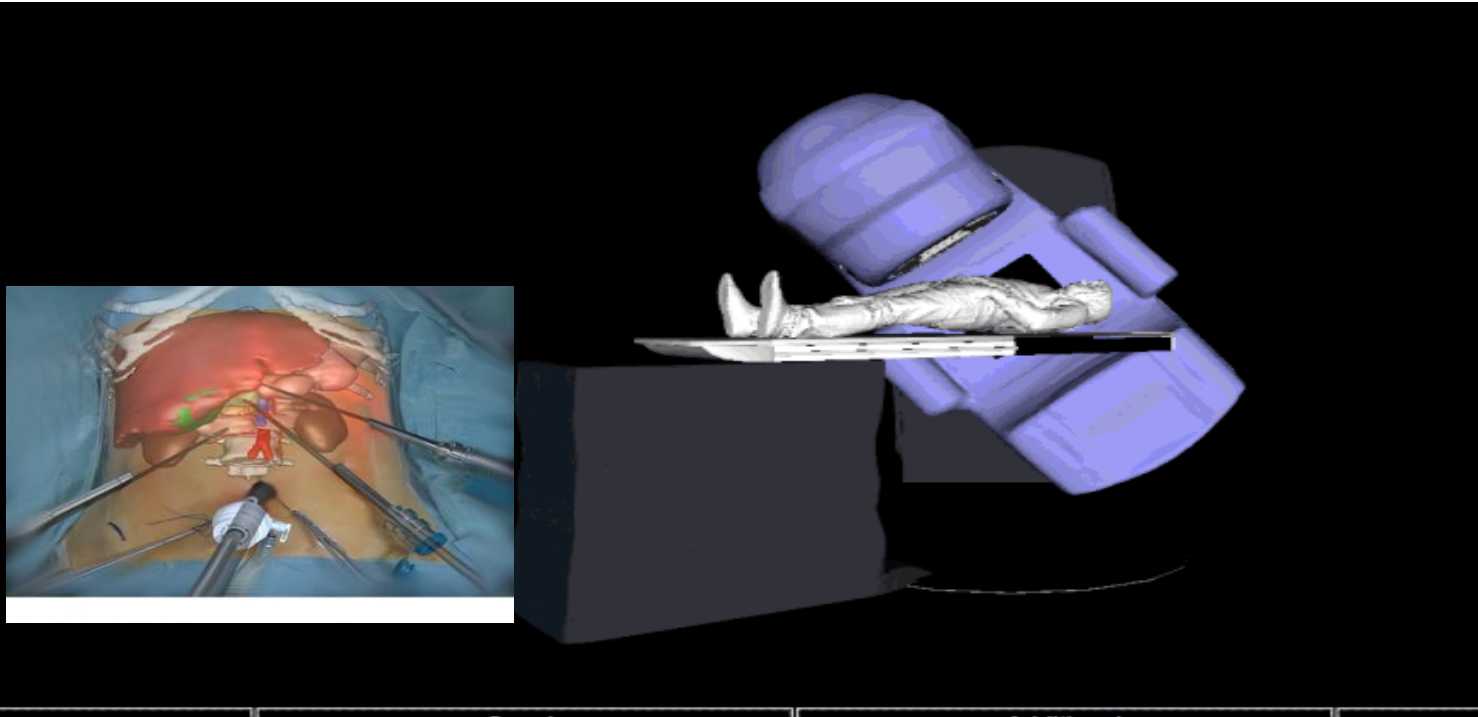
## AUTOMATIQUE

**ROBOTIQUE** : Conception de machines automatiques (+/-  
grand niveau d'autonomie)



**AUTOMATIQUE** : Science qui traite de la  
MODELISATION, l'ANALYSE, l'IDENTIFICATION, et  
la COMMANDE des systèmes dynamiques

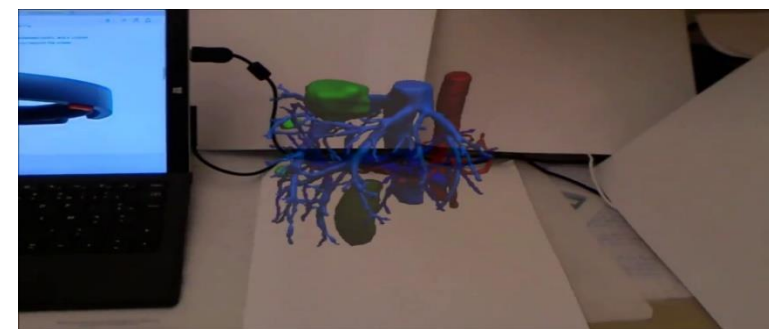
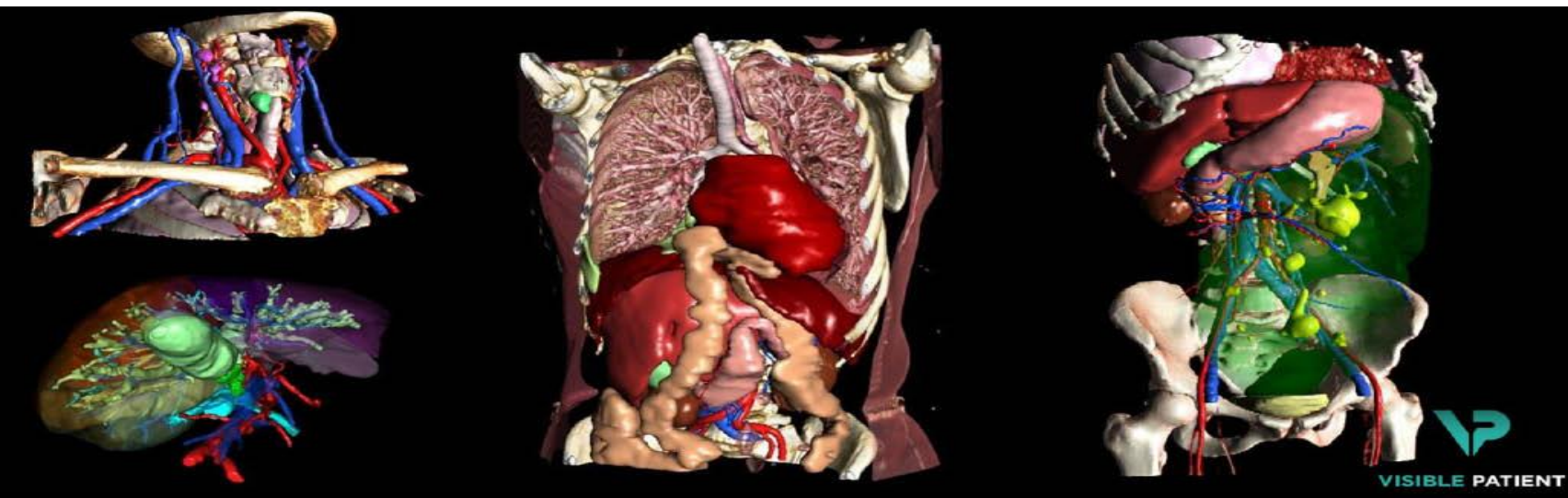




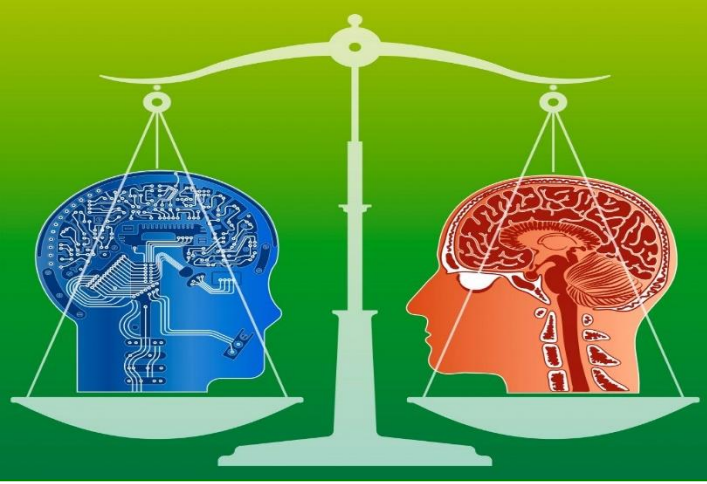
# RÉALITÉ AUGMENTÉE



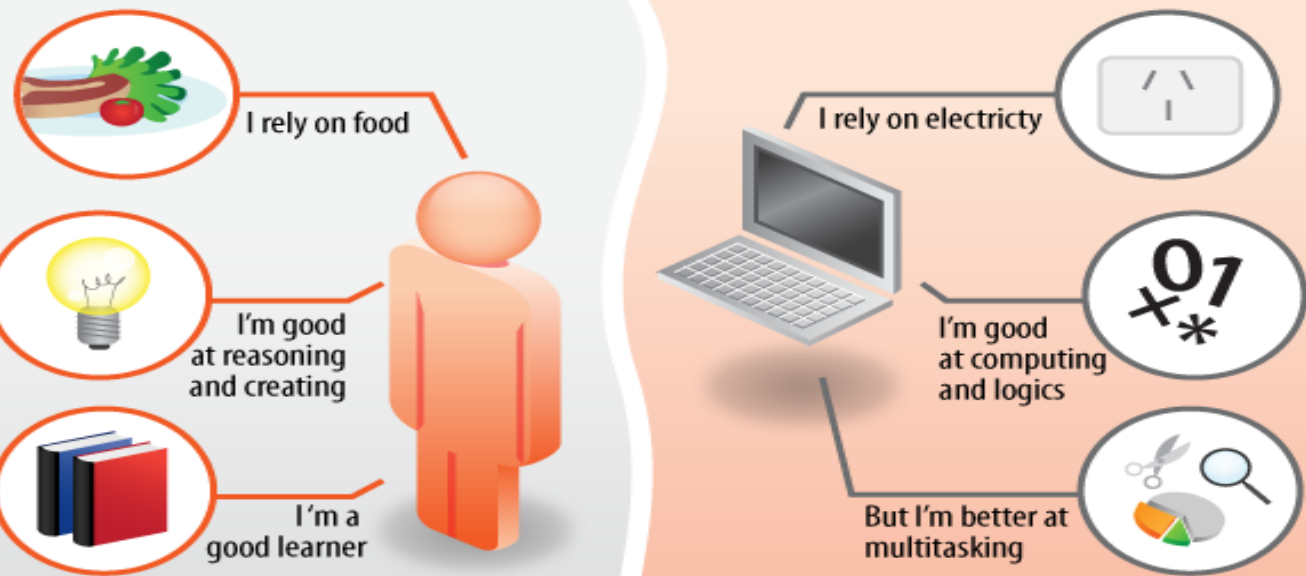
VISIBLE PATIENT



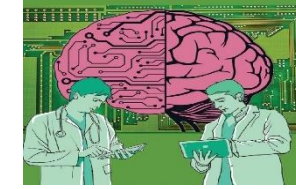




# Difference Between Human & Computer



# DifferenceBetween.net



Microsoft 23 mai 2013 Les Bites
VIVA MAY 23-25 TECHNOLOGY

## le grand entretien

**« Dans la santé, nous ne sommes plus à l'heure du sachant tout-puissant »**

**NATHALIE COLLIN**  
Directrice générale de Pfizer  
**ALAIN TOLESIANO**  
Président de l'Association française de Neurologie

**Le grand entretien** est une émission de radio qui propose un échange de vues entre deux personnalités de la vie intellectuelle et professionnelle. Cette semaine, c'est Nathalie Collin, directrice générale de Pfizer, et Alain Toleciano, président de l'Association française de Neurologie, qui sont invités.

**Nathalie Collin** est née en 1961 à Paris. Elle est diplômée de l'École Polytechnique et de l'École Normale Supérieure. Elle a travaillé pour la société de conseil McKinsey & Company avant de rejoindre Pfizer en 2007. Elle est membre du conseil d'administration de l'Association française de Neurologie.

**Alain Toleciano** est né en 1947 à Paris. Il est diplômé de l'École Polytechnique et de l'École Normale Supérieure. Il a travaillé pour la société de conseil McKinsey & Company avant de rejoindre l'Association française de Neurologie en 2007. Il est membre du conseil d'administration de l'Association française de Neurologie.

**Le grand entretien** est une émission de radio qui propose un échange de vues entre deux personnalités de la vie intellectuelle et professionnelle. Cette semaine, c'est Nathalie Collin, directrice générale de Pfizer, et Alain Toleciano, président de l'Association française de Neurologie, qui sont invités.



## 2018 This Is What Happens In An Internet Minute



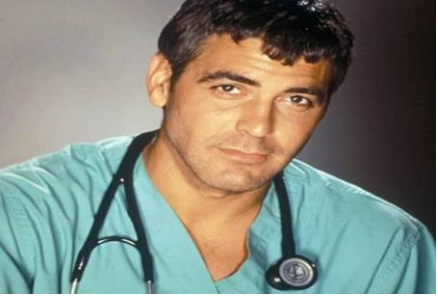
## Randomized Trial Comparing a Web-Mediated Follow-up With Routine Surveillance in Lung Cancer Patients

Fabrice Denis, Claire Lethrosne, Nicolas Pourel, Olivier Molinier,



**Conclusions:** A web-mediated follow-up algorithm based on self-reported symptoms improved OS due to early relapse detection and better performance status at relapse.





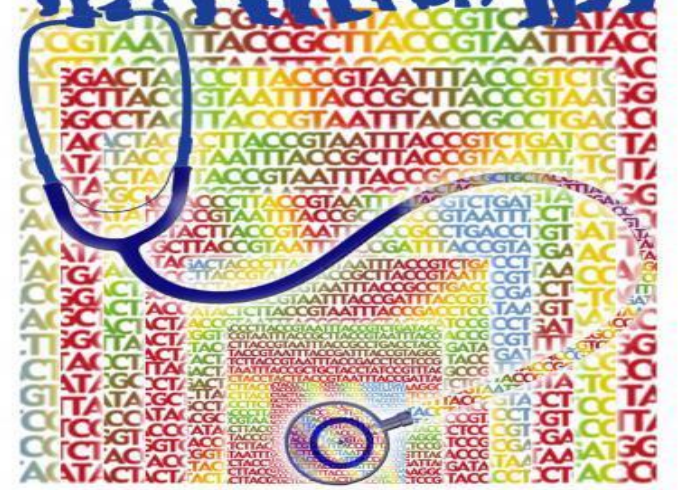
# REDEFINIR LE MEDECIN DE DEMAIN

La Pluridisciplinarité au Cœur de  
la Stratégie Thérapeutique

René-Théophile-Hyacinthe Laennec, (1781-1926)



Médecin Français, Inventeur et metteur au point  
du diagnostic médical par auscultation (1819). Inventeur du stéthoscope



BIO TECHNO CLINIQUE

# MAUVAISE PREDICTION, BONNE PERSPECTIVE



« Dans 10 ans nous aurons vaincu le cancer... »

RICHARD NIXON, 1971

Quintuple le budget du NCI en 10 ans  
> **Révolution Biologie Moléculaire**

- **La Survie des Cancers à 5 ans, fin 1960 = 38%**
- **La Survie des Cancers à 5 ans, en 2010 = 68%**

Human Genome Project



1937

## NATIONAL CANCER ACT

### SECTION 404 (a) (1)

The Director shall "collect, analyze and disseminate information...useful in the prevention, diagnosis, and treatment of cancer, including the establishment of an international cancer research data bank...(for) cancer research undertaken in any country for the use of any person involved in cancer research in any country."

11/83

National Cancer Act, 1971

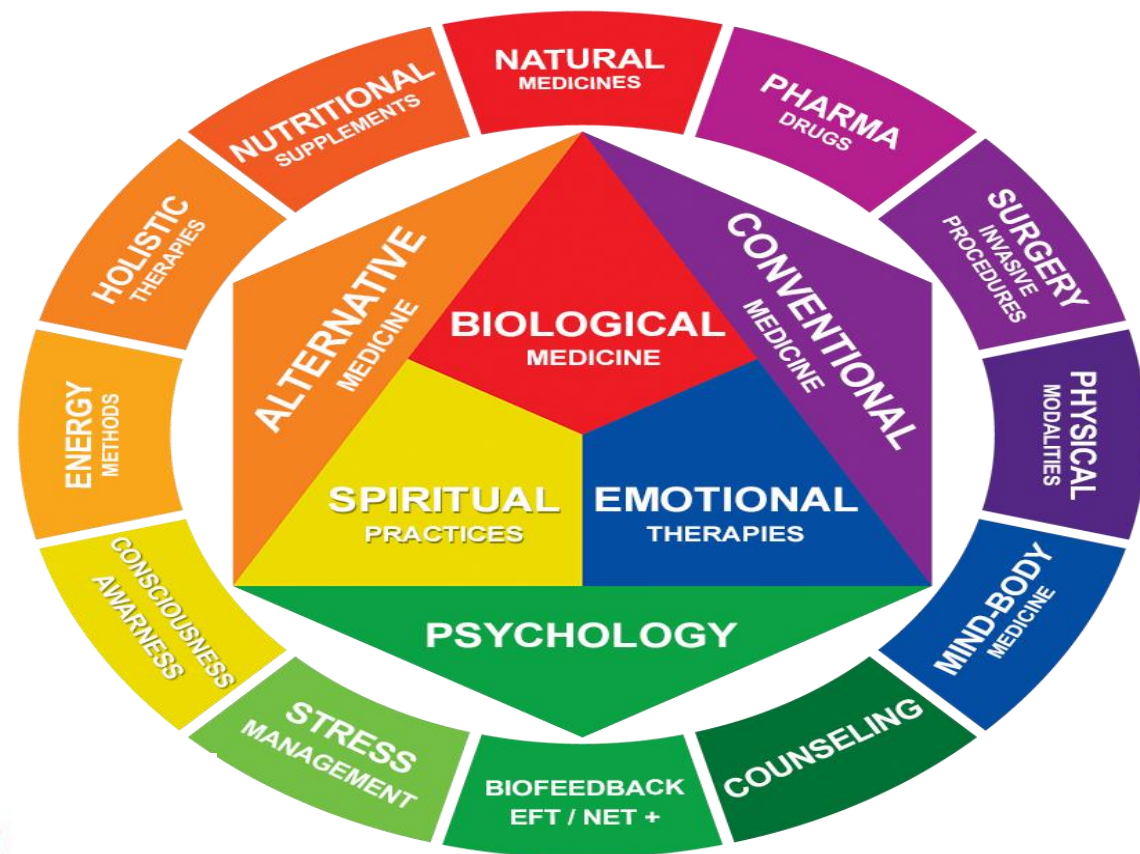
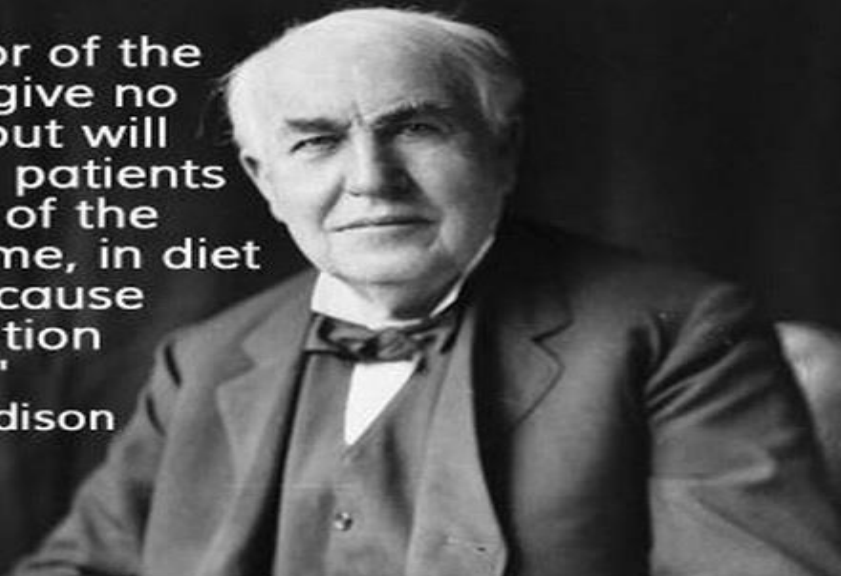


«Pour ce qui est de l'avenir, il ne s'agit pas de le prévoir mais de le rendre possible »

- Antoine de Saint-Exupéry



"The doctor of the future will give no medicine, but will interest his patients in the care of the human frame, in diet and in the cause and prevention of disease."  
~ Thomas Edison



## ETHIQUE



## COLLOQUE ÉTHIQUE ET GÉNÉTIQUE

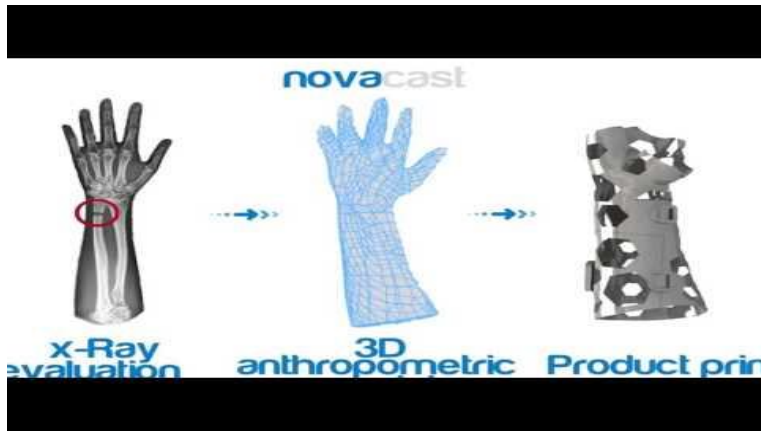
Réflexion Ethique en Génétique Prédictive

29 mars 2017

PALAIS BRONGNIART, PARIS

9H00 - 17H30

# Impression 3D



# Réalité Virtuelle



# Réalité augmentée



# Santé Connectée



# Silico Trial



# Intelligence Artificielle



# Biologie synthétique



# Robotique



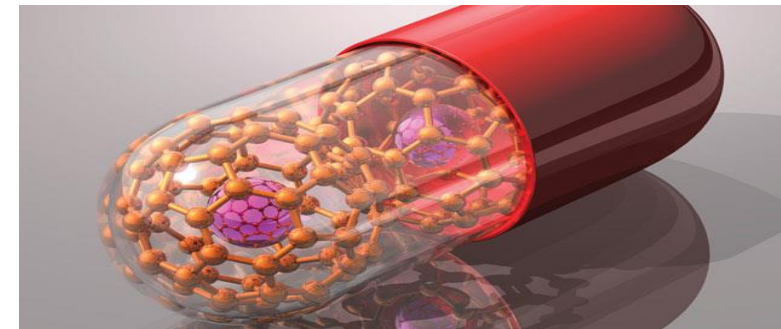
# Tricorder Médical



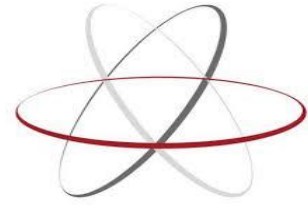
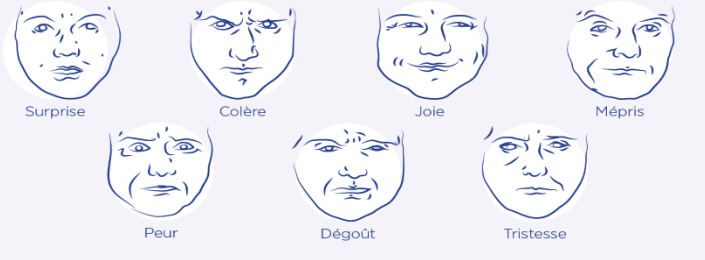
# Séquençage génétique



# Nanomedecine







Institut  
**Rafaël**  
Maison de l'après cancer

