

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

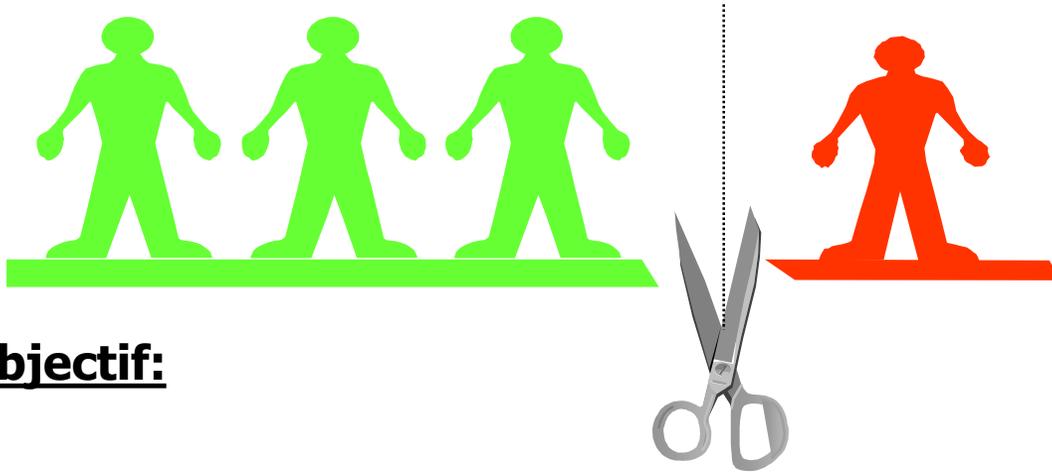
18^e siècle

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



VOLTAIRE

La Statistique \neq Médecine personnalisée



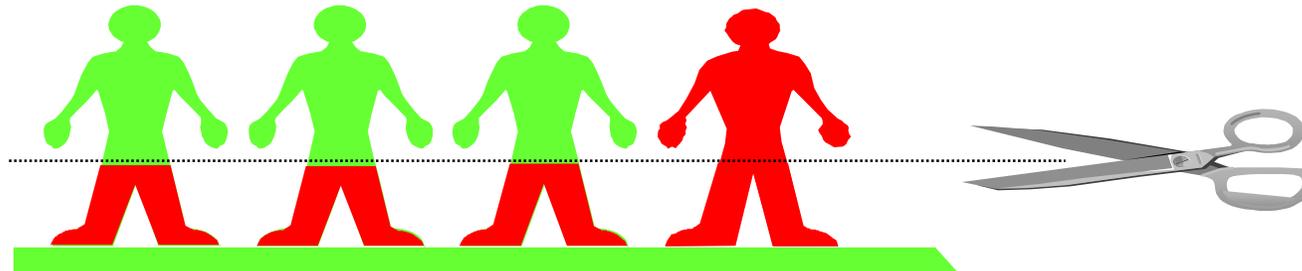
Un seul patient rechutera

\Rightarrow Ce patient seul recevra un traitement maximal

Objectif:

Réalité:

please cut here



Statistiquement, chaque patient a un risque de rechute.

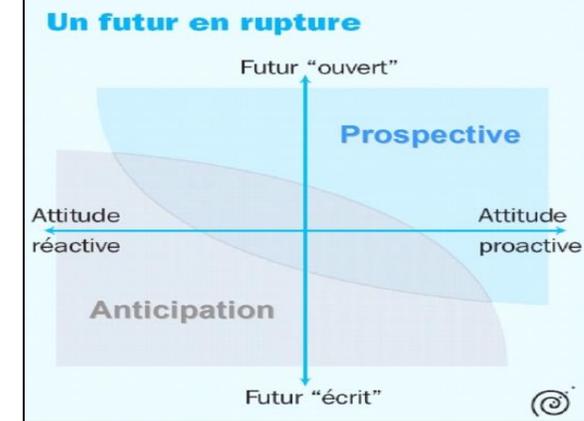
\Rightarrow Chaque patient reçoit un traitement maximal, “probablement” efficace

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^{a,*,b}, Mayada Bourmech^a, Hanah Lamallem^{a,b}, Marc Bollet^{a,b}, Olivier Bauduceau^{a,b}, Pascal Pujol^{a,b,c}, Patrick Bloch^b, David Khayat^{a,b}

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

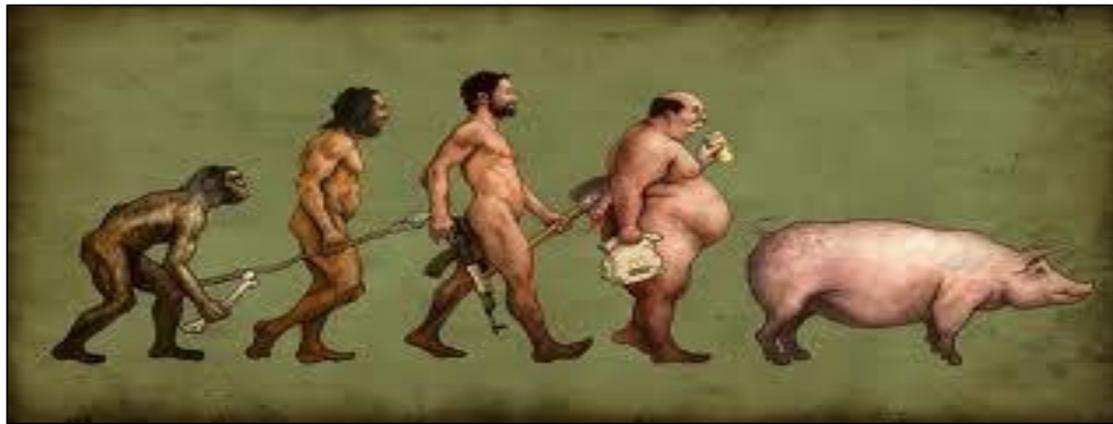
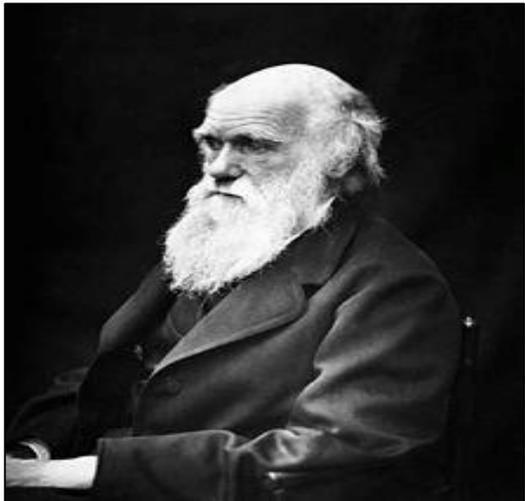
Le Futur :

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

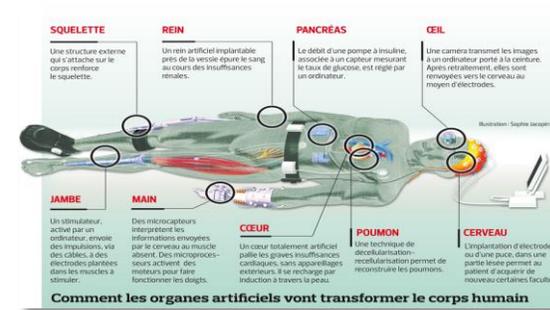
PROSPECTIVE A 10 ANS ...

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**

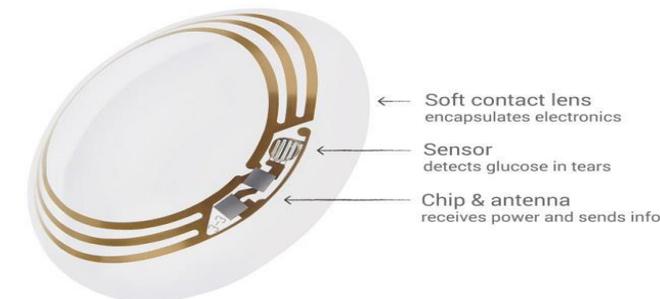
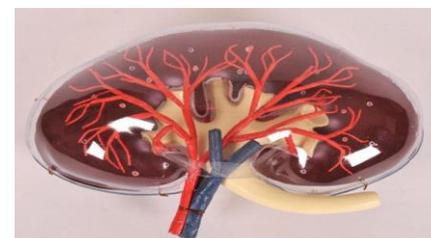
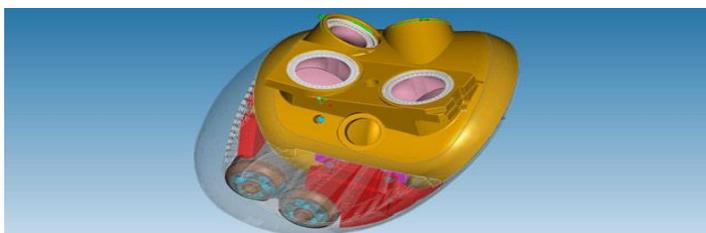
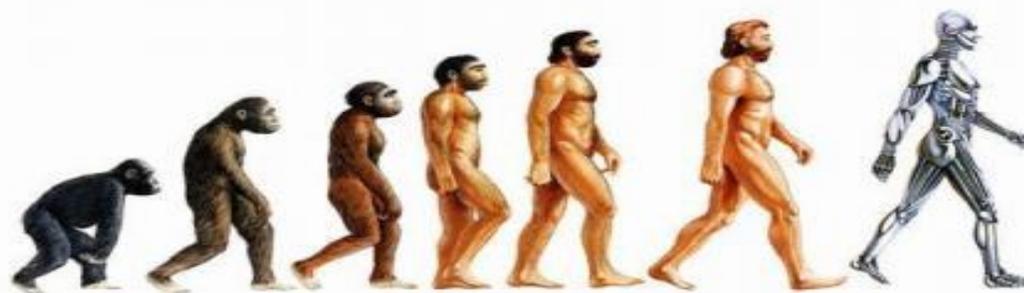
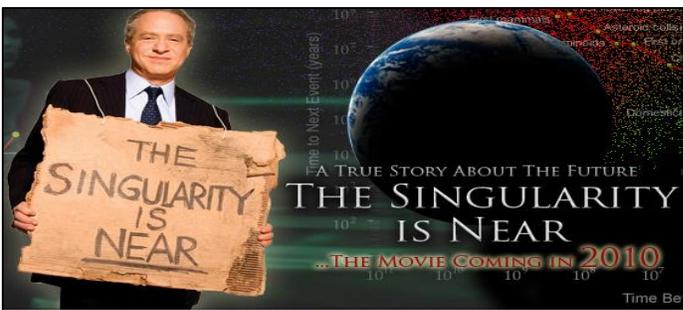
Modification Culturelle

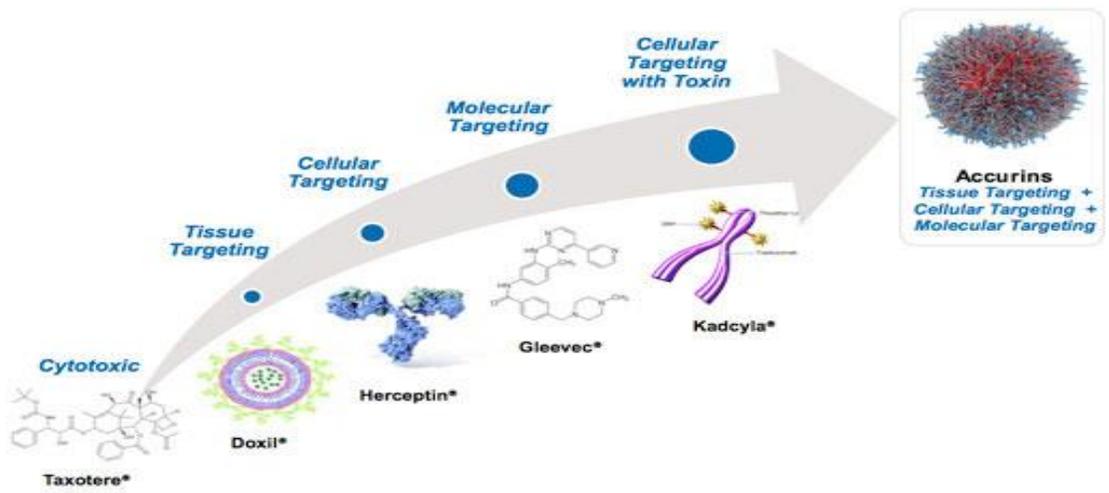


Charles Darwin, 1869

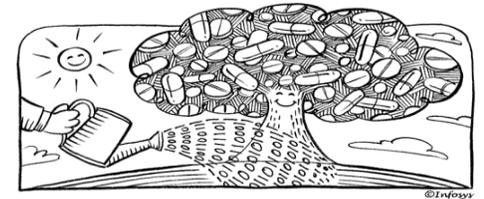


Ray Kurzweill, 2013





NEW DRUGS

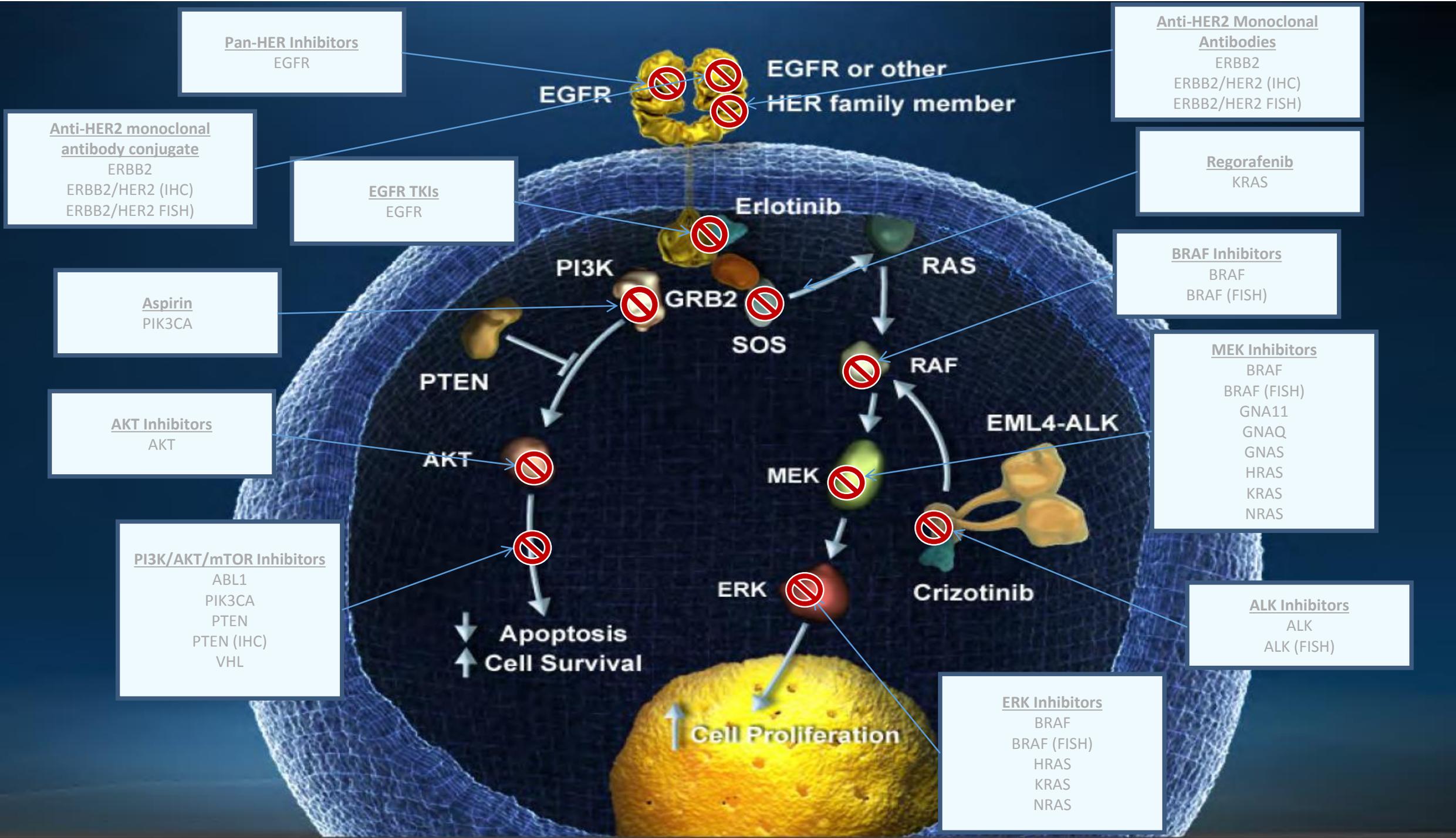


« Les médecins administrent des médicaments dont ils savent très peu, à des malades dont ils savent moins, pour guérir des maladies dont ils ne savent rien.. »



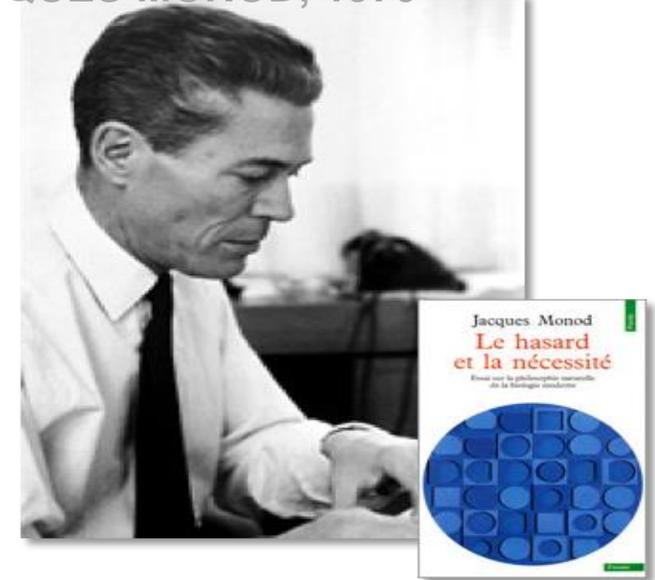
VOLTAIRE





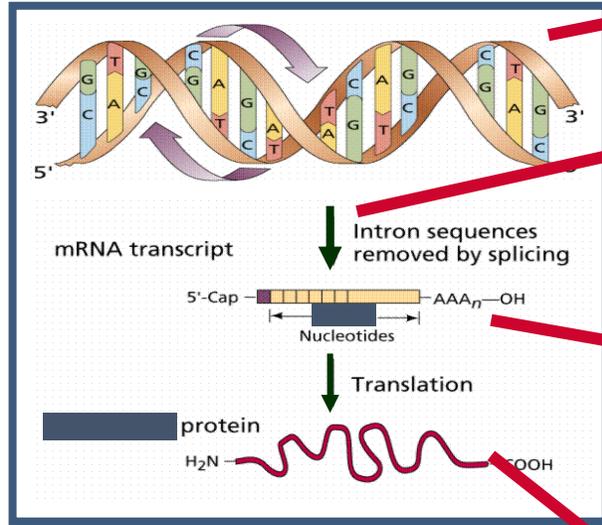
LA REVOLUTION GENETIQUE

JACQUES MONOD, 1970



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

Continuum

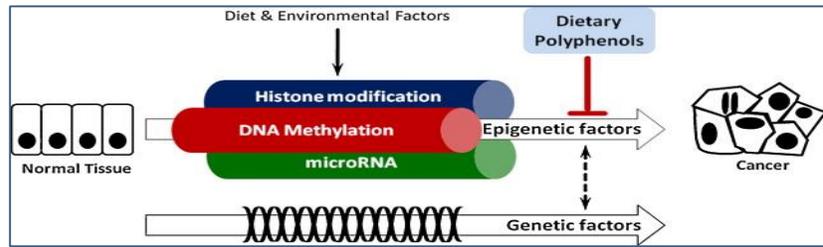


Genomics

Epigenomics

Transcriptomics

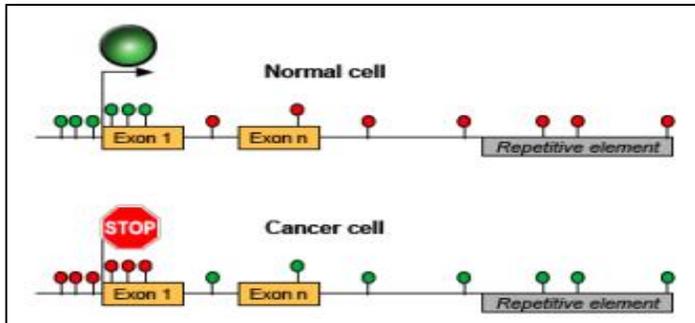
Proteomics



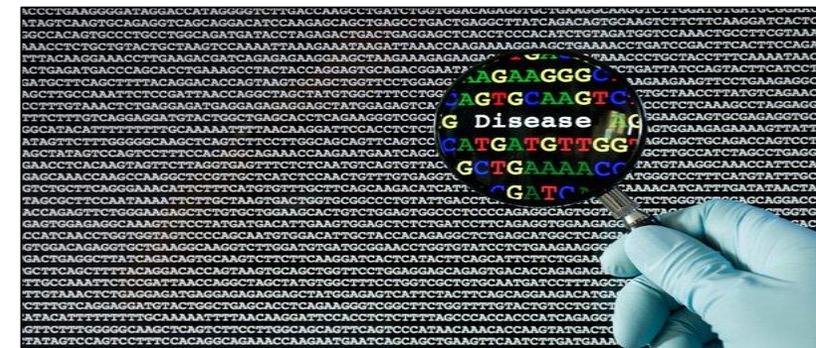
< 10 000 bases DNA during a whole life



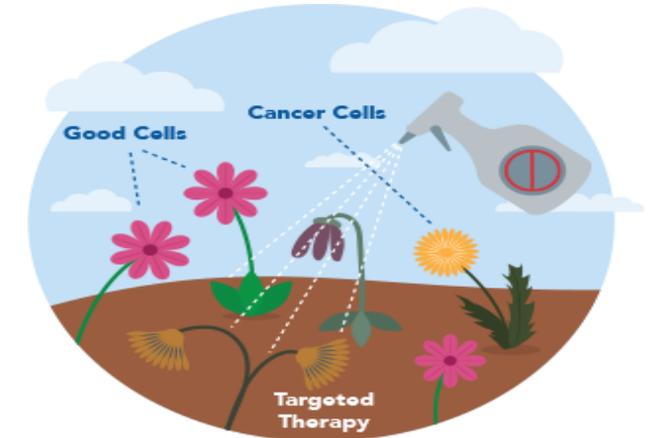
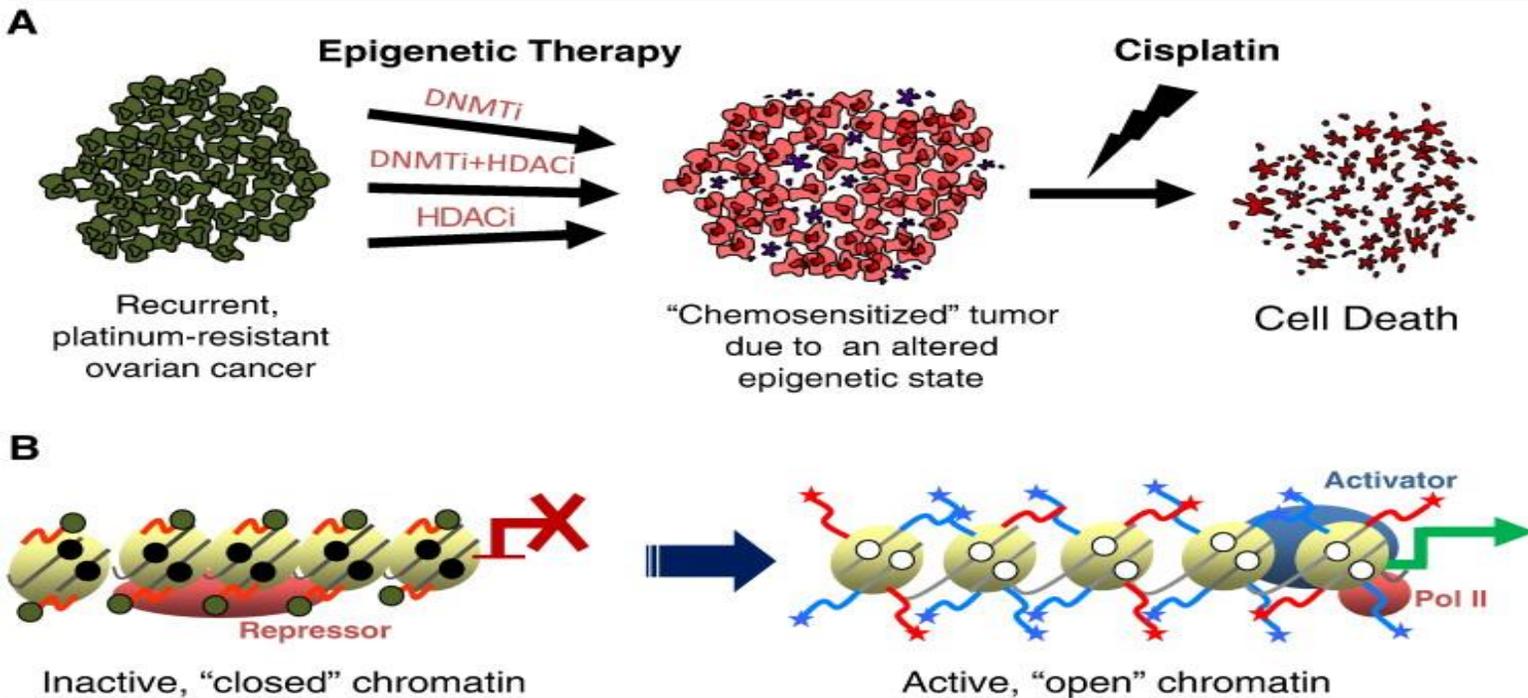
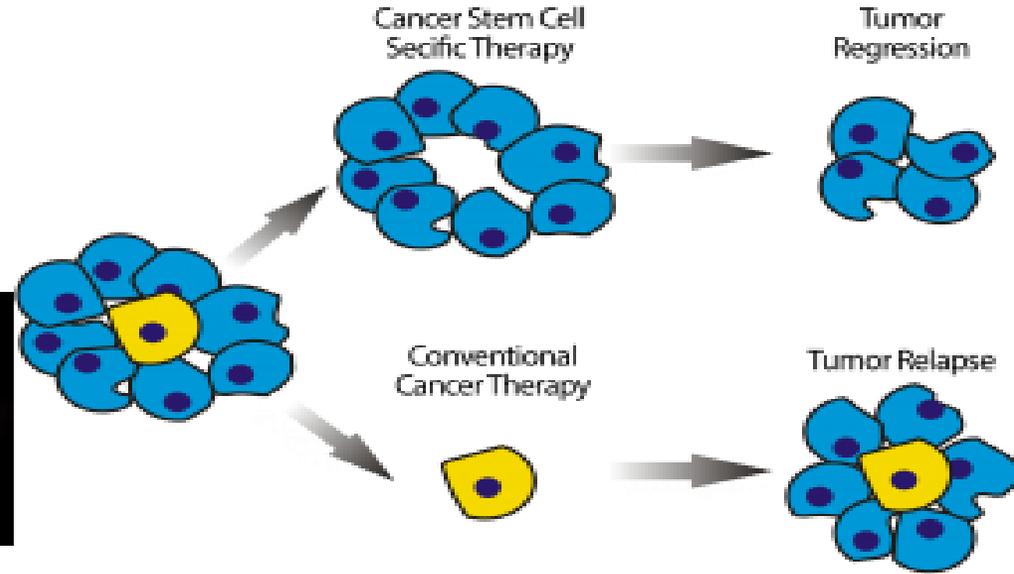
50 milliards per hour



Next Generation Sequencing



EPIDRUGS



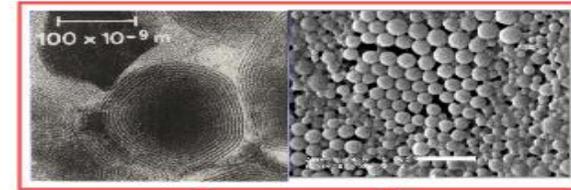
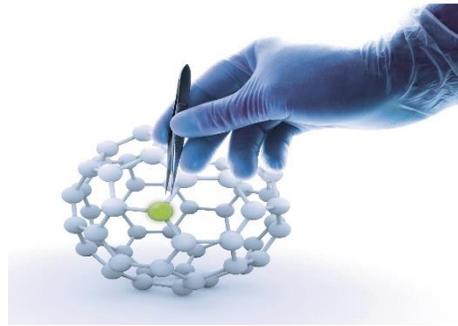
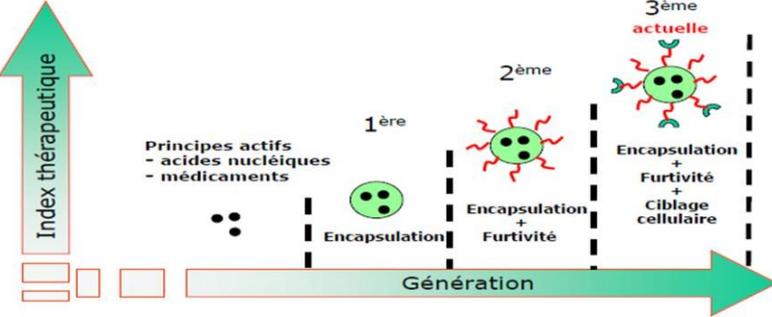
Détruire les cellules souches tumorales

CURRENT CONCEPTS

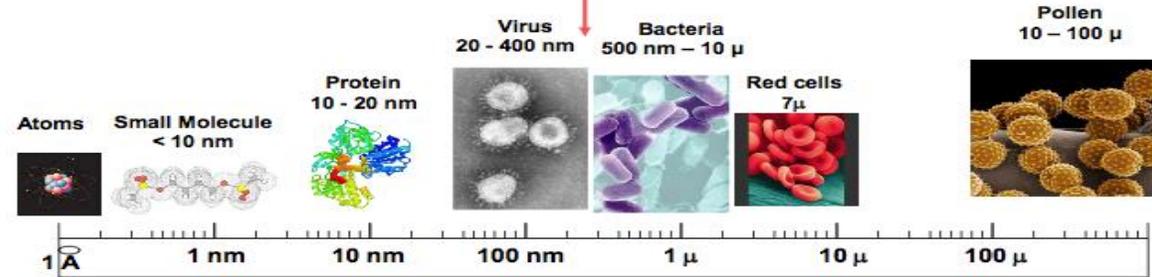
Nanomedicine

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

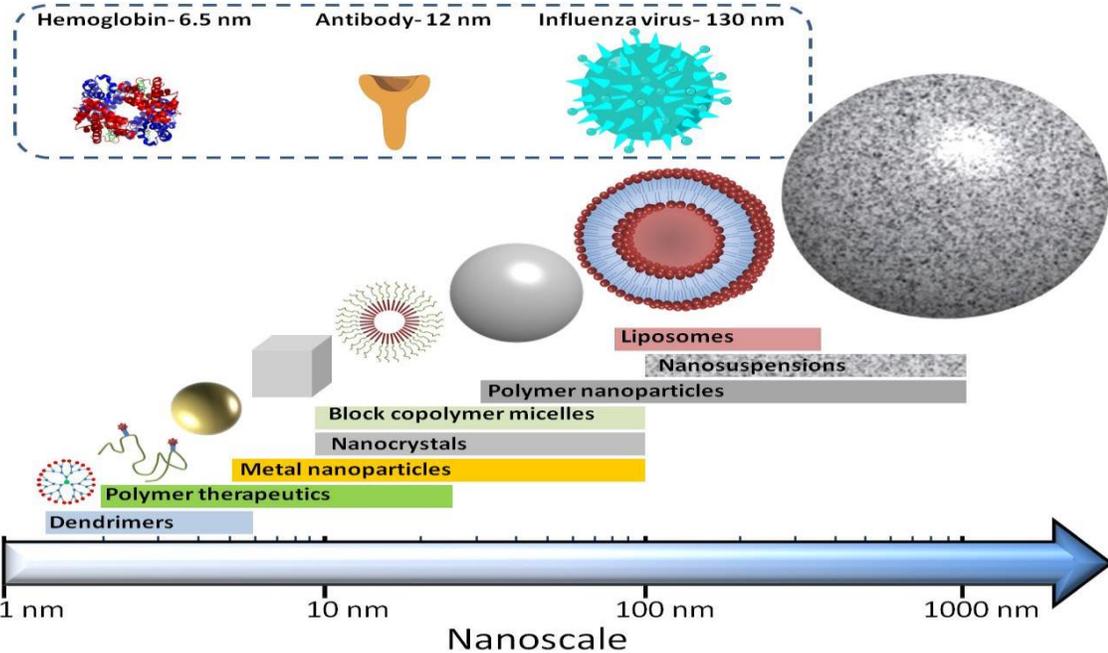


Double défi des nanomédicaments:

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

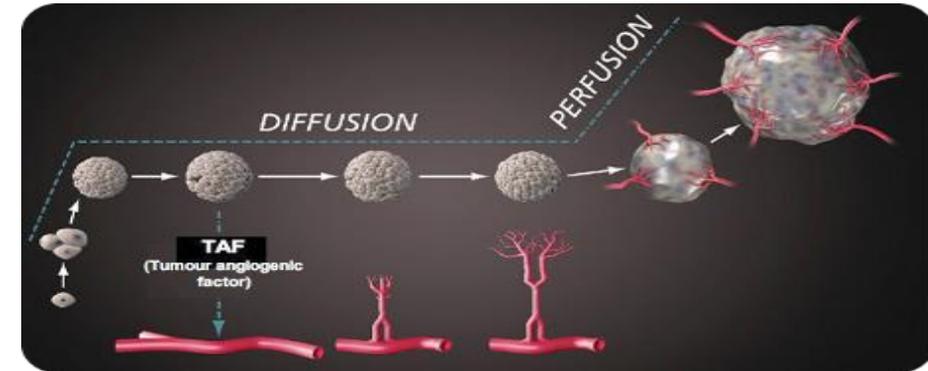
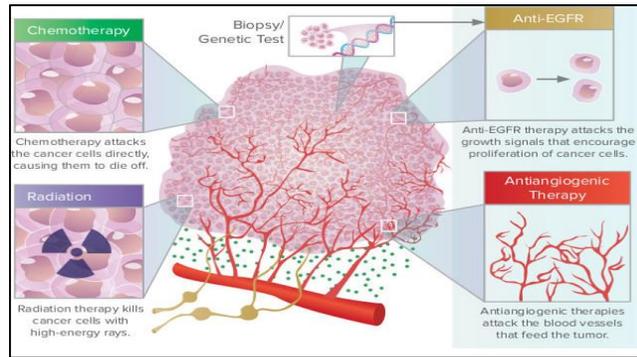
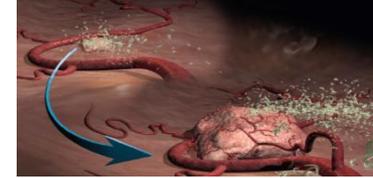


ADRESSER sélectivement vers le tissu ou cellule cible, et d'en contrôler la libération.



ANGIOGENESE TUMORALE

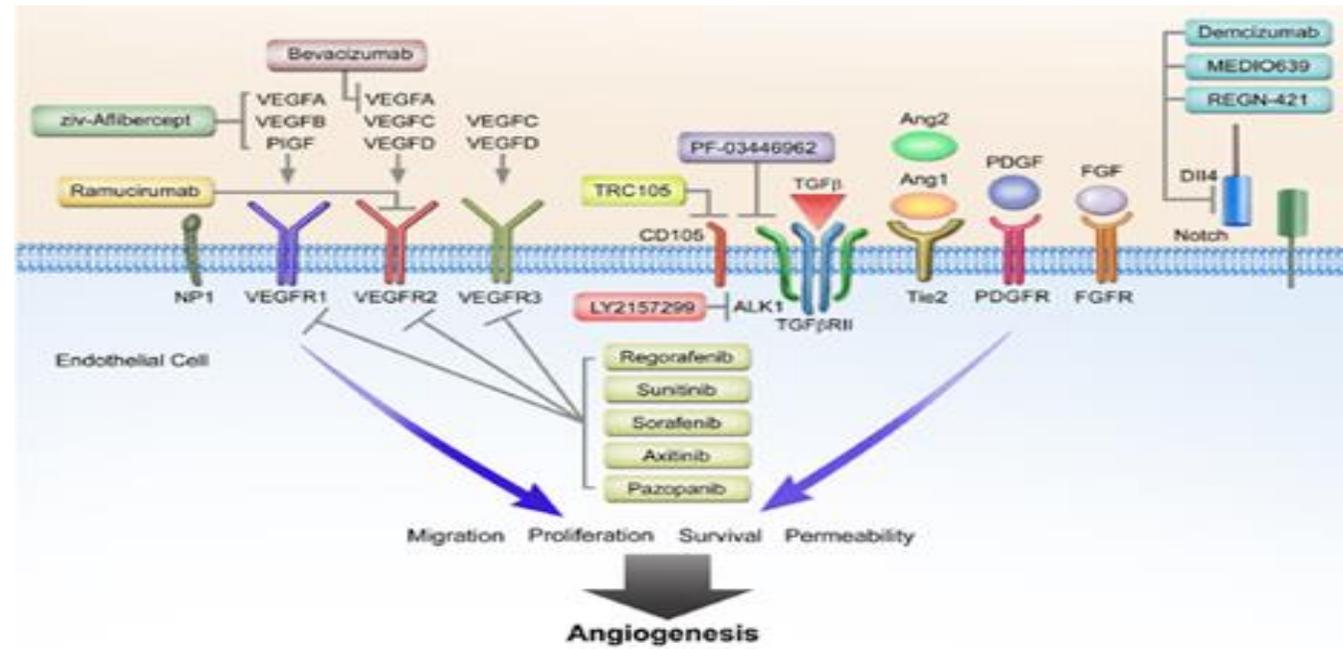
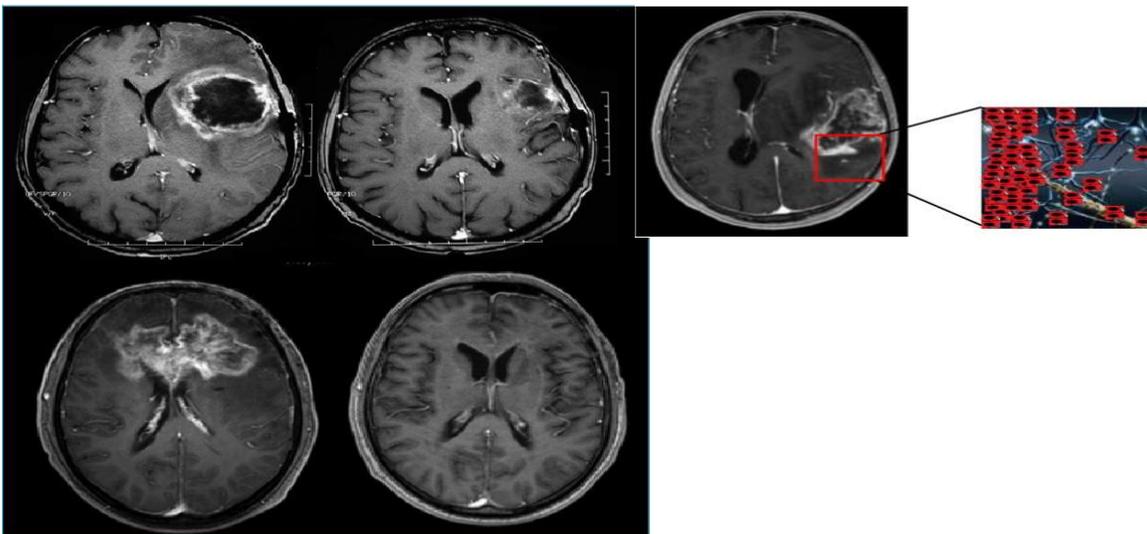
Judah Folkman, père fondateur de l'angiogénèse, NEJM 1971



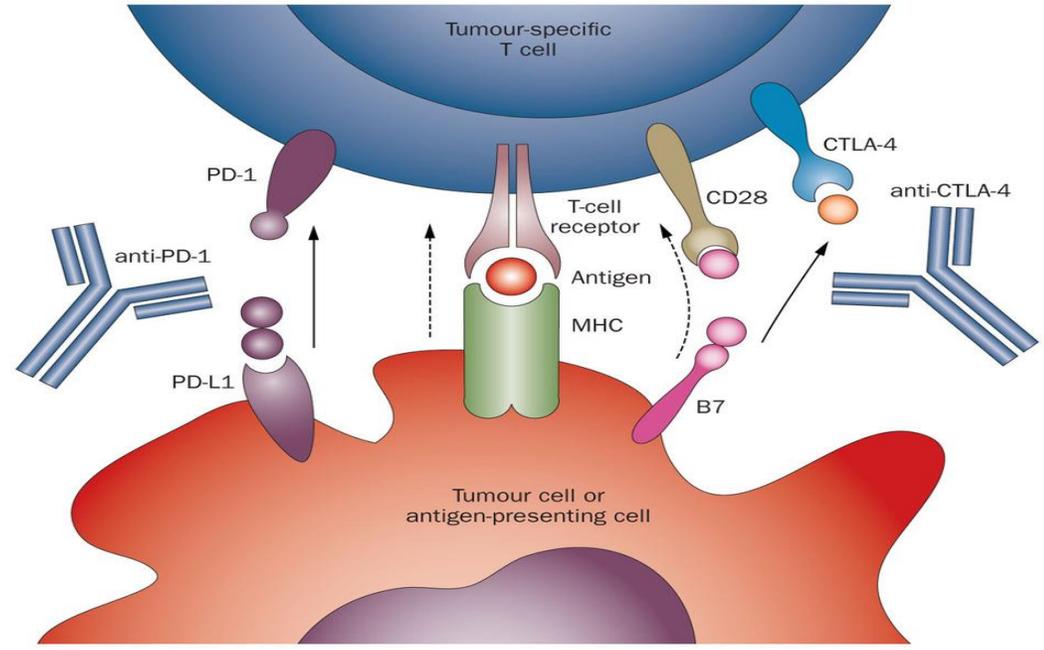
La croissance, l'invasion tissulaire et la dissémination des cancers dépendent de la capacité des cellules tumorales à développer un réseau vasculaire

Décédé le 14 Janvier 2008

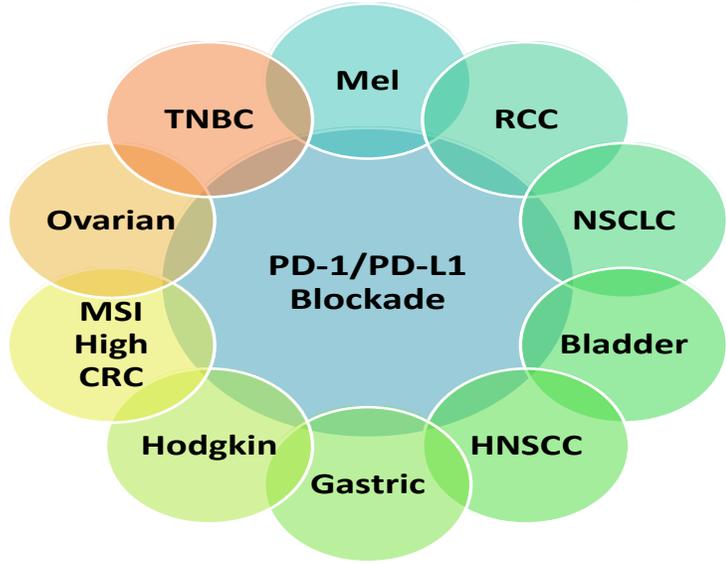
A affronté pendant 30 ans le scepticisme de la communauté médicale



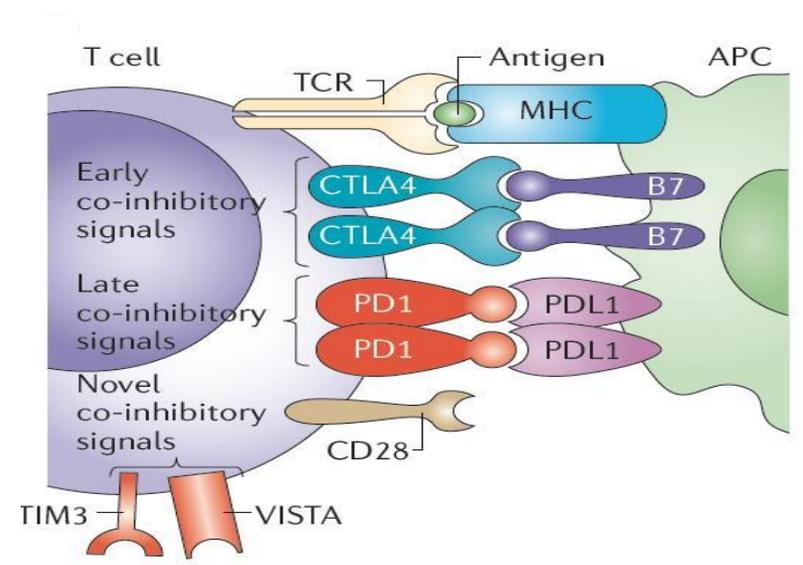
2015 FDA Approved Immunotherapies



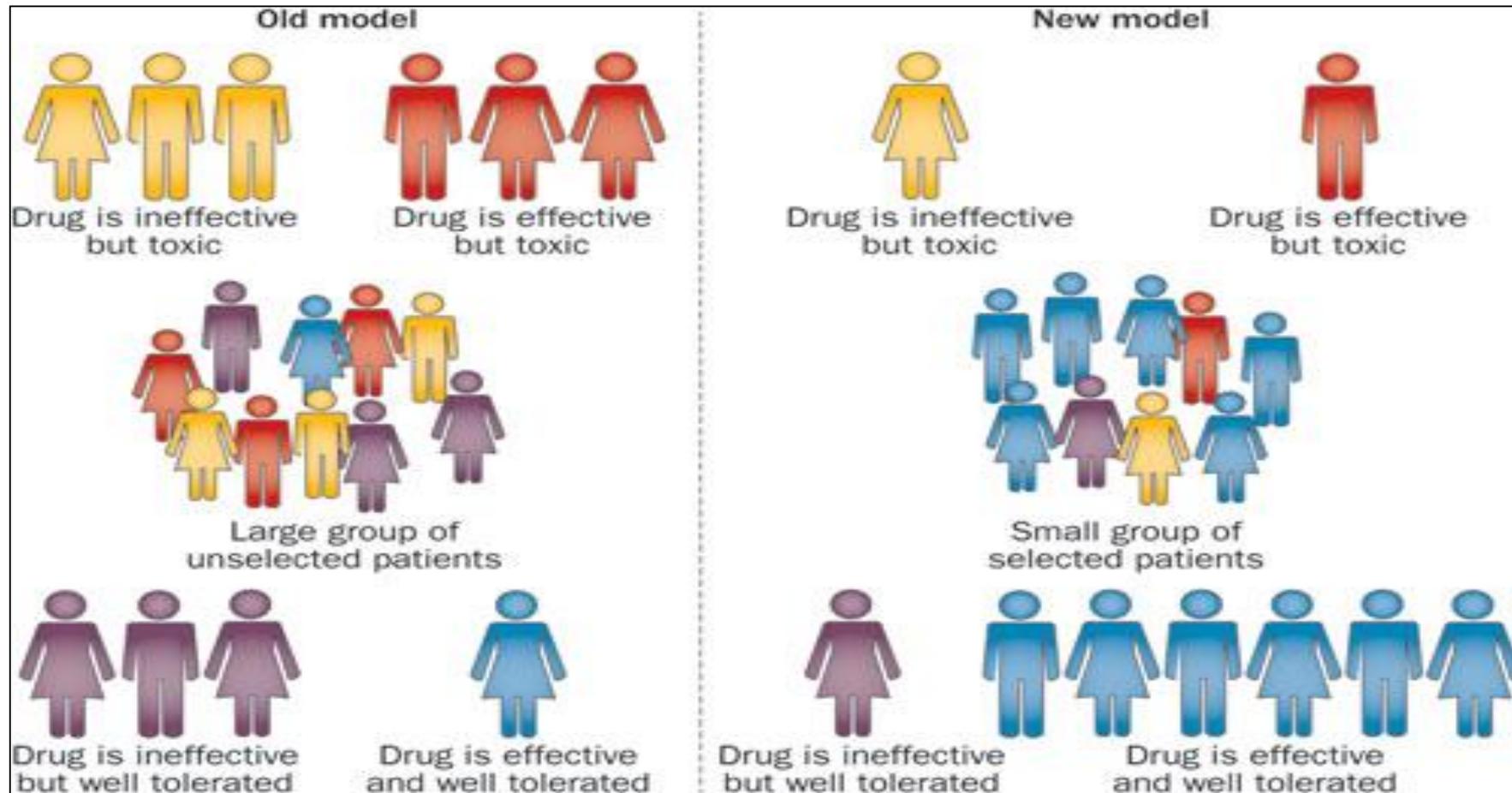
Immunomodulation as a new weapon in our armamentarium to fight cancer



Lymphocyte Inhibition



PHARMACOGÉNOMIQUE

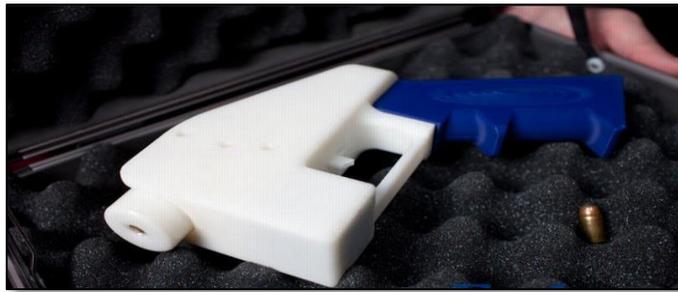


3D-PRINTED- DRUG

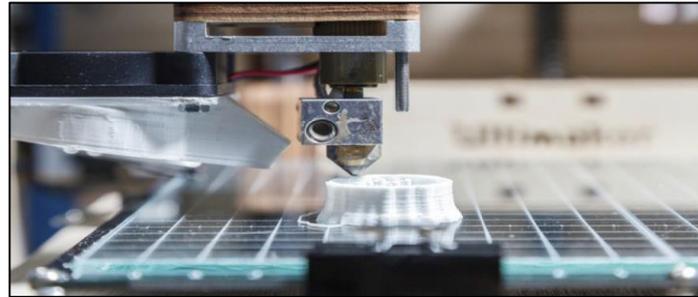
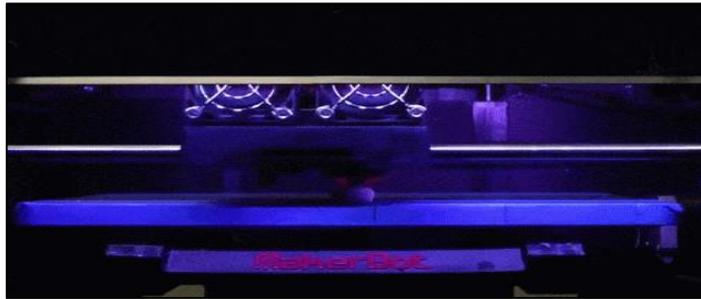


Lee Cronin, Chimiste écossais

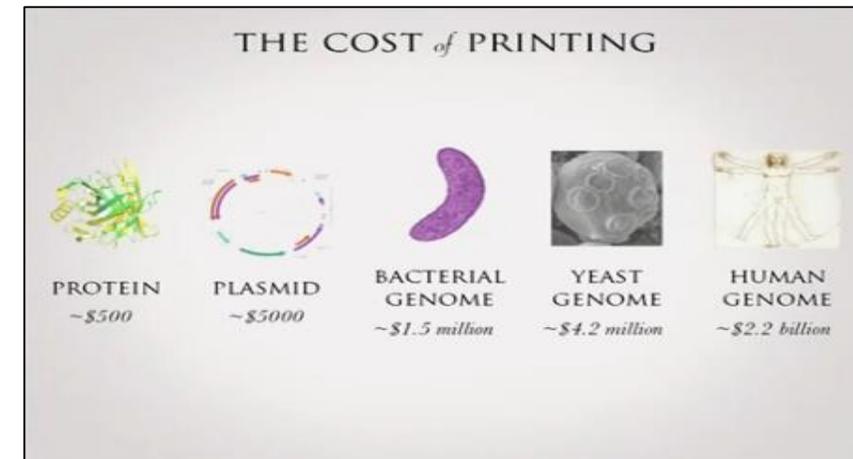
Ultimately, Cronin says, "For me the cool bit, going into the future, is the idea of taking your own stem cells with your own genes and environment and printing your own medicine."



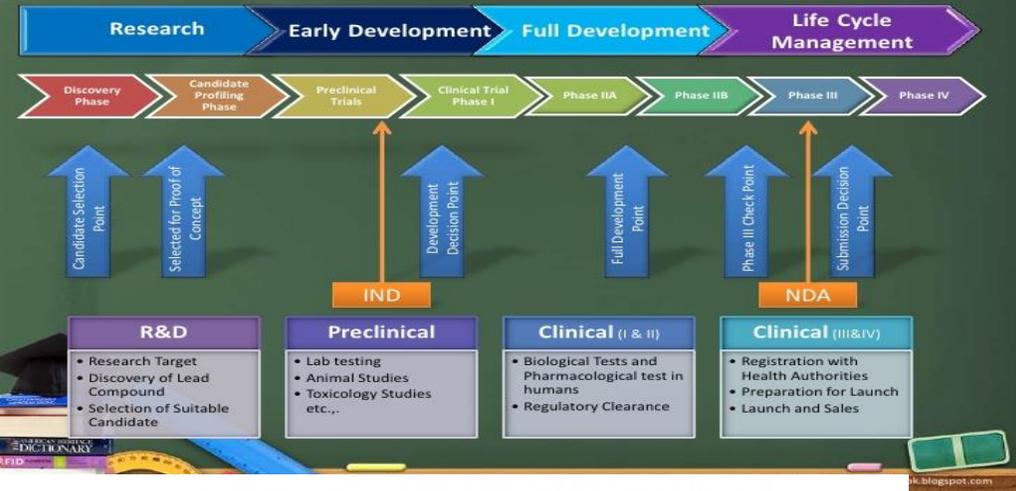
États-Unis : un pistolet créé avec une imprimante 3D



SPRITAM : 1^{ER} MÉDICAMENT 3D-FABRIQUE
Approuvé par FDA - 2016



New Drug Development Process



MODIFIER LE PROCESSUS DE DEVELOPPEMENT DES MEDICAMENTS ?



ESSAI BASKET

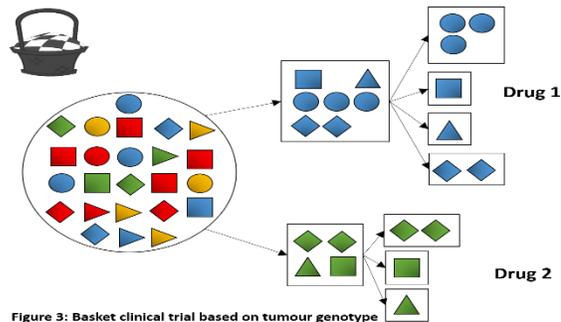
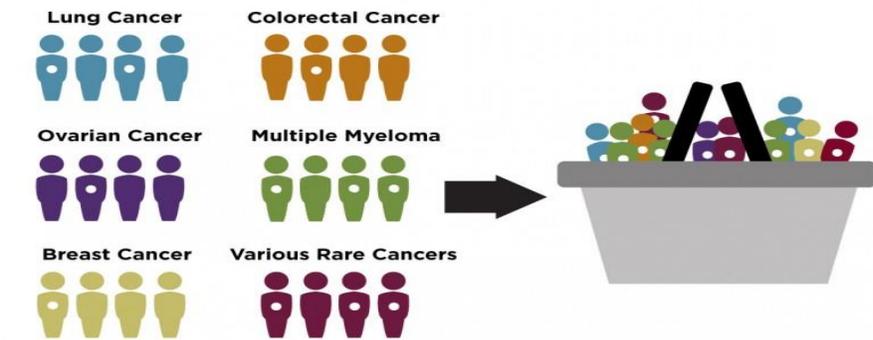
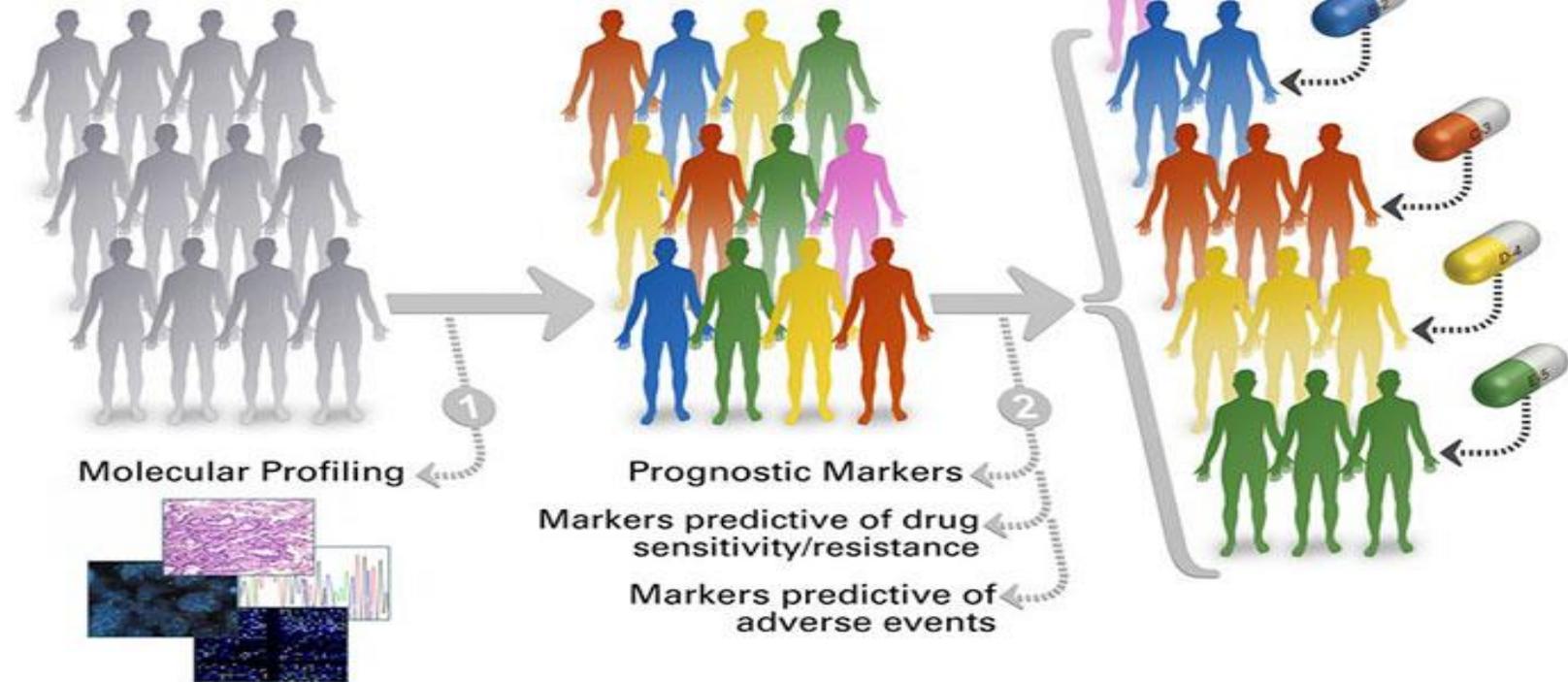
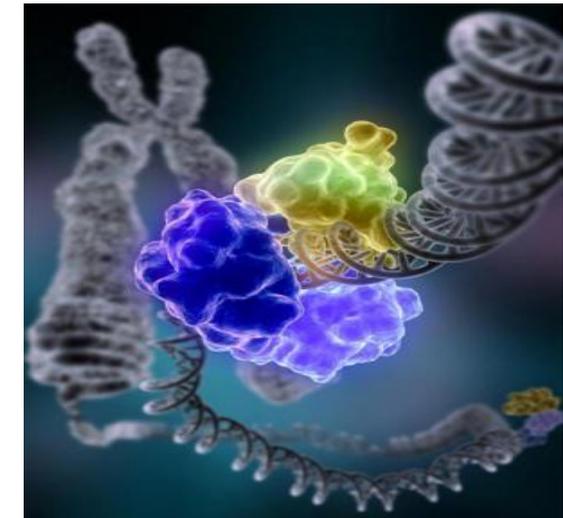
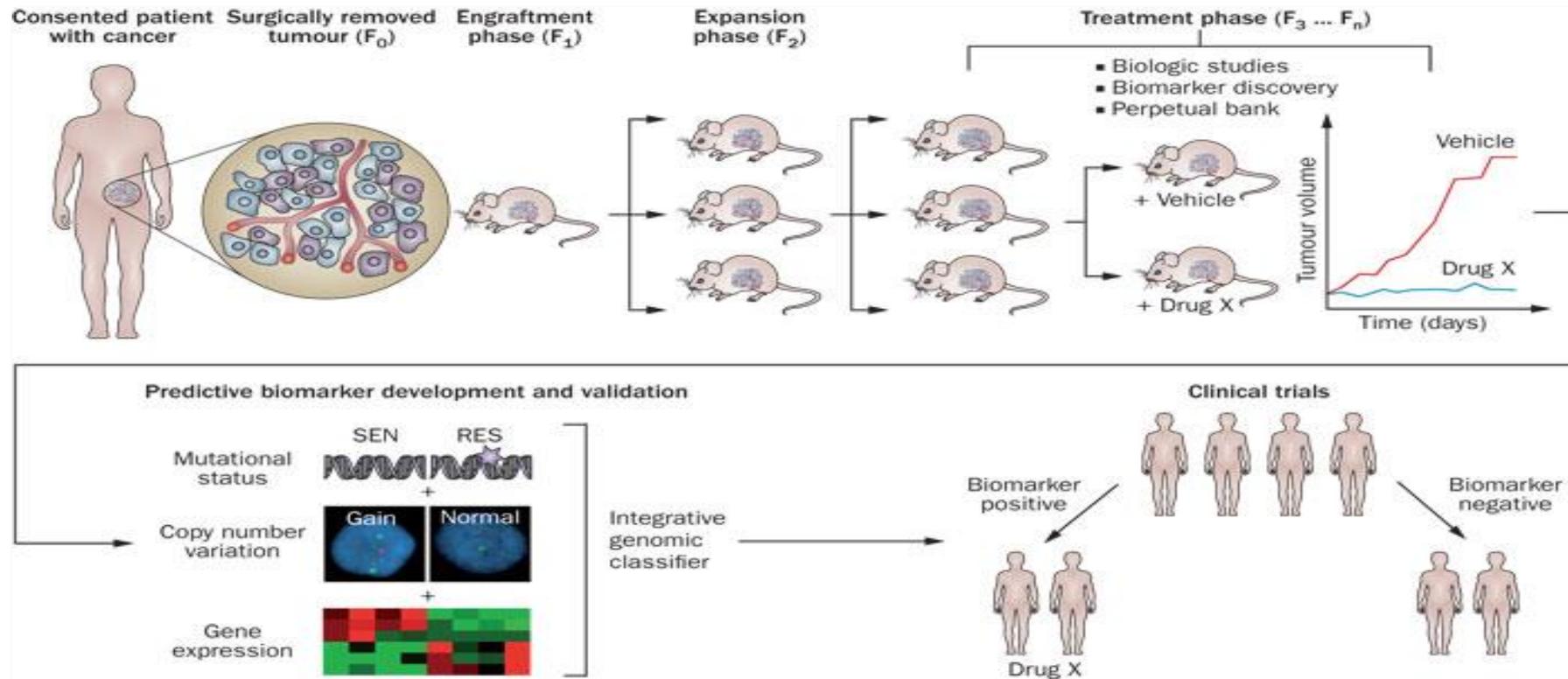


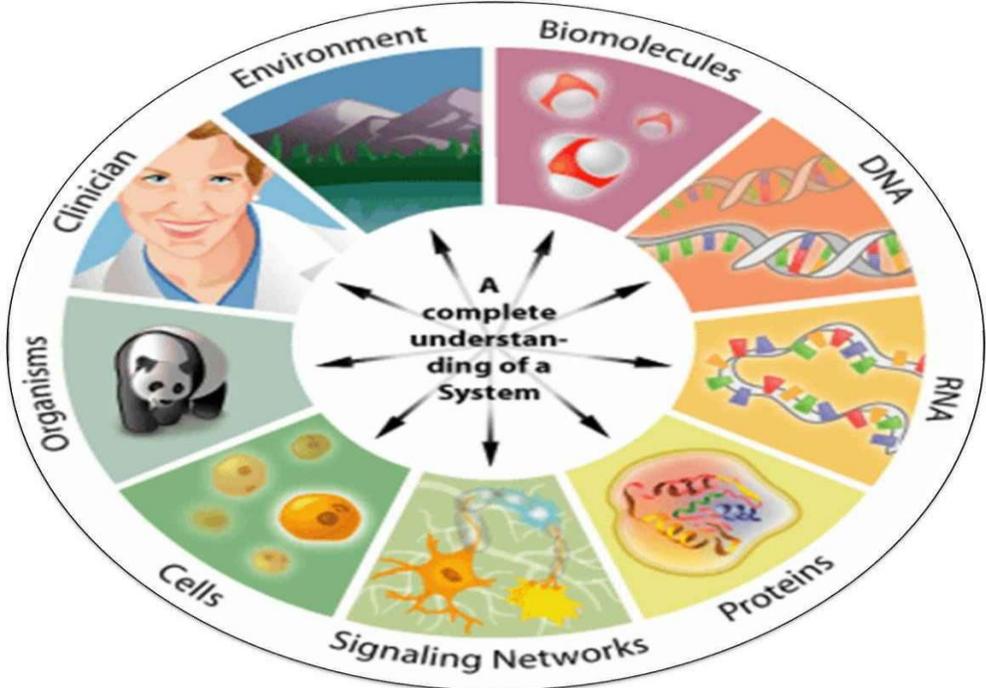
Figure 3: Basket clinical trial based on tumour genotype

Targeted Cancer Therapy

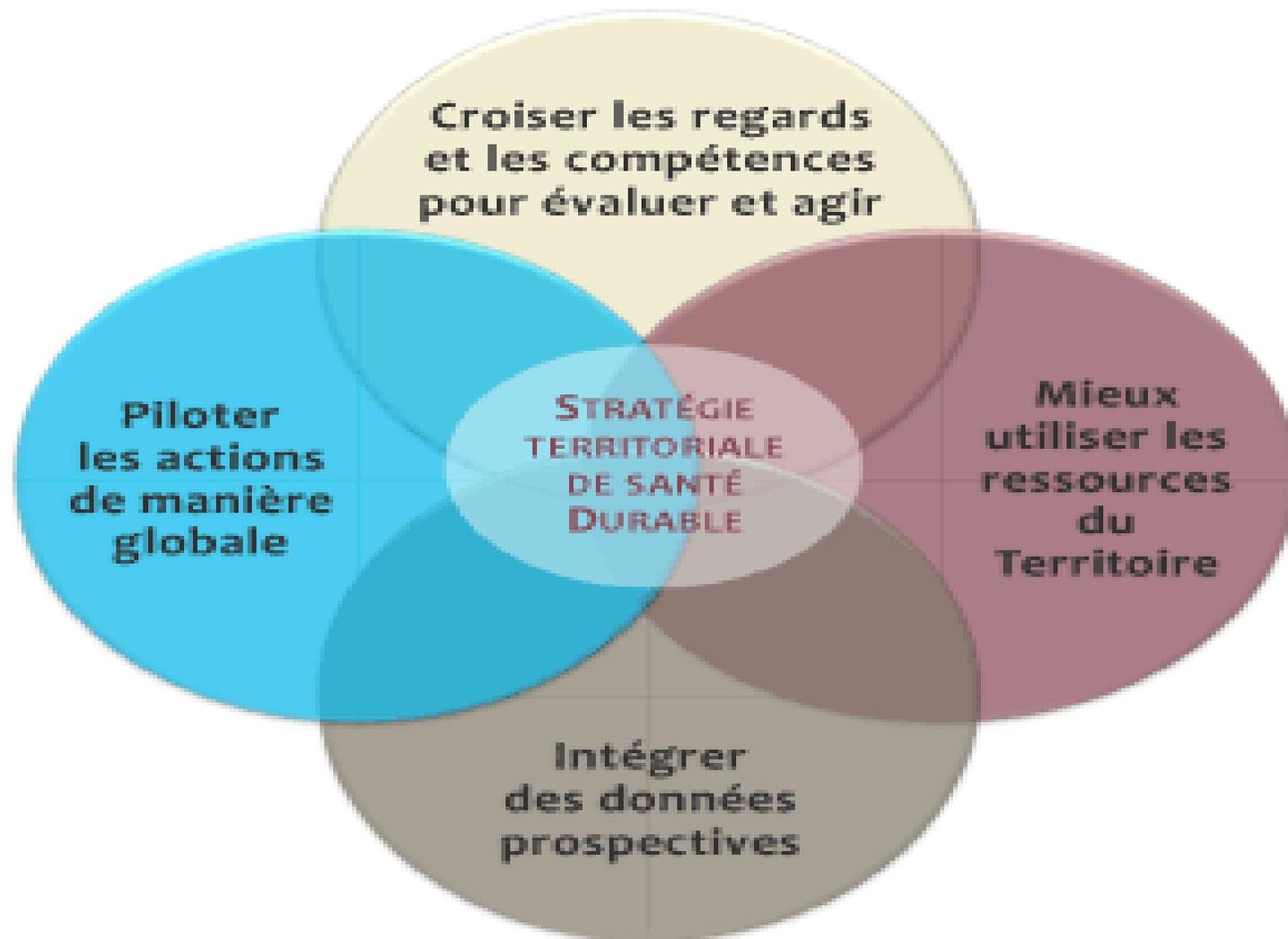


XENOPATIENTS : REDÉFINIR LA RECHERCHE CLINIQUE





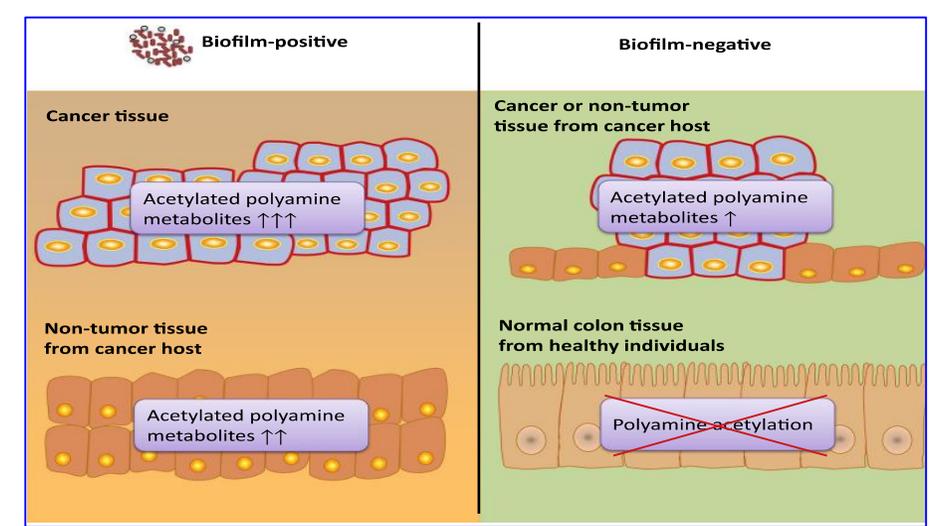
SANTE ENVIRONNEMENTALE



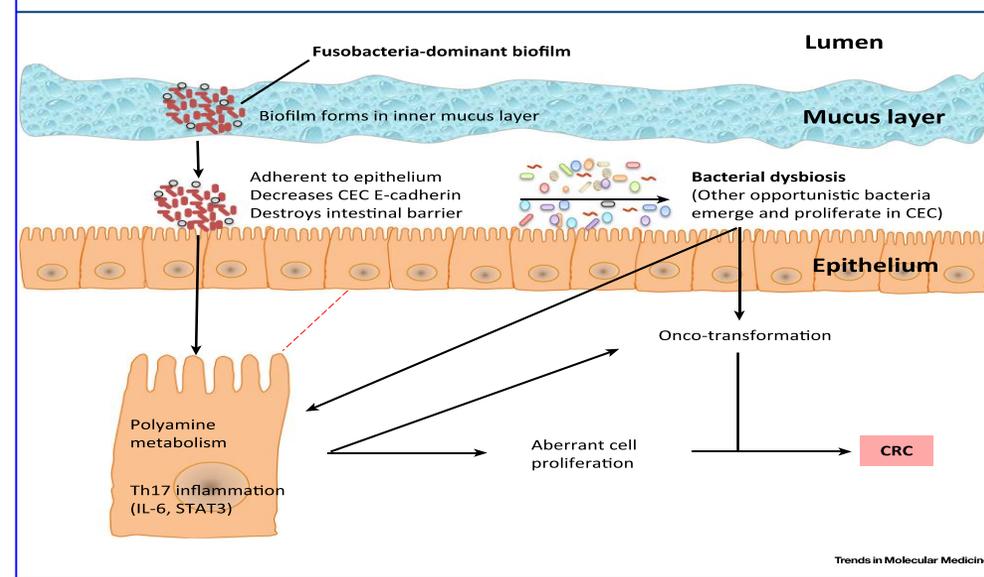
Bacterial Biofilms in Colorectal Cancer Initiation and Progression

Shan Li,¹ Sergey R. Konstantinov,¹ Ron Smits,¹ and Maikel P. Peppelenbosch^{1,*}

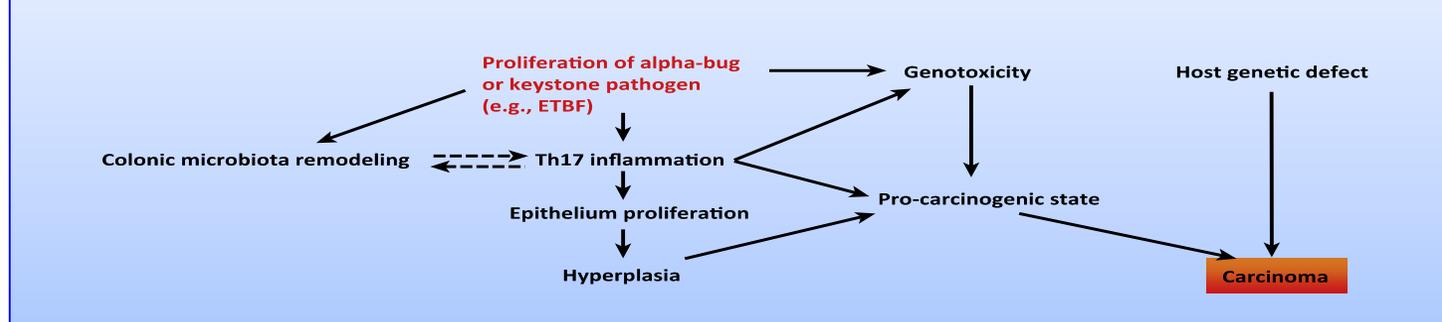
structures termed biofilms. We explore here the concept that a polymicrobial biofilm promotes pro-carcinogenic activities that may partially underlie progression along the adenoma-CRC axis.



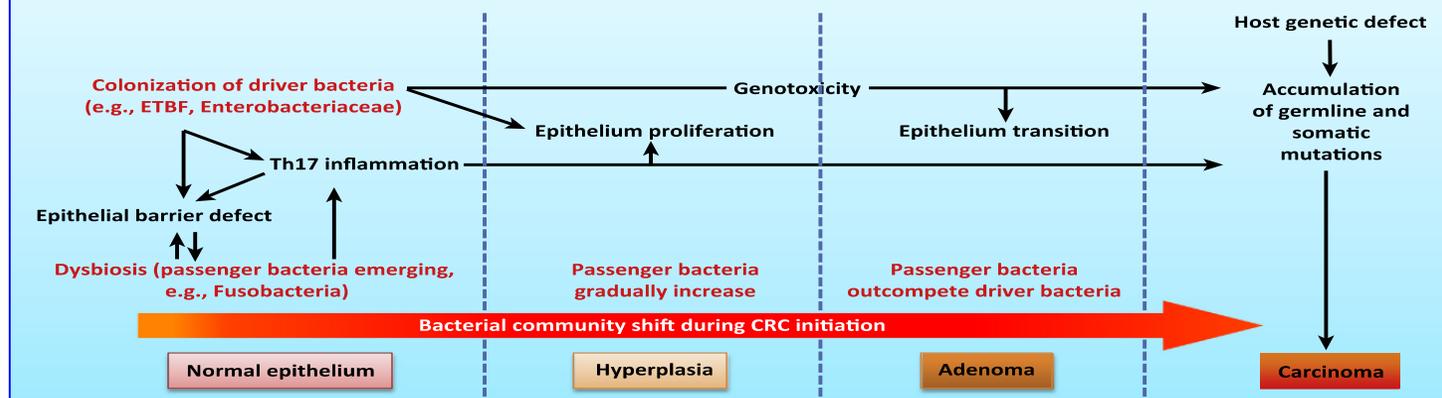
The Biofilm-Driven Colorectal Cancer (CRC) Carcinogenesis Model



(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 Lock¹, Ahmad Muinuddin², Walter I. Kocha³, Robert Dinniwell⁴, George Rodrigues⁵, David D'souza⁶

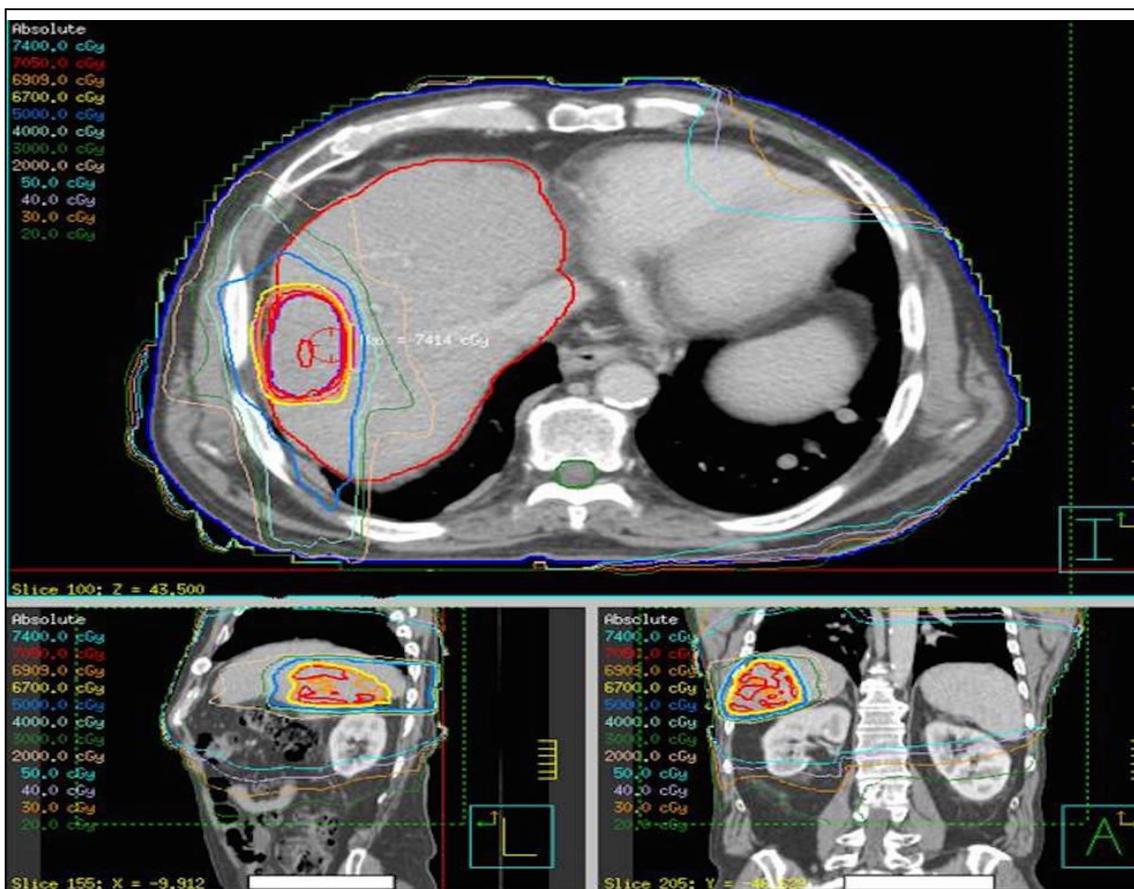


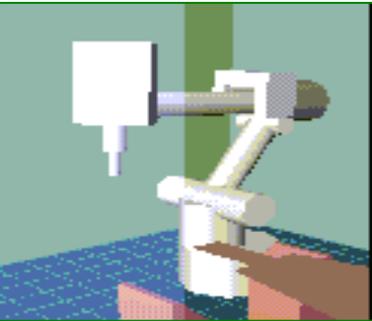
FIGURE 2: Radiation dosimetry plan for liver treatment

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^{1*} and Silvia C. Formenti²

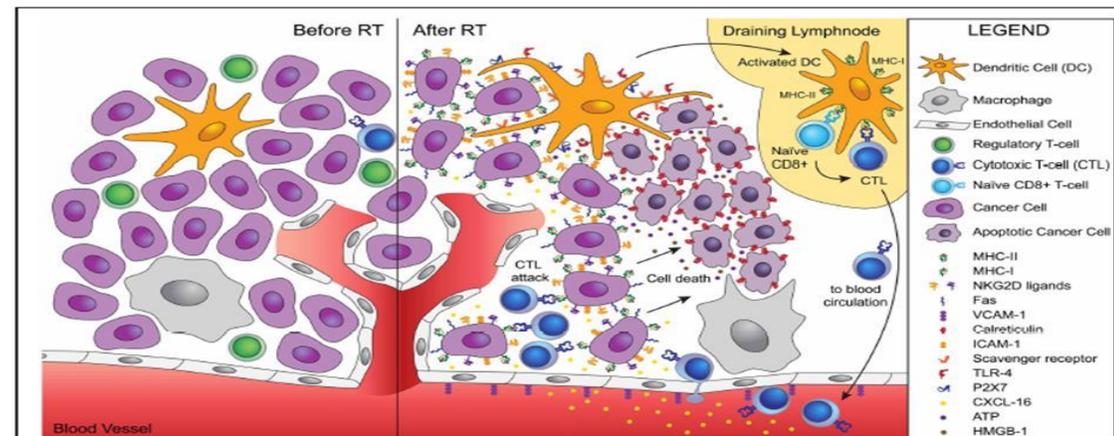
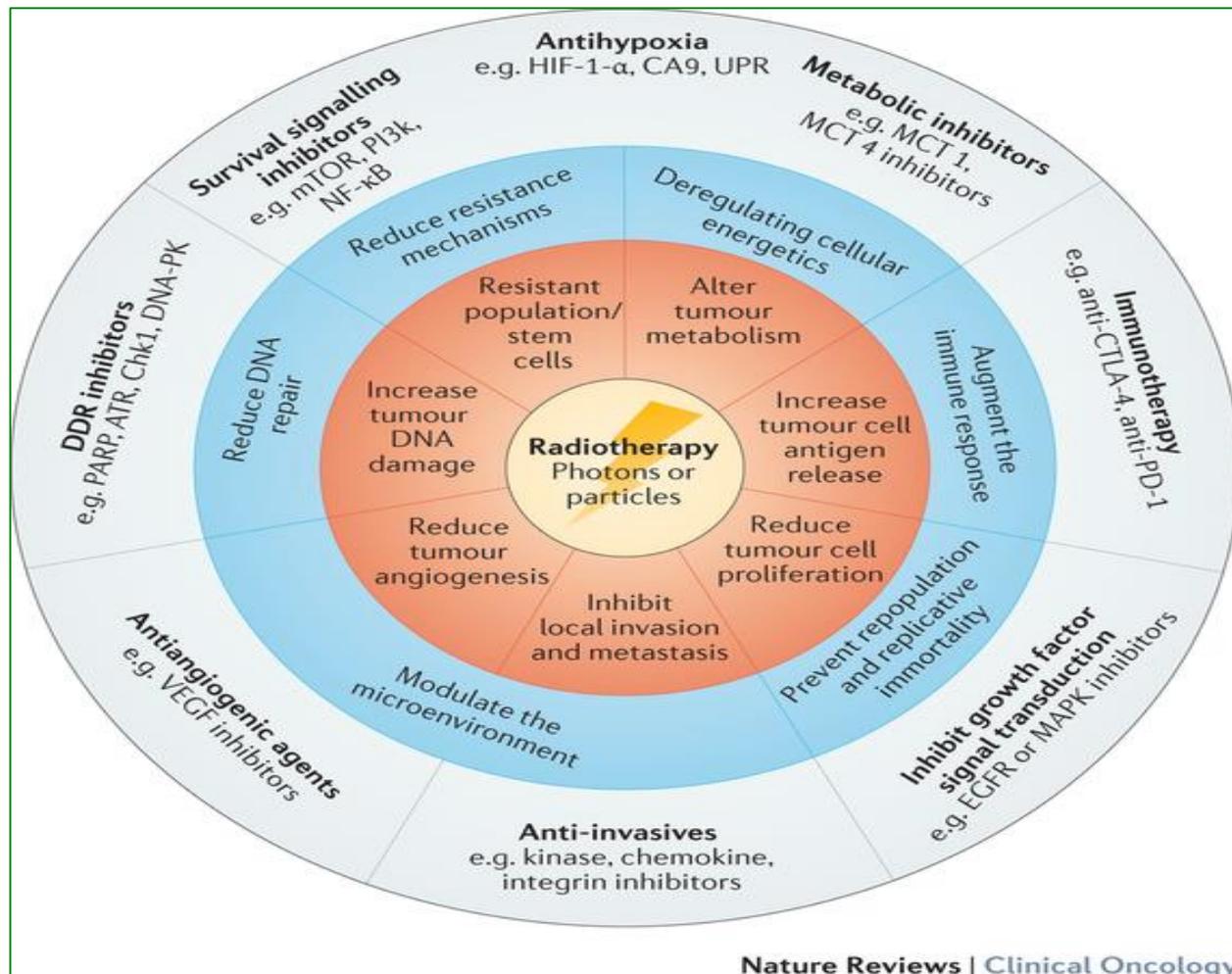
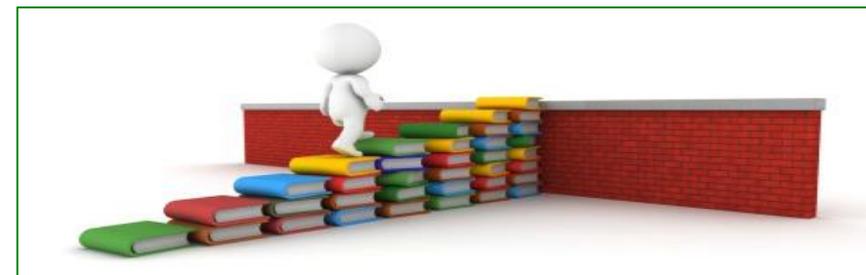


FIGURE 1 | Ionizing radiation acts as a modifier of the tumor microenvironment converting the tumor into an *in situ* vaccine. Radiation induces an immunogenic cell death of tumor cells characterized by calreticulin translocation to the surface of dying cells, and release of HMGB-1 and ATP. Calreticulin 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 Gaya¹, Charles A. Akle², Satvinder Mudan³, John Grange⁴

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 ²), 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 ²) concurrent LDFRT given as 60 cGy bid 2 days weekly for 6 weeks	Gemcitabine 1,250 mg/m ² at 10 mg/m ² /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 ² , 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 ² 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.

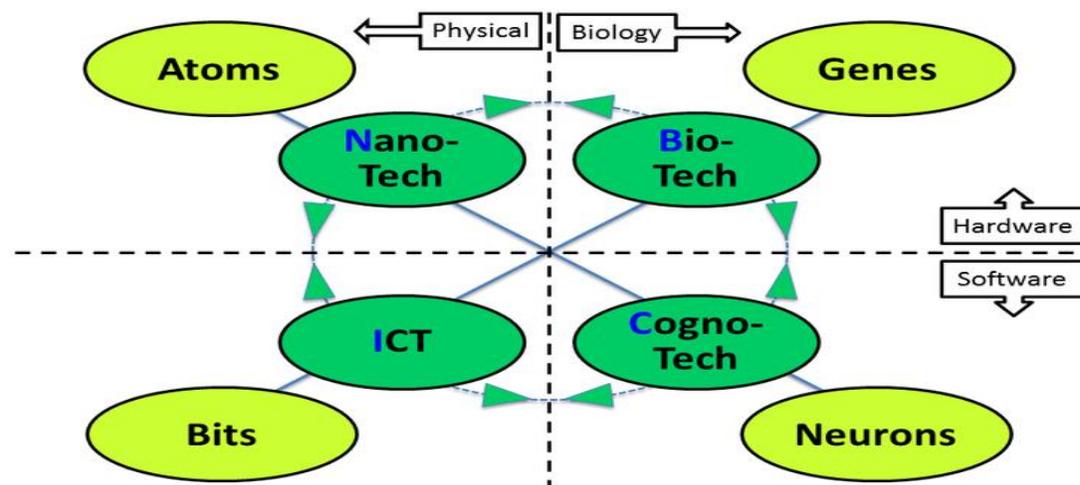
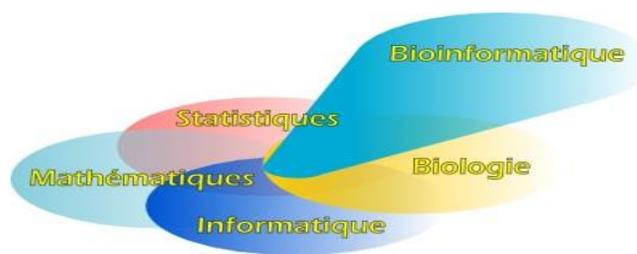
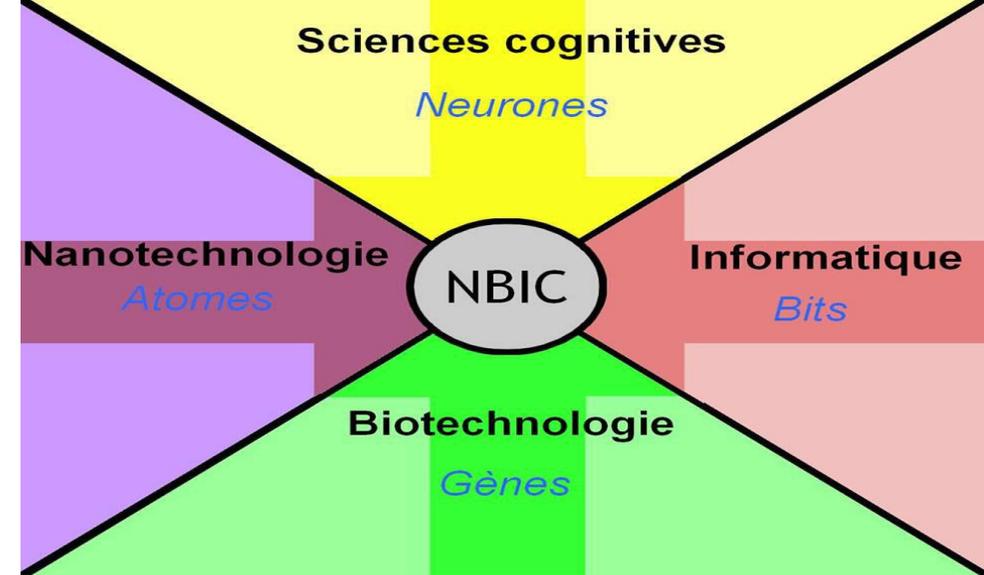
« *Tout est poison, rien n'est poison, Il n'y a que le dose... »* »

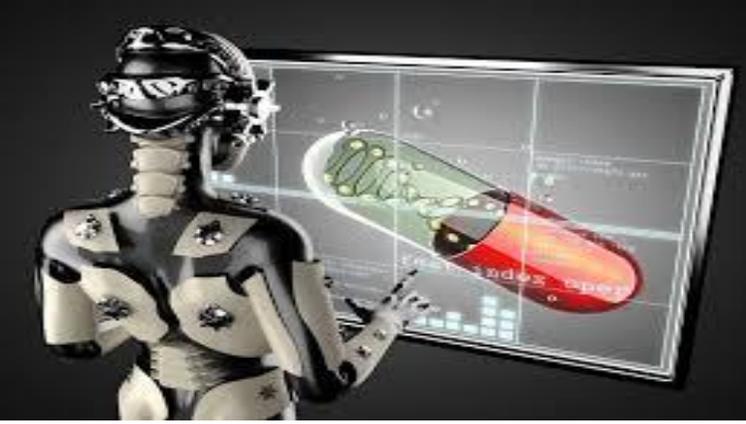


FIGURE 1: Paracelsus (Theophrastus Bombastus von Hohenheim) 1493-1541
Engraving from life by Augustin Hirschvogel in 1538.



HORMESE





BIOPEN

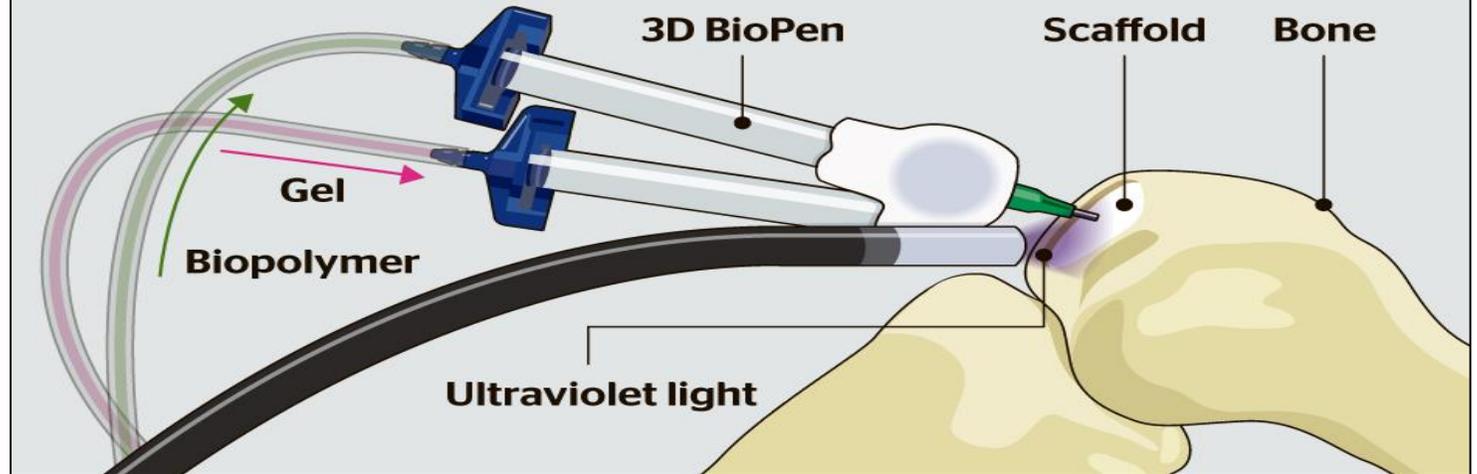


How it works

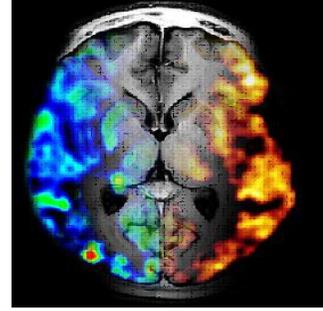
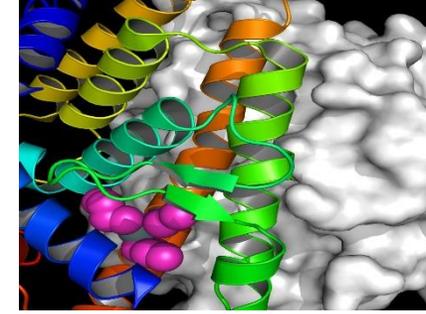
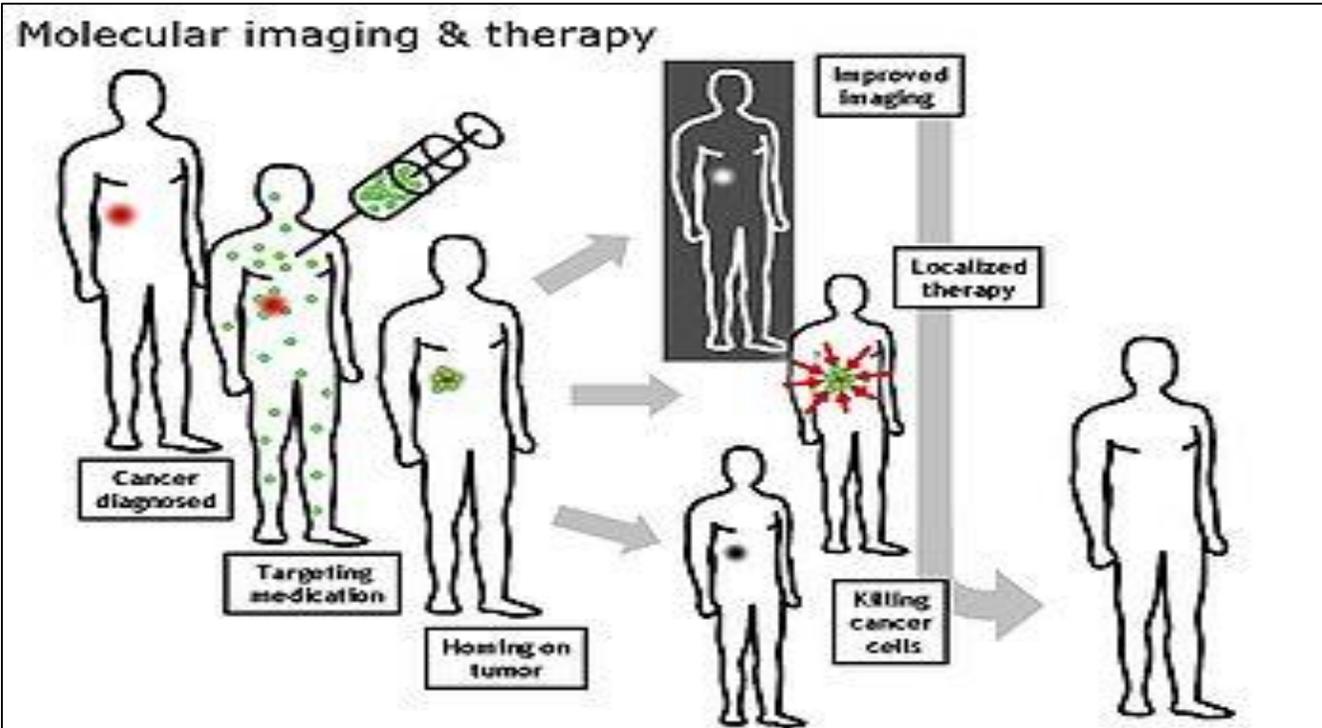
1 BioPen uses cell material inside a biopolymer such as alginate, which is in turn encased in a layer of gel

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

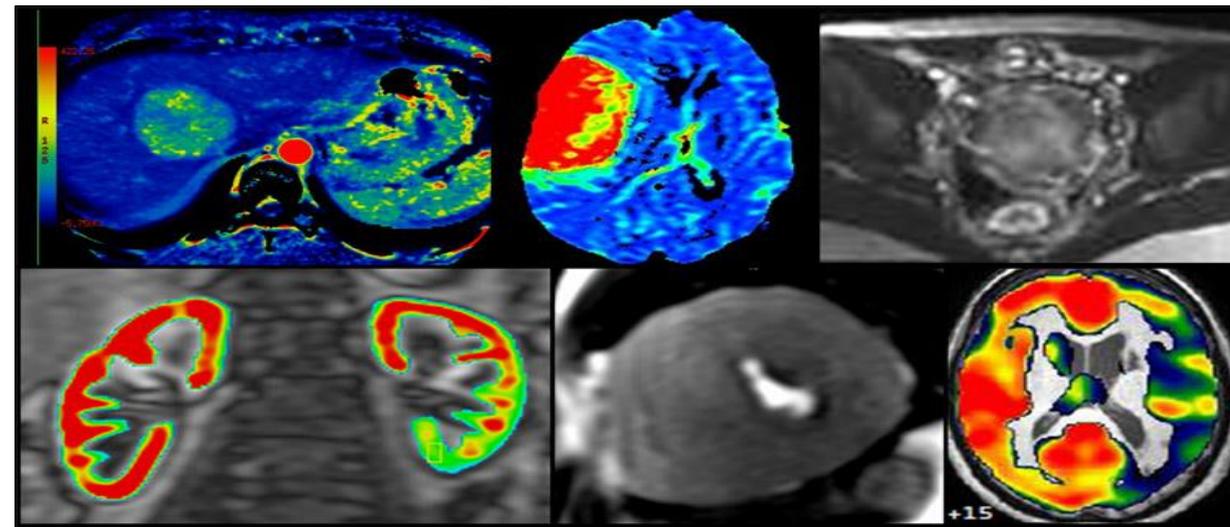
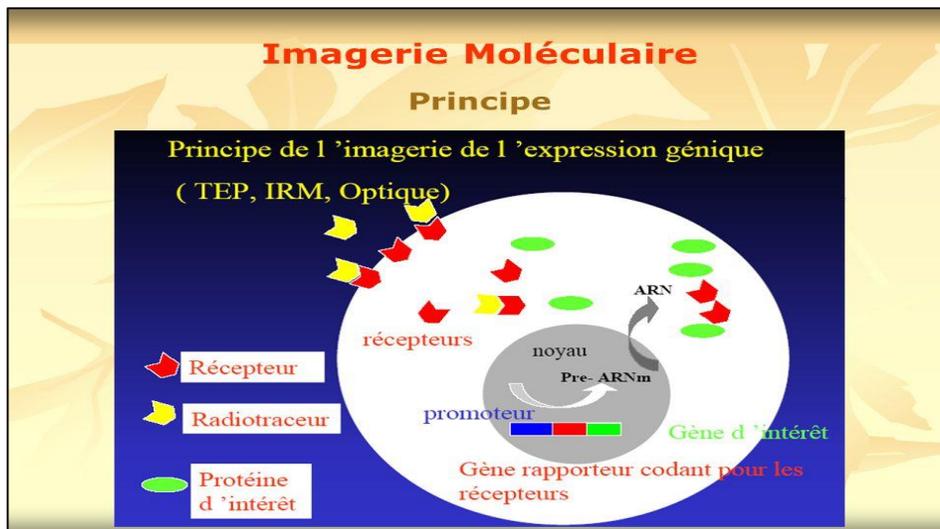
3 Ultraviolet light hardens the gel and protects the cells that are built up to create a 3D scaffold on the wound site



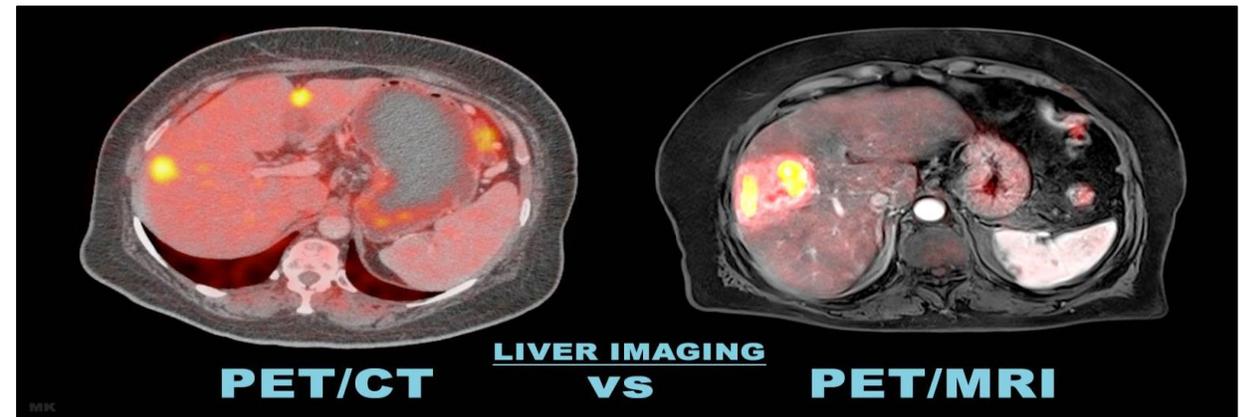
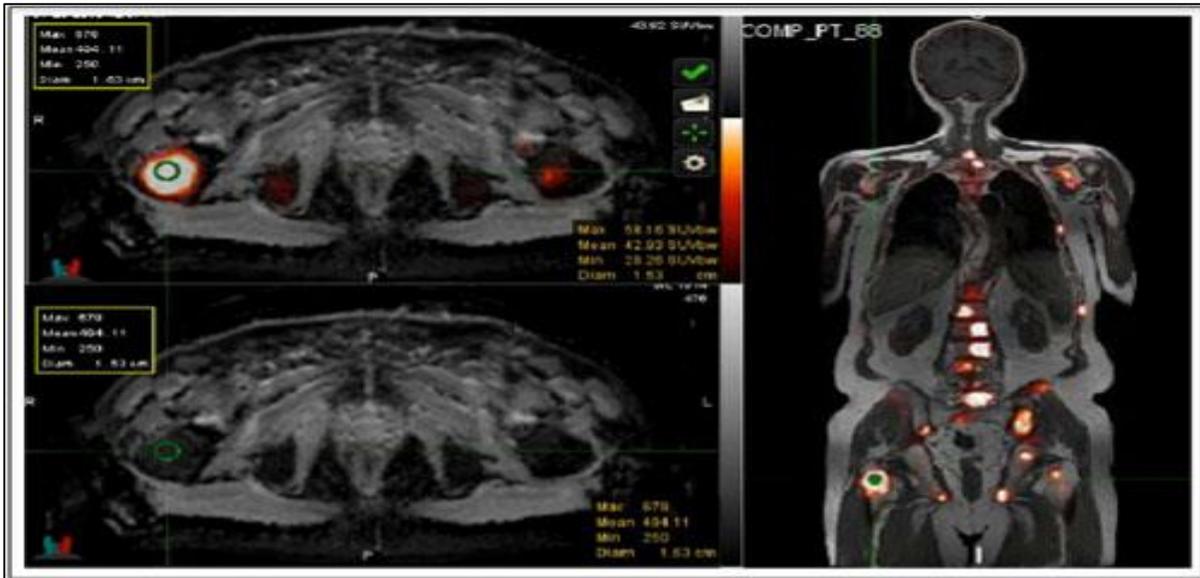
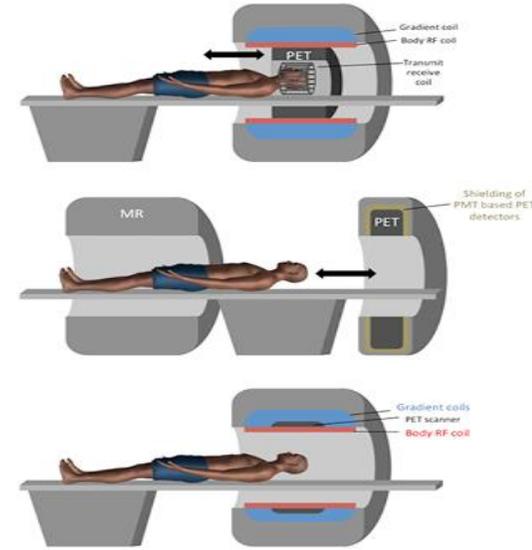
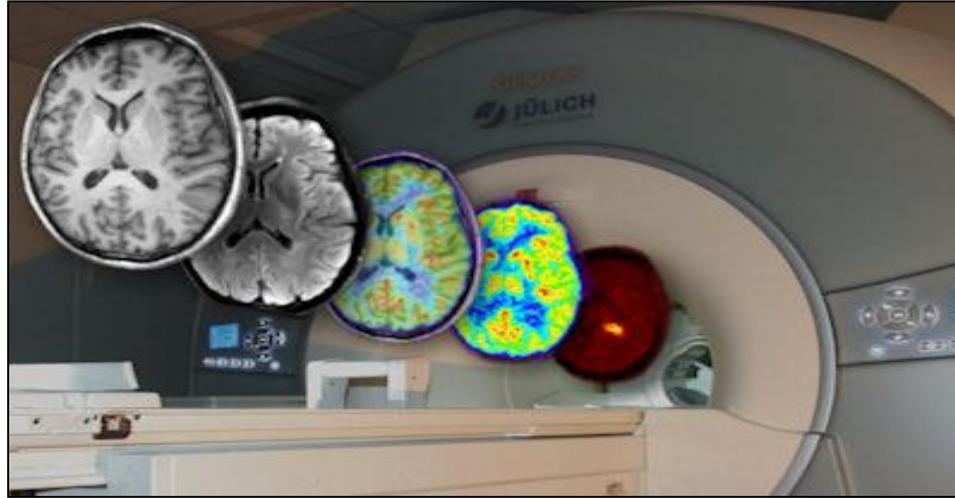
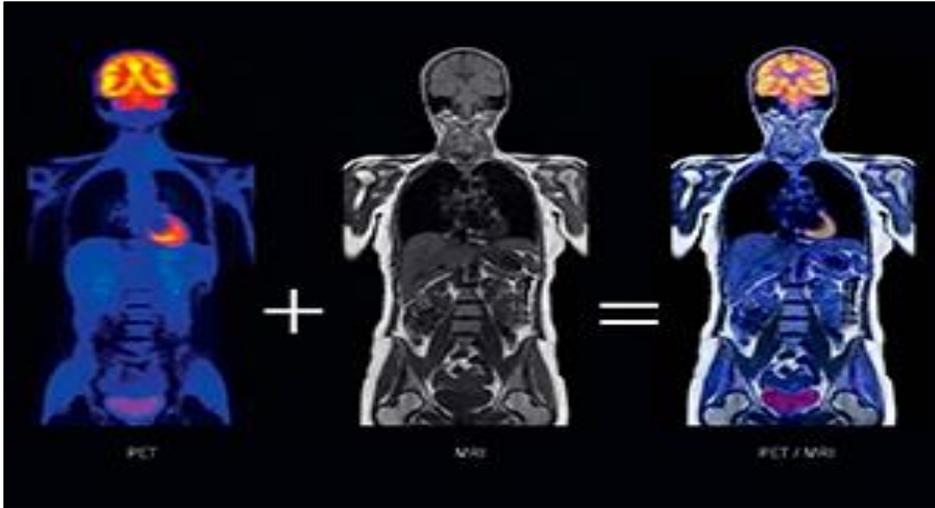
THERANOSTIC

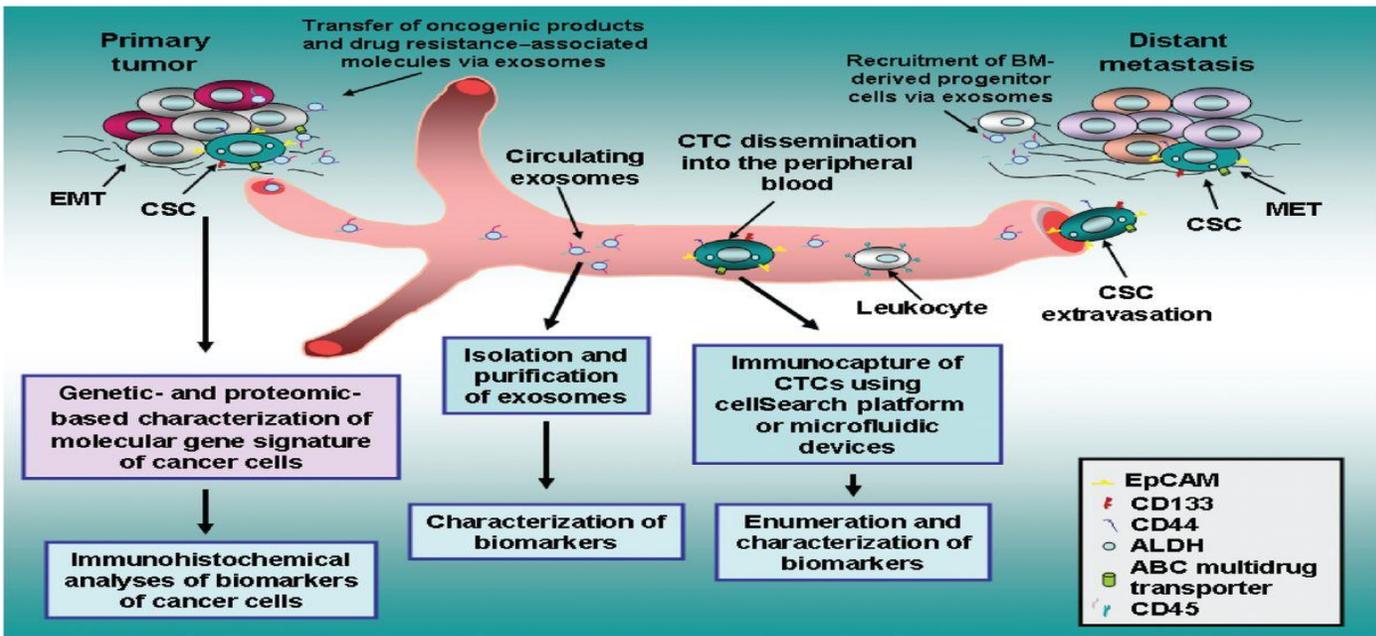


IMAGERIE DE FLUORESCENCE

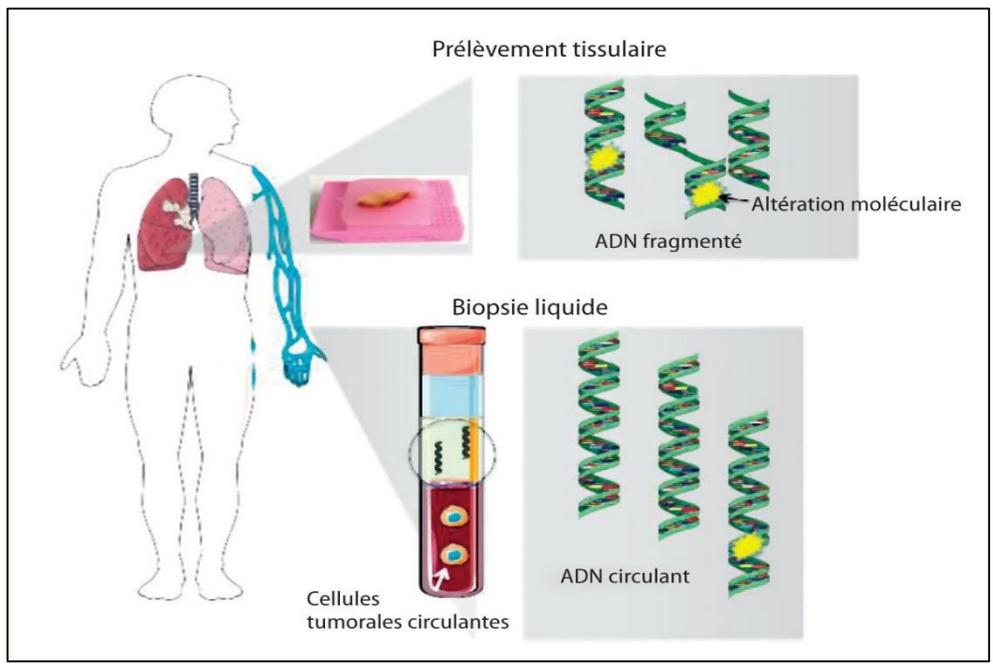


TEP IRM



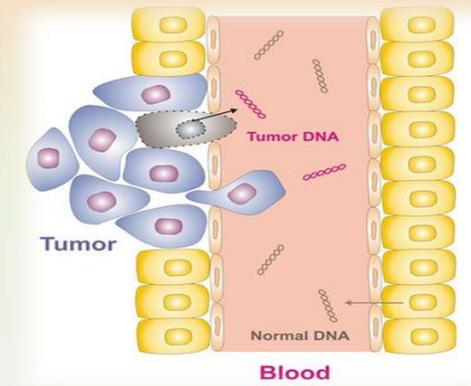


CTC, ADN circulant : Biopsies liquides



ADN tumoral circulant (ADNct)

- Surveiller la dynamique de la tumeur
- ADN tumoral circulant ≈ 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.



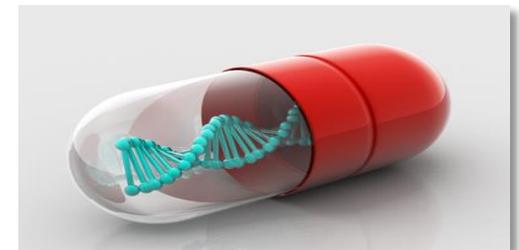
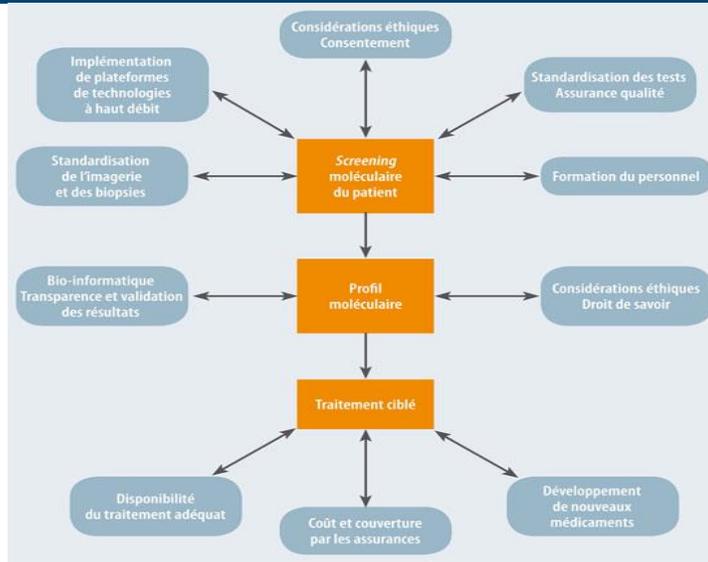
NOW:
Robotic Assistance

2 hour procedures and minimal blood loss mean faster recoveries.



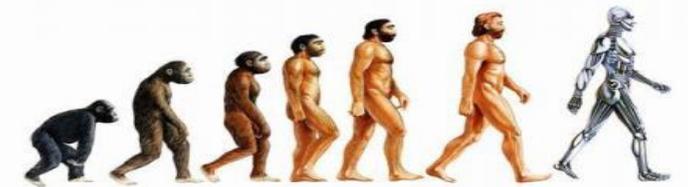
SOON:
Precision Medicine

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)

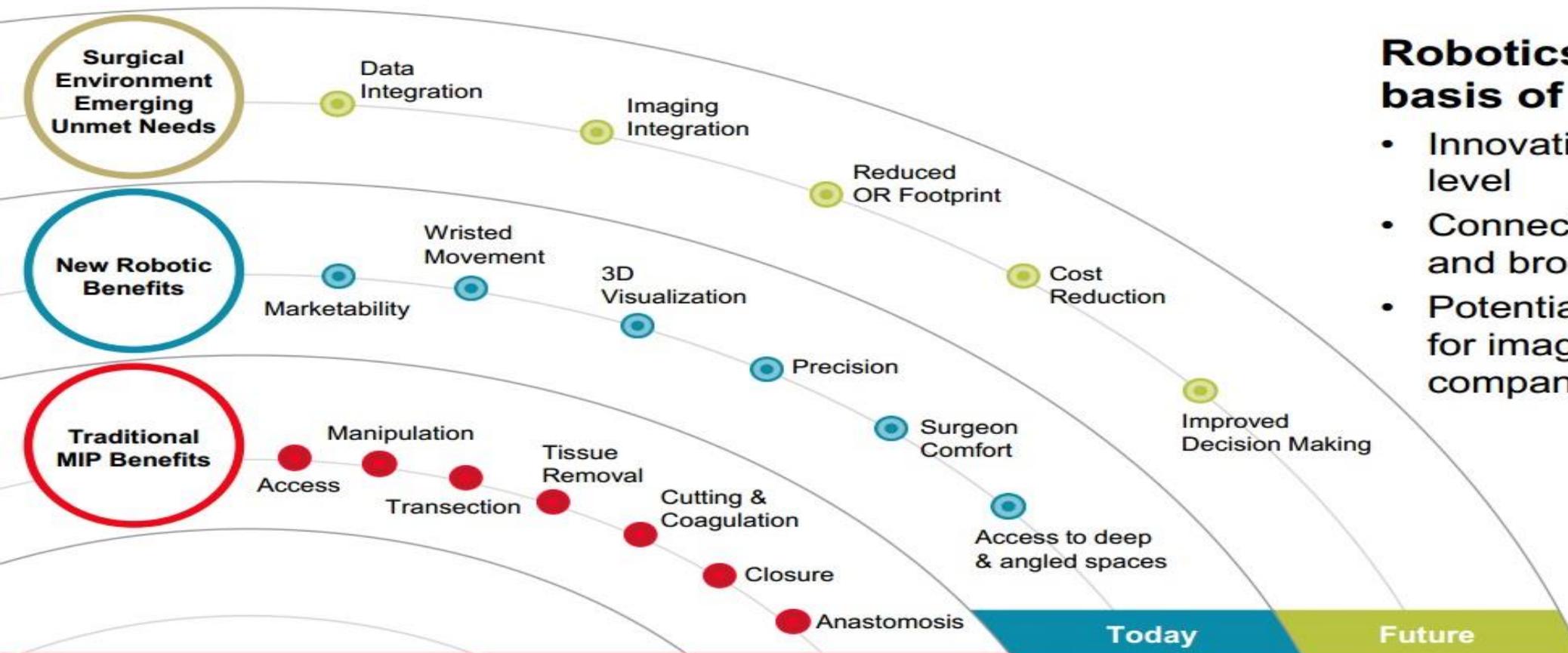
Did you like this answer?

LIKE DISLIKE

Ask MedWhat

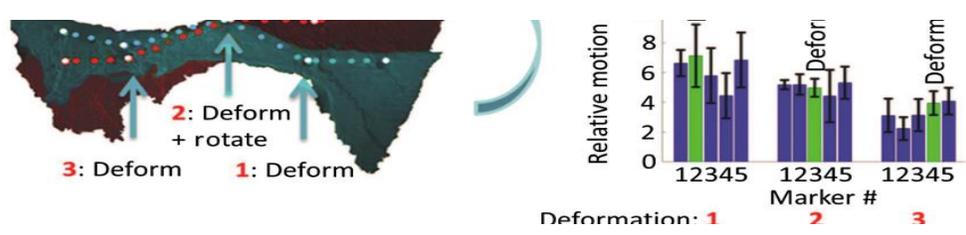


Robotics Opportunities: Today and Future



Robotics is shifting the basis of competition

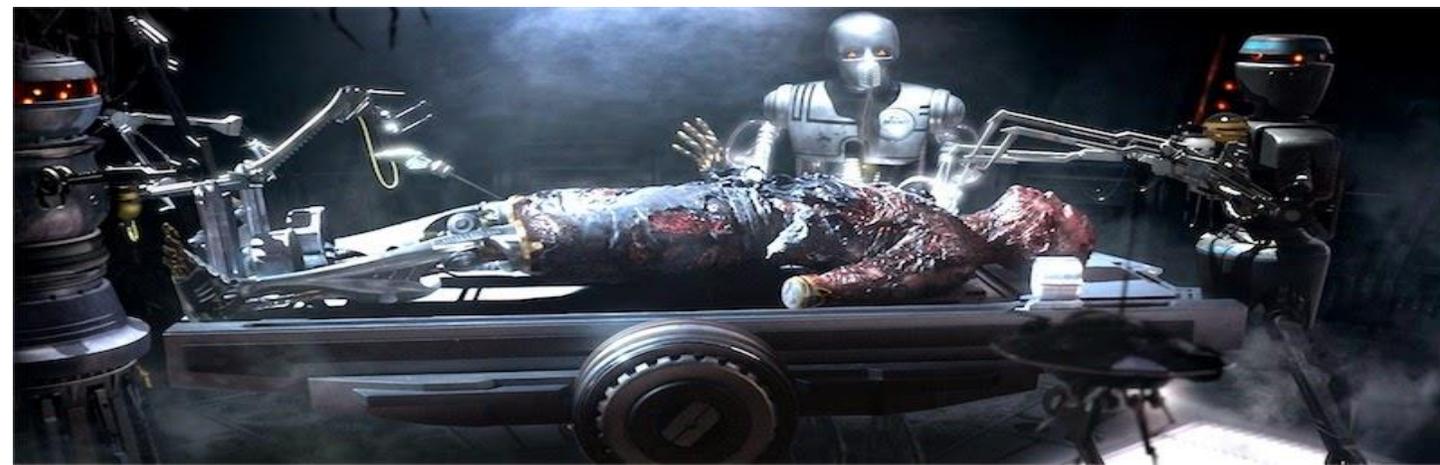
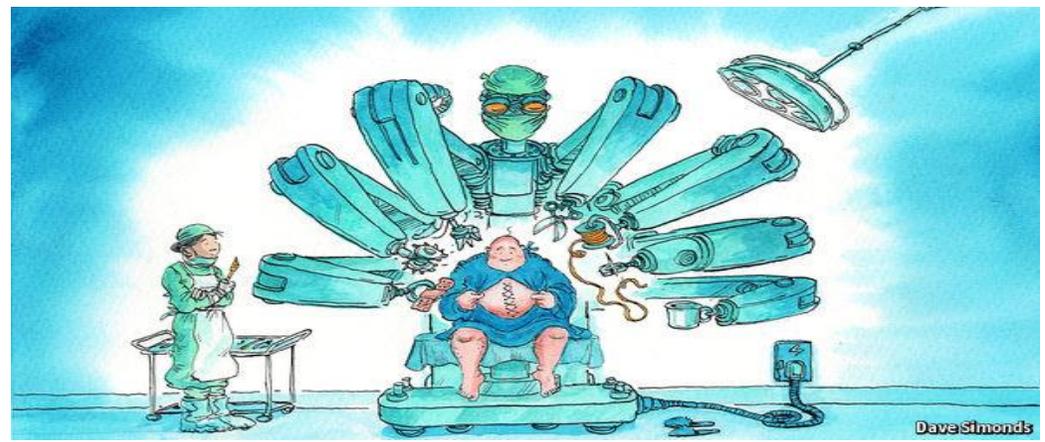
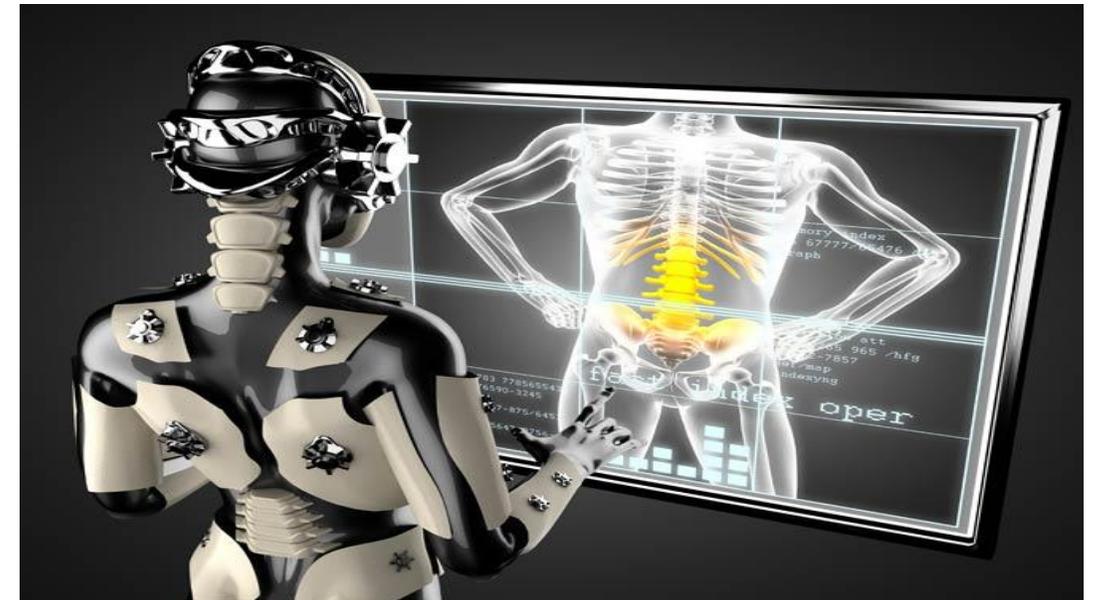
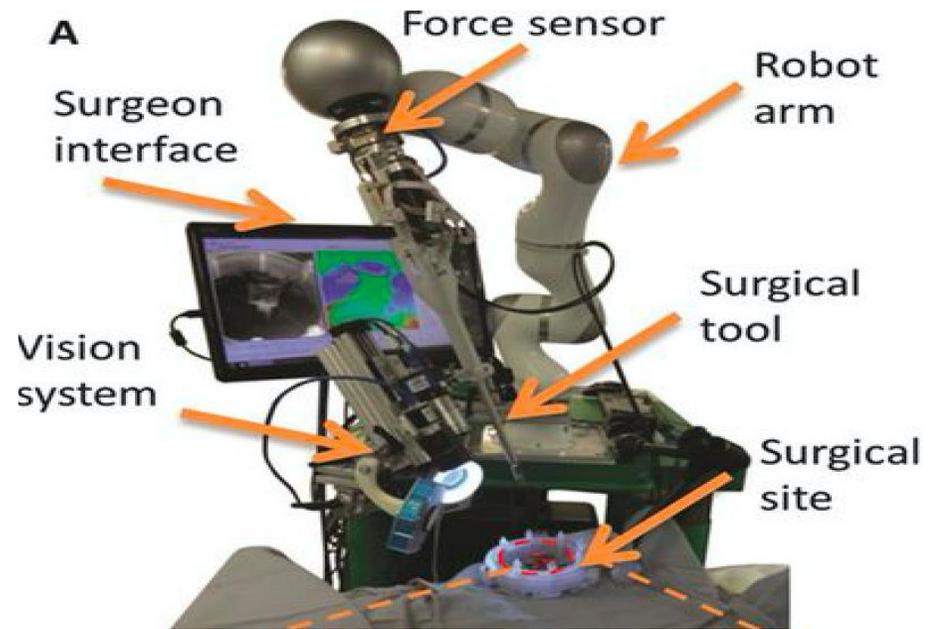
- Innovation at the system level
- Connection between OR and broader environment
- Potential bridge to the OR for imaging & diagnostic companies

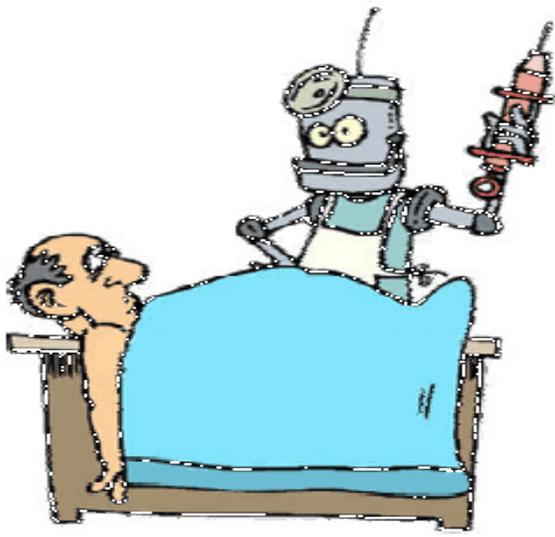


ENGINEERING

Supervised autonomous robotic soft tissue surgery

Azad Shademan,¹ Ryan S. Decker,¹ Justin D. Opfermann,¹ Simon Leonard,²
Axel Krieger,¹ Peter C. W. Kim^{1*}





Notre mission

Inventer des technologies de robotique chirurgicale de dernière génération

Une triple ambition

Augmenter le confort et la sécurité des patients

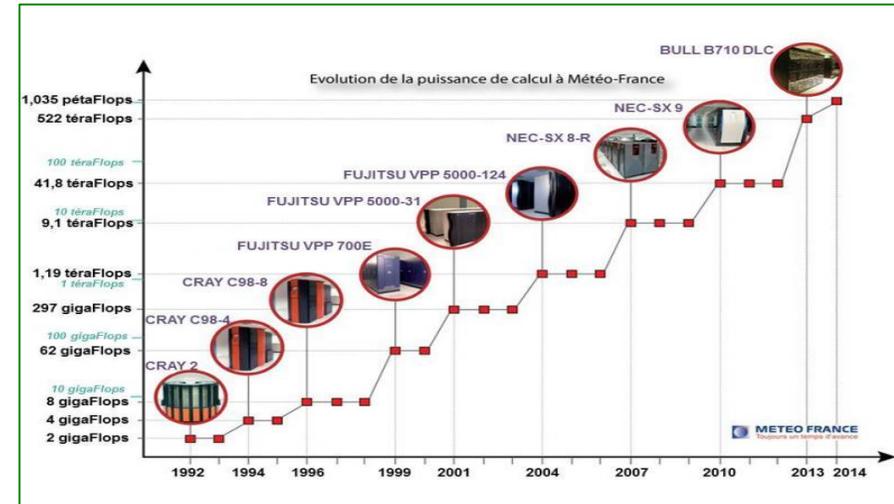
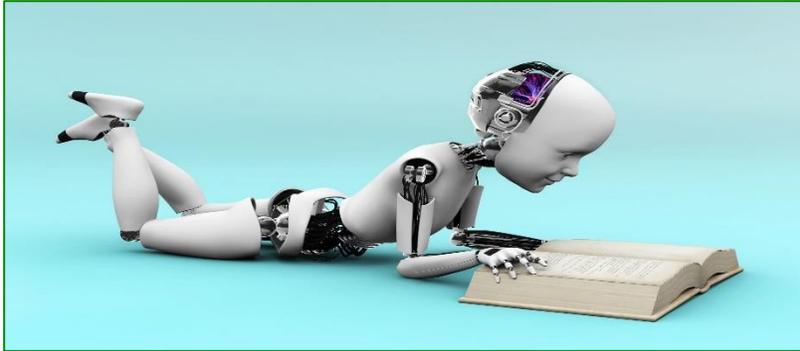
Assister et fiabiliser le geste des chirurgiens

Contribuer à améliorer la performance des hôpitaux

INTELLIGENCE si :

- Reproduction
- Curiosité

INTELLIGENCE ARTIFICIELLE



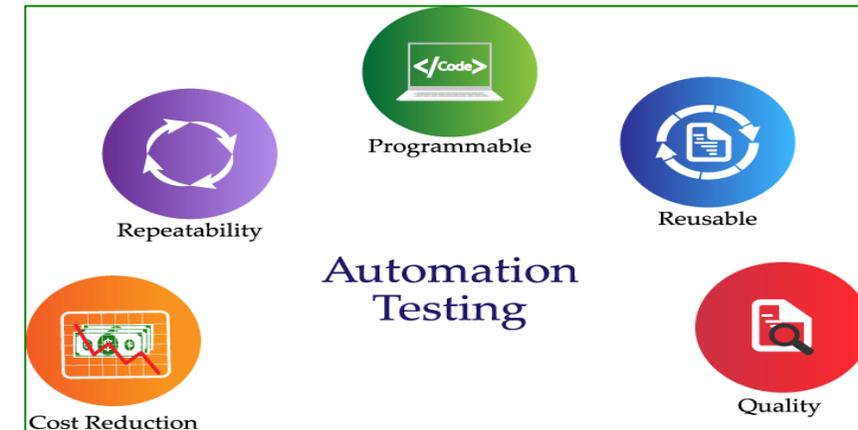
Une machine peut être programmée pour pouvoir réécrire, restructurer sa
Connaissance initiale, à partir d'informations reçues ou perçues

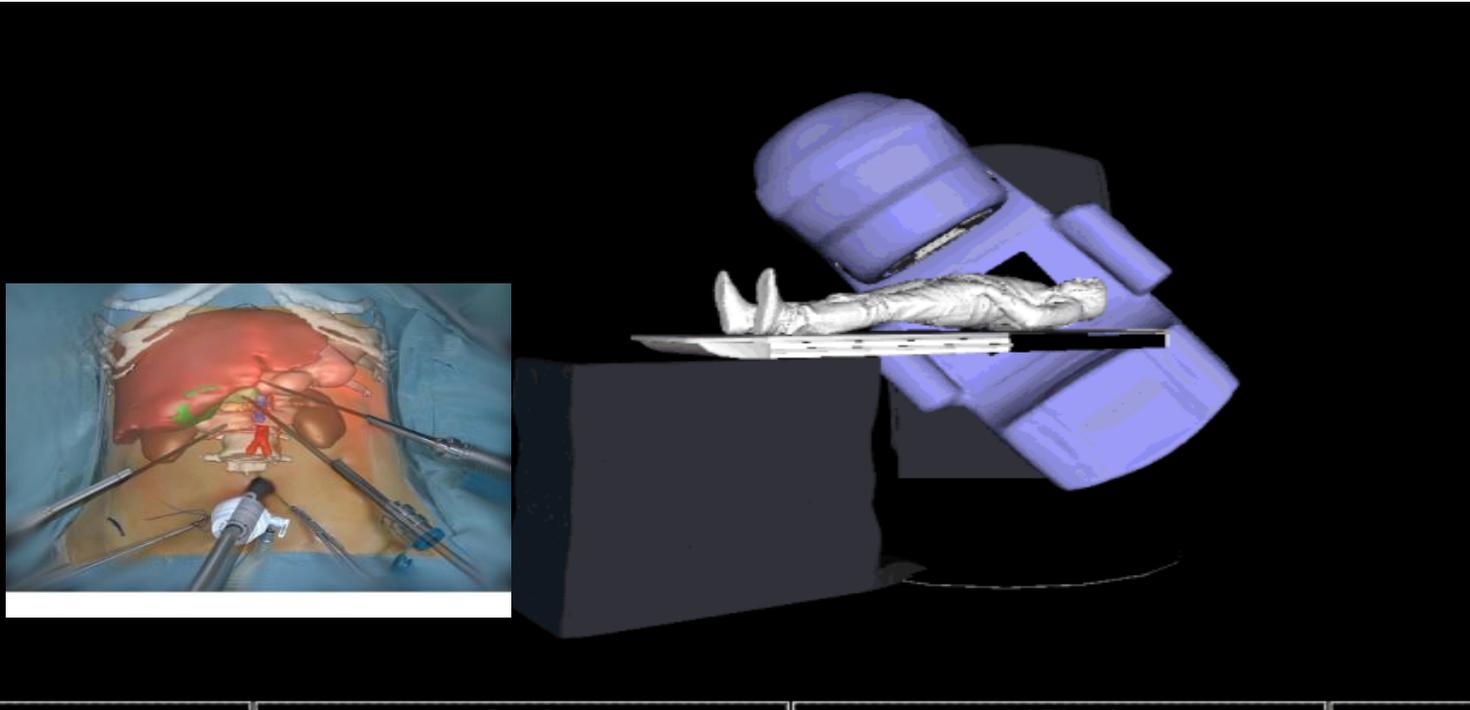
AUTOMATIQUE

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

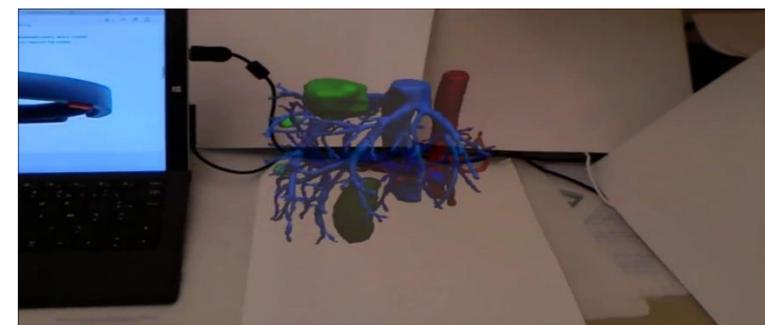
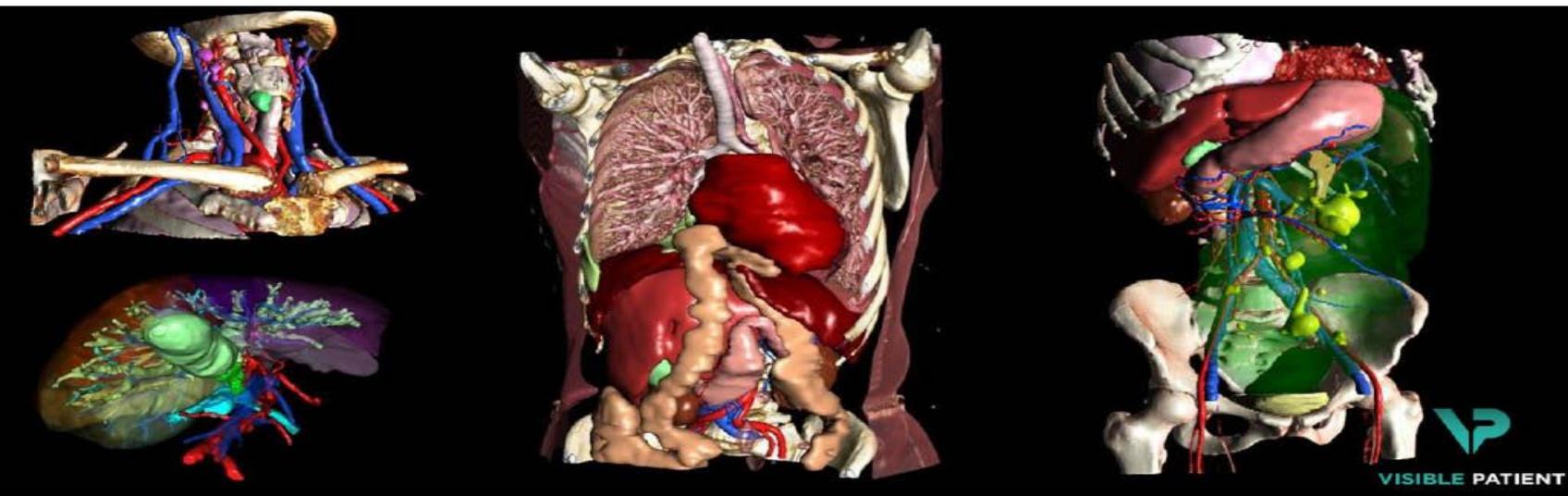




RÉALITÉ AUGMENTÉE



VISIBLE PATIENT





2018 This Is What Happens In An Internet Minute

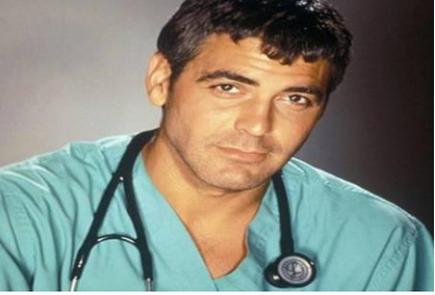


Randomized Trial Comparing a Web-Mediated Follow-up With Routine Surveillance in Lung Cancer Patients

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

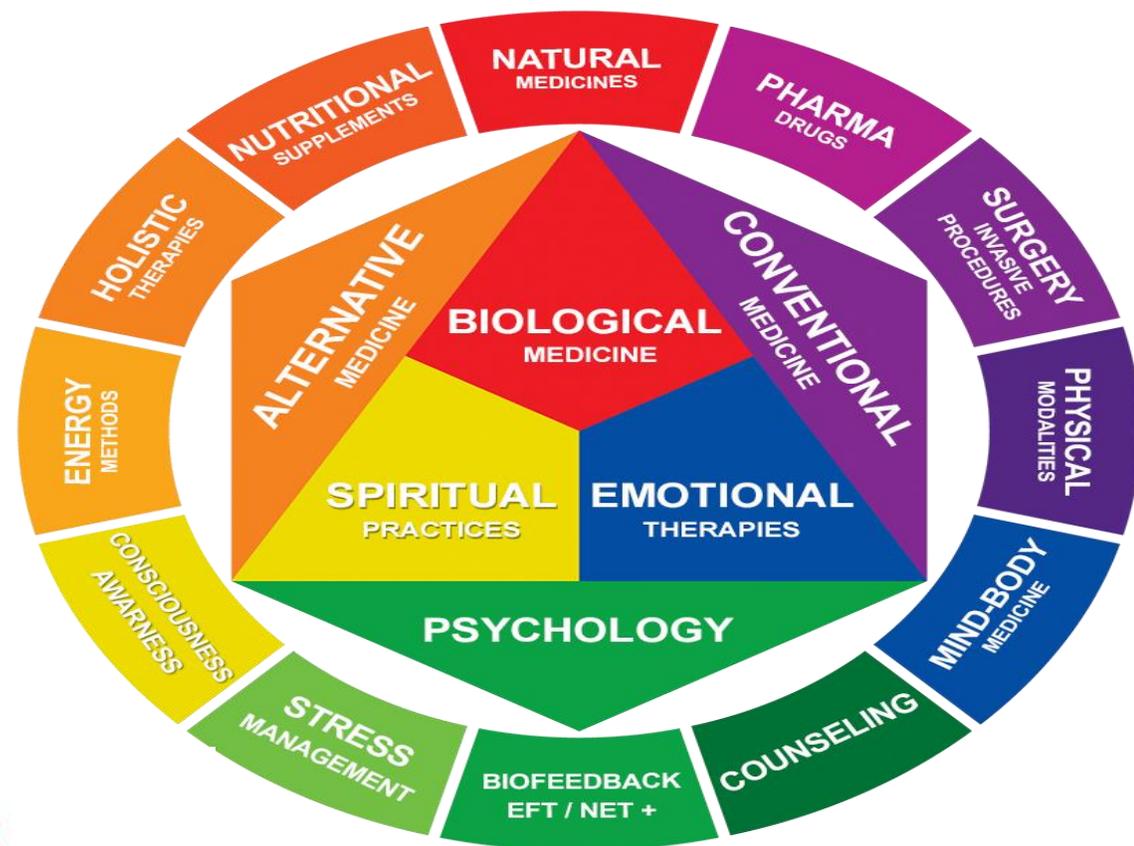
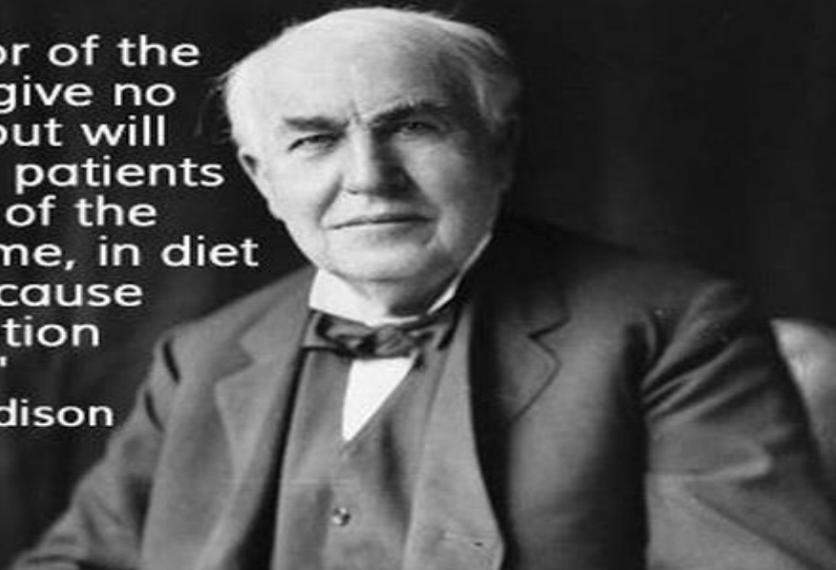
National Cancer Act, 1971



«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

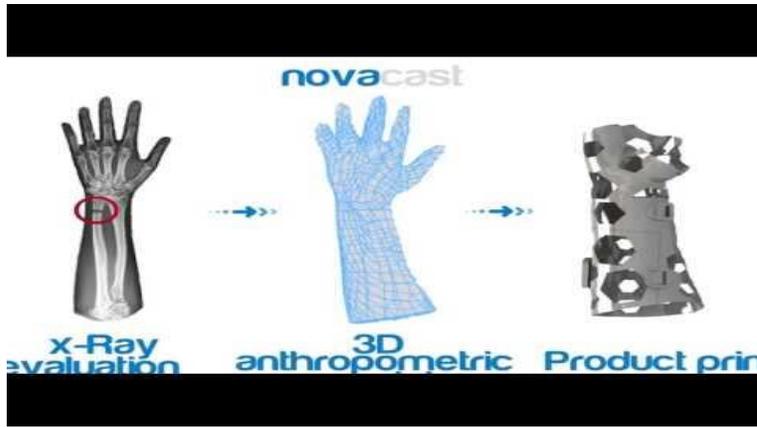
Réflexion Ethique en Génétique Prédictive

29 mars 2017

PALAIS BRONGNIART, PARIS

9H00 - 17H30

Impression 3D



Réalité Virtuelle



Réalité augmentée



Santé Connectée



Silico Trial



Intelligence Artificielle



Biologie synthétique



Robotique



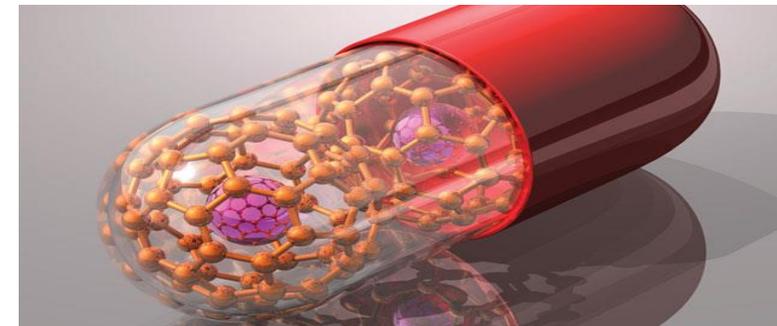
Tricorder Médical

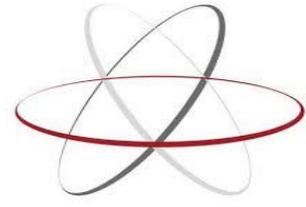
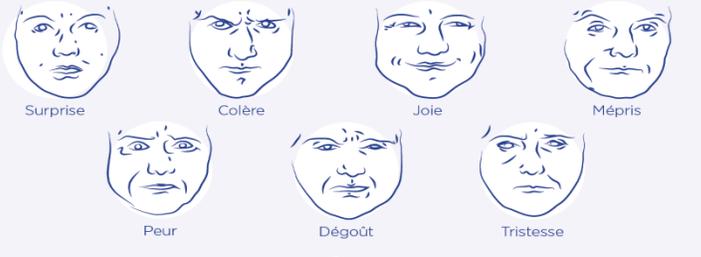


Séquençage génétique



Nanomedecine





Institut
Rafaël
Maison de l'après cancer

