Medicina di Precisione,Farmaci Intelligenti,Genetica: il futuro che ci attende

Marco A. Pierotti

Istituto FIRC di Oncologia Molecolare (IFOM)/ Cogentech S.B. srl

Piacenza, 1 dicembre 2018

“Premesse”

@ Il passato come formazione del presente;

@ la comunicazione del presente come responsabilita’ per un futuro sostenibile;

@ il cancro come paradigma della nuova medicina.

L’esperienza personale :

“Dal male oscuro alla medicina di precisione, una storia di uomini,topi e molecole”

Da dove tutto partì

Gennaio 1970 - Nixon dichiara Guerra al Cancro

Nixon firma The National Cancer Act, Dec. 1971

"I will also ask for an appropriation of an extra $100 million to launch an intensive campaign to find a cure for cancer…"

La promessa di Nixon: "Conquest of cancer by 1976 (Country Bicentellian),as Kennedy conquest of the Moon". Perché' falli"?

- Conquista della Luna

*L'obiettivo era un oggetto conosciuto
*La necessaria conoscenza era disponibile
*Opportuni investimenti e l'obiettivo era raggiungibile

- Conquista del Cancro

*L'obiettivo era una malattia ad origine ancora sconosciuta con due ipotesi prevalenti.

La ipotesi virale

@"The circumstantial evidence continues to point to viral causation of several kinds of cancers, however" National Panel on the Conquest of Cancer, pp 17-18 / tobacco document

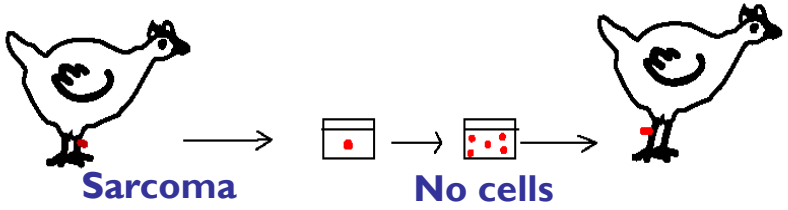
L'ipotesi ambientale

@"Firts report of occupation-induced cancer of scrotum in chimney sweepers" Percival Pott St.Bartholomew's Hospital London 1775.

L' Ipotesi virale

FRANCIS PEYTON ROUS

1910
@Lavoro di F.P. Rous



The experiment satifies Koch's postulates

A TRANSMISSIBLE AVIAN NEOPLASM.[1]
(SARCOMA OF THE COMMON FOWL.)

By PEYTON ROUS, M.D.

(From the Laboratories of the Rockefeller Institute for Medical Research, New York.)

Plates LXVI–LXVIII.

Among the many recent observations on transmissible neoplasms are several which may have greatly enlarged our knowledge of tumor behavior and certainly, for the present, have somewhat confused it. The tumors of the lower animals first studied experimentally—those of the rat and mouse—were found to conduct themselves much as do human neoplasms; and results with them rather strengthened than changed our conception of tumor-characters. But there have since been discovered a number of transmissible new growths of unusual behavior, among them a sarcoma of the dog, transmissible at coitus (Sticker, Ewing), an endemic

Premio Nobel1966

1975
Joho RM
Billeter MA,
Weissmann C
1977
Hanafusa H.

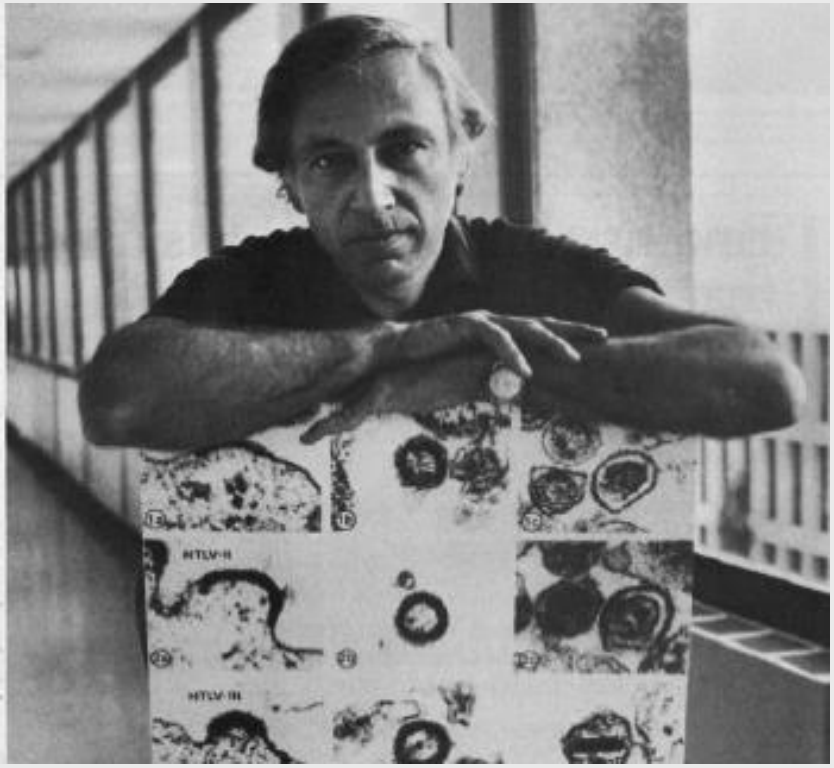
V-src identificato:
Rous Sarcoma virus con 4 geni Gag-pol-env-src

Il PRIMO oncoretrovirus

“La fine dell’Ipotesi virale”

- @ L’attivita’ tumorigenica dei retrovirus e’dovuta all’inserimento nel loro genoma di un gene cellulare attivato (oncogene) che questi virus possono incorporare nel loro genoma e poi replicarsi come oncoretrovirus.

L'effetto positivo di un fallimento



@"The technologies
put in place to identify
the cancer virus
(and a little help
from L. Montagneir and F. Barre'-
Sinoussi 2008
nobelists)
enabled Robert Gallo's lab
to identify
the origin of AIDS"

“La fine dell’Ipotesi Virale”

Human endogenous retroviruses (HERVs): un update

❑ **Il progetto genoma umano ha trovato molte migliaia di ERV, classificate in 24 famiglie (*ASM News, 2001*).**

❑ Gli HERV costituiscono circa **l’8% del genoma umano** (98,000 elementi e frammenti)(PNAS 2004). Nessuno capace di replicazione, tutti defettivi, con delezioni o mutazioni nonsenso (2005). Tuttavia molto studiati per l’evoluzione: **HERV-K** (HML2), costituisce <1% degli elementi HERV, è attivo da quando l’uomo si è differenziato dagli scimpanzè. Ci sono indicazioni che HERV-K106 e HERV-K116 siano attivi nell’uomo da 800.000 anni, e che HERV-K106 possa aver infettato i moderni esseri umani 150.000 anni fa.

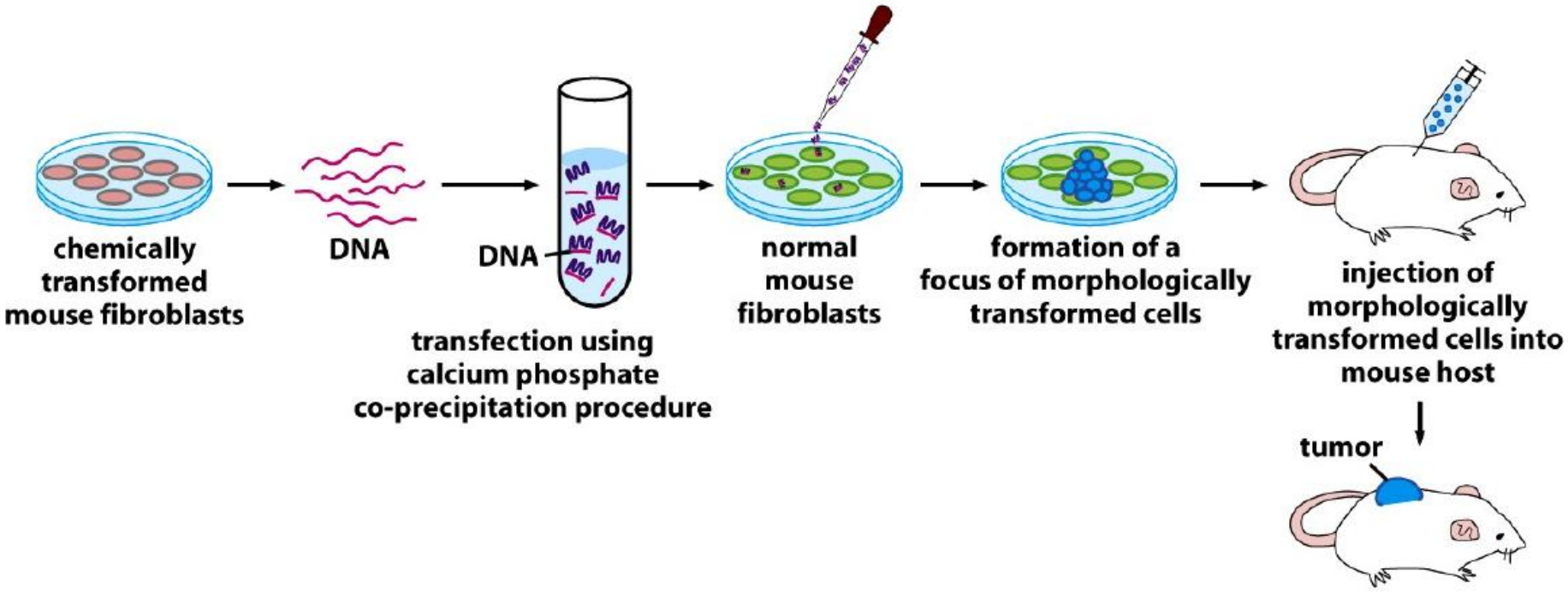
❑ Alcuni studi li hanno associati allo sviluppo di malattie autoimmuni, in particolare sclerosi multipla → retrovirus W detto "**MS-associated retrovirus**" (MSRV).

❑ 2004: sono stati trovati Ab anti-HERV con maggior frequenza in pazienti affetti da **schizofrenia**. Inoltre nel liquido cerebrospinale di tali pazienti sono stati trovati marker retrovirali (RT) 4 volte maggiori che nei controlli, suggerendo che l’infezione/riattivazione di HERV possano essere un trigger per tale malattia.

❑ 2007: due gruppi (S. Francisco e Toronto) hanno pubblicato che c’è evidenza di una risposta cellulo-mediata anti-HERV nei pazienti **HIV**, ipotizzando che HIV possa indurre l’espressione di HERV nelle cellule infettate.

I nemici sono dentro noi: gli Oncogeni e l'origine del cancro (da v-onc a c-onc)

La metodologia (magica) della "transfection"



Il primo Oncogene umano: l'equivalente dell' oncogene v-HRAS dei roditori

Nature. 1982 Apr 1;296(5856):404-9.

Isolation and preliminary characterization of a human transforming gene from T24 bladder carcinoma cells.

Goldfarb M, Shimizu K, Perucho M, Wigler M.

Abstract

DNA from T24, a cell line derived from a human bladder carcinoma, can induce the morphological transformation of NIH 3T3 cells. Using techniques of gene rescue to clone the gene responsible for this transformation, we have found that it is human in origin, less than 5 kilobase pairs in size and is homologous to a 1,100-base polyadenylated RNA species found in T24 and HeLa cells. Blot analysis indicates extensive restriction endonuclease polymorphism near this gene, in human DNAs.

Cell. 1982 May;29(1):161-9.

Isolation of a transforming sequence from a human bladder carcinoma cell line.

Shih C, Weinberg RA.

Abstract

We have isolated the component o
oncogenic sequence was isolated
carrying the human oncogene. A s
vector pBR322. The subcloned onc
appears to derive from sequences
between the oncogene and its norr
variety of other types of human tun
contrast, the EJ bladder oncogene
line. The oncogene appears to hav

Proc Natl Acad Sci U S A. 1982 May;79(9):2845-9.

Oncogenes in human tumor cell lines: molecular cloning of a transforming gene from human bladder carcinoma cells.

Pulciani S, Santos E, Lauver AV, Long LK, Robbins KC, Barbacid M.

Abstract

The presence of dominant transforming genes in human tumor cell lines has been investigated. High molecular weight DNAs isolated from cell lines established from carcinomas and sarcomas of various organs as well as from a glioblastoma and two melanomas were utilized to transfect NIH/3T3 mouse fibroblasts. The DNAs of T24 and A2182, two cell lines derived from a bladder and a lung carcinoma, respectively, and of HT-1080, a cell line established from a fibrosarcoma, were able to transform recipient NIH/3T3 cells. First-cycle transformants exhibited anchorage-independent growth and were tumorigenic in athymic and immunocompetent mice. Moreover, they contained human DNA sequences and were able to transmit their malignant phenotype in additional cycles of transfection. Southern blot analysis of T24-derived transformants showed that a single fragment of human DNA specifically cosegregated with the malignant phenotype, suggesting that it contained the T24 oncogene. Therefore, these human sequences were molecularly cloned with lambda Charon 9A as the cloning vector. The resulting recombinant DNA molecule, designated lambda T24-15A, was shown to contain a 15-kilobase-pair EcoRI insert of human cellular DNA. lambda T24-15A DNA (either intact or EcoRI digested) transformed NIH/3T3 fibroblasts with a specific activity of 20,000 focus-forming units per pmol of cloned DNA. Our results indicate that we have molecularly cloned a biologically active oncogene present in T24 human bladder carcinoma cells.

I nemici sono dentro noi: gli "Oncogeni" e l'origine del cancro

@ Quesito aperto: l'oncogene e' tale SOLO nel tessuto tumorale di un individuo?

The Washington Post

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FRIDAY, FEBRUARY 10, 1984

Higher in Areas Approximately 75 Miles From District of Columbia (See Box on A2)

Cancerous Process in Gene Identified

By Victor Cohn
Washington Post Staff Writer

Scientists have identified the crucial mutation, or change in a single chemical molecule, that turned a potential cancer gene cancerous in a smoker's lung.

The achievement by four scientists at the National Institutes of Health and two Italian co-workers is potential cancer genes, and that these genes can be turned into malignant genes (oncogenes) by some event or events. In this patient's case, the trigger probably was exposure to carcinogens in the cigarette smoke he had long inhaled.

Genes are segments of the thin twisted strands of DNA, or deoxyribonucleic acid, that dictate the role author of the new report in today's issue of Science.

Drs. Santos, Dionisio Martin-Zanca, E. Premkumar Reddy and Mariano Barbacid, all of the National Cancer Institute, did the research with Drs. Marco Pierotti and Guiseppe Della Porta of Italy's National Institute for the Study and Cure of Tumors in Milan.

retaliate for the U.S. shellin
Associated Press reported.
cannot stand neutral watchi
barbaric bombardment practi
the Sixth Fleet against Le
civilians," Damascus' gover
radio said. It warned that Syri
be compelled to react."]

[The official Soviet new
Pravda Thursday charged th
United States had "pra
started an undeclared war
Lebanon" and accused U.S. fo
wiping Beirut "off the face
earth," United Press Intern
n Moscow.]

ican official he
BANON, A23, Col.

ys decision on
ns. Pa

Science. 1984 Feb 17;223(4637):661-4.

Malignant activation of a K-ras oncogene in lung carcinoma but not in normal tissue of the same patient.

Santos E, Martin-Zanca D, Reddy EP, Pierotti MA, Della Porta G, Barbacid M.

Abstract

A single genetic alteration, a guanine-to-cytosine transversion, is responsible for the acquisition of malignant properties by K-ras genes of two human tumor cell lines established from carcinomas of the bladder (A1698) and lung (A2182). As a consequence, arginine instead of the normal glycine is incorporated into the K-ras-coded p21 proteins at amino acid position 12. This mutation creates a restriction enzyme polymorphism that can be used to screen human cells for transforming K-ras genes. This approach was used to identify the mutational event responsible for the malignant activation of a K-ras oncogene in a squamous cell lung carcinoma of a 66-year-old man; this point mutation was not present in either the normal bronchial or parenchymal tissue or in the blood lymphocytes. Hence, malignant activation of a ras oncogene appears to be specifically associated with the development of a human neoplasm.

Dr. Jekill e Mr.Hyde

@ proto-oncogene = gene che nella cellula normale ,in maniera regolata, determina la sua crescita e il suo differenziamento.

@ oncogene (c-onc) = forma "attivata" di un proto-oncogene che sregolato partecipa alla conversione di una cellula normale in tumorale

I nemici sono dentro noi: gli "Oncogeni" e l'origine del cancro

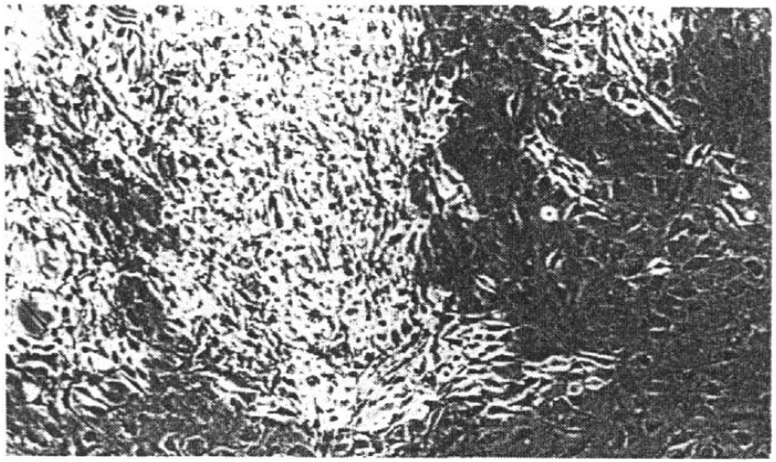
RET e TRK: due oncogeni made in Italy

Reprinted from Nature, Vol. 328, No. 6126, p. 170-172, 9 July 1987

A new oncogene in human thyroid papillary carcinomas and their lymph-nodal metastases

A. Fusco*, M. Grieco*, M. Santoro*, M. T. Berlingieri*, S. Pilotti†, M. A. Pierotti‡, G. Della Porta‡ & G. Vecchio*

* Dipartimento di Biologia e Patologia Cellulare e Molecolare, Centro di Endocrinologia ed Oncologia Sperimentale del CNR, II Facoltà di Medicina e Chirurgia, Università di Napoli, Via S. Pansini 5, 80131 Naples, Italy
† Divisione di Anatomia Patologica e Citologia, Istituto Nazionale Tumori, Via Venezian 1, 20133 Milan, Italy
‡ Divisione di Oncologia Sperimentale, Istituto Nazionale Tumori, Via Venezian 1, 20133 Milan, Italy



Oncogene (1989), **4**, 1457–1462

High frequency of activation of tyrosine kinase oncogenes in human papillary thyroid carcinoma

I. Bongarzone[1], M.A. Pierotti[1], N. Monzini[1], P. Mondellini[1], G. Manenti[1], R. Donghi[1], S. Pilotti[2], M. Grieco[3], M. Santoro[3], A. Fusco[3], G. Vecchio[3] & G. Della Porta[1]

[1]*Divisione di Oncologia Sperimentale A and* [2] *Divisione di Anatomia Patologica, Istituto Nazionale Tumori, Via G. Venezian 1, 20133 Milan;* [3]*Centro di Endocrinologia ed Oncologia Sperimentale del CNR, Dipartimento di Biologia e Patologia Cellulare e Molecolare, II Facoltà di Medicina e Chirurgia, Università di Napoli, Via S. Pansini 5, 80131 Naples, Italy*

I nemici sono dentro noi: gli "Oncogeni" e l'origine del cancro. Attivazione di oncogeni per radiazioni ionizzanti: la lezione di Chernobyl.

[CANCER RESEARCH 55, 5617–5620, December 1, 1995]

Oncogenic Rearrangements of the *RET* Proto-Oncogene in Papillary Thyroid Carcinomas from Children Exposed to the Chernobyl Nuclear Accident[1]

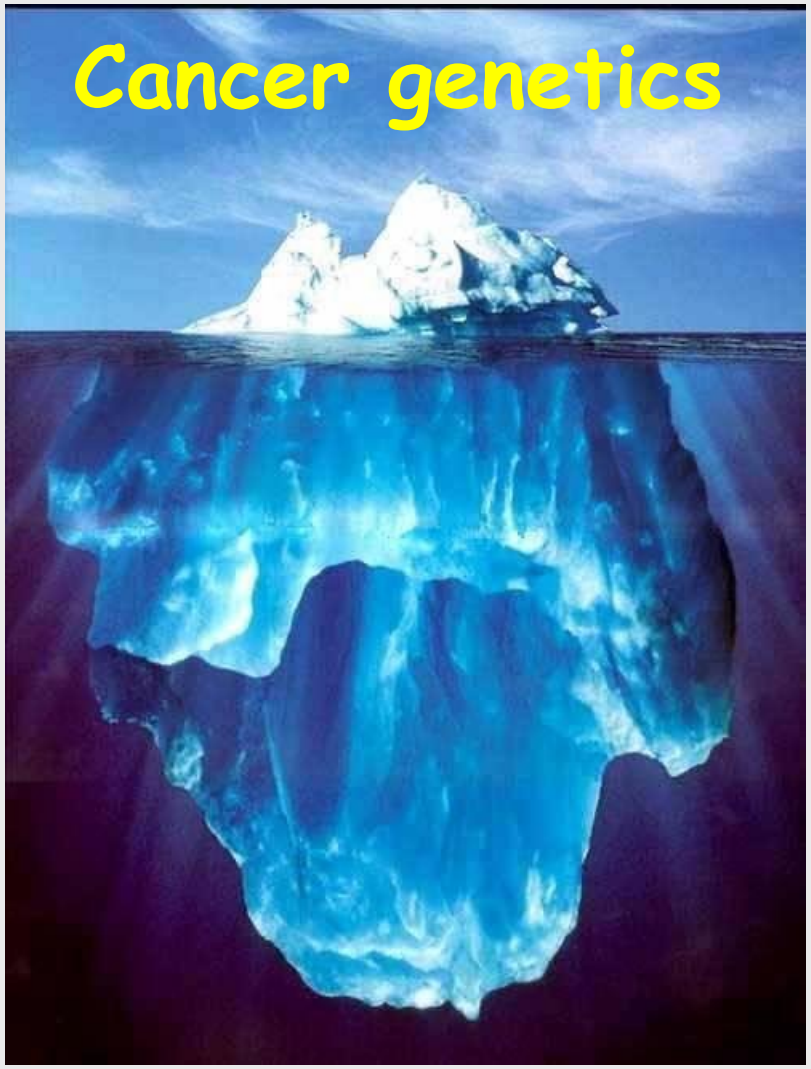
Laura Fugazzola, Silvana Pilotti, Aldo Pinchera, Tatiana V. Vorontsova, Piera Mondellini, Italia Bongarzone, Angela Greco, Larisa Astakhova, Marta G. Butti, Eugene P. Demidchik, Furio Pacini, and Marco A. Pierotti[2]

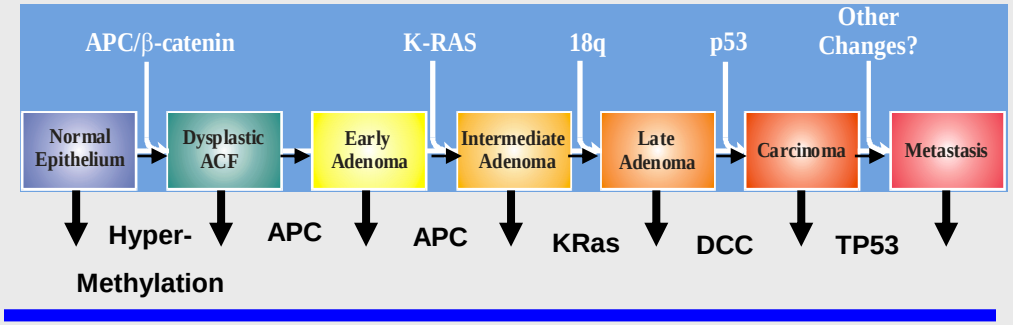
Istituto di Endocrinologia, Universita' di Pisa, V.le del Tirreno 64, 56018 Tirrenia Pisa [L. F., A. P., F. P.]; Divisione di Anatomia Patologica e Citologia [S. P.] and Divisione di Oncologia Sperimentale A [P. M., I. B., A. G., M. G. B., M. A. P.], Istituto Nazionale Tumori, Via G. Venezian 1, 20133 Milano, Italy; and Institute of Radiation Medicine [T. V. V., L. A.] and Oncology Center of Thyroid [E. P. D.], Minsk, Byelorussia

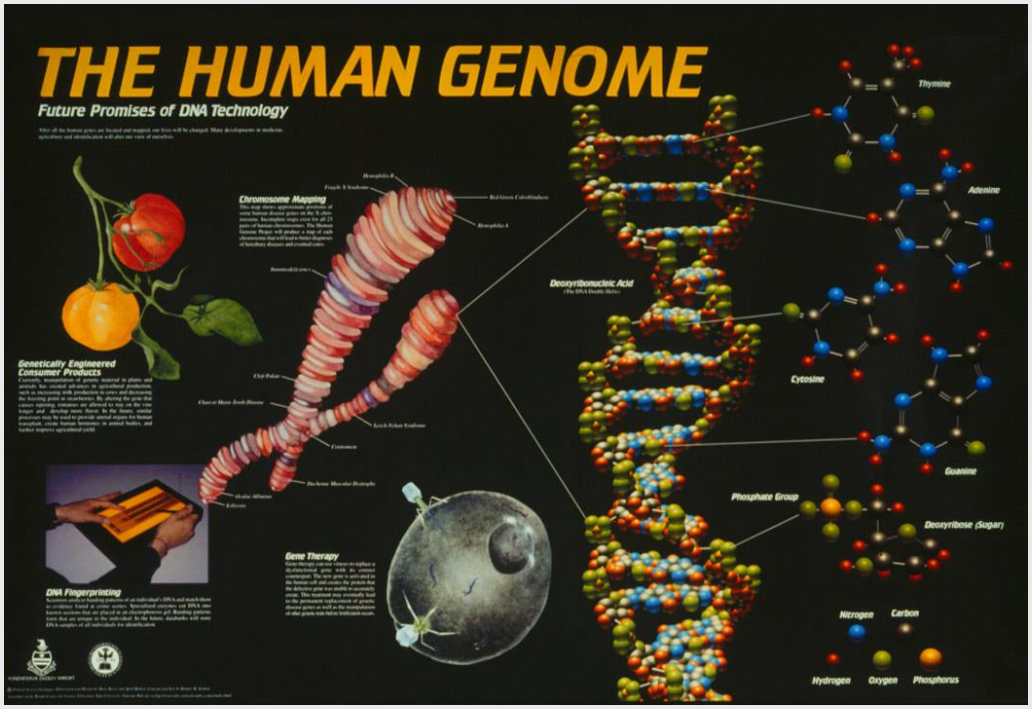
Chernobyl accident

Hiroshima bombing

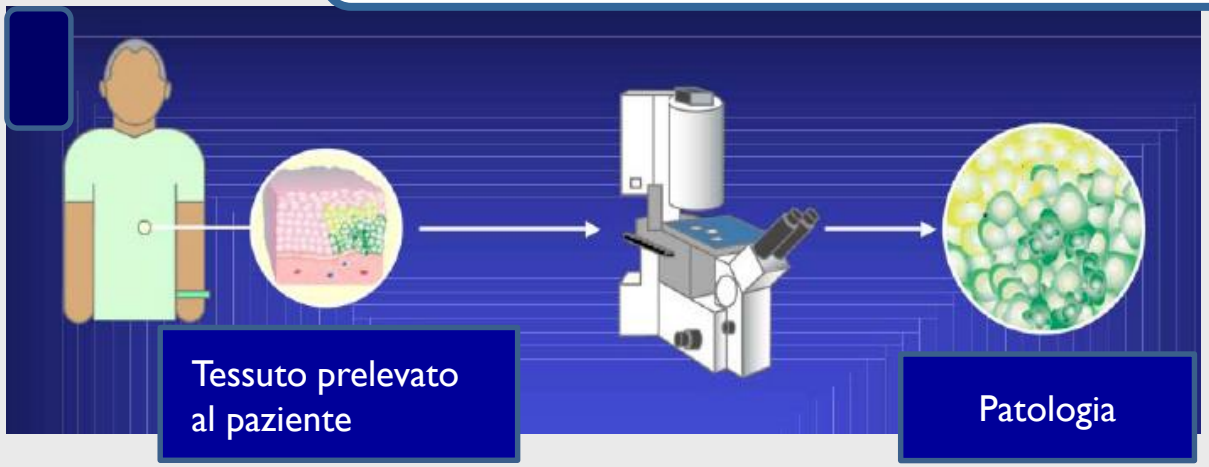
Il Cancro e'una malattia genetica somatica ed e' un processo che avviene a stadi multipli



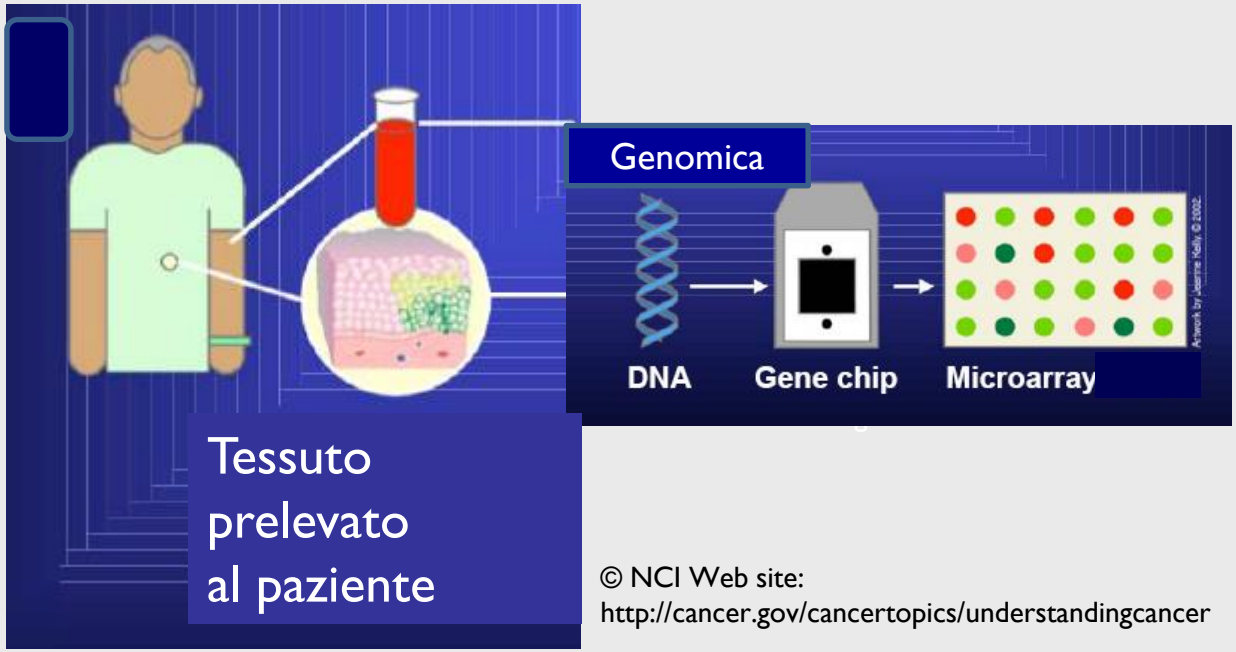




Un Nuovo Scenario per la Diagnostica dei Tumori

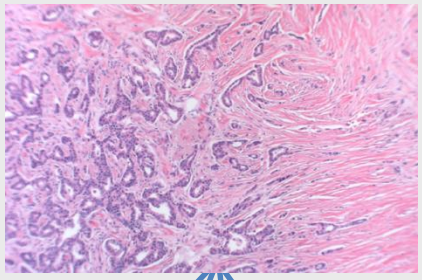


La diagnosi molecolare dei tumori

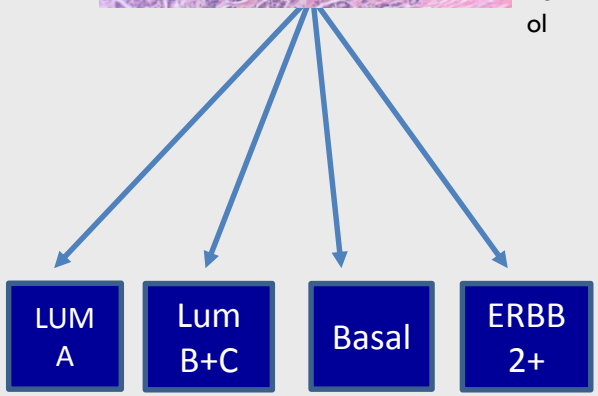


© NCI Web site:
http://cancer.gov/cancertopics/understandingcancer

Carcinoma mammario duttale infiltrante



© Brown Medical School

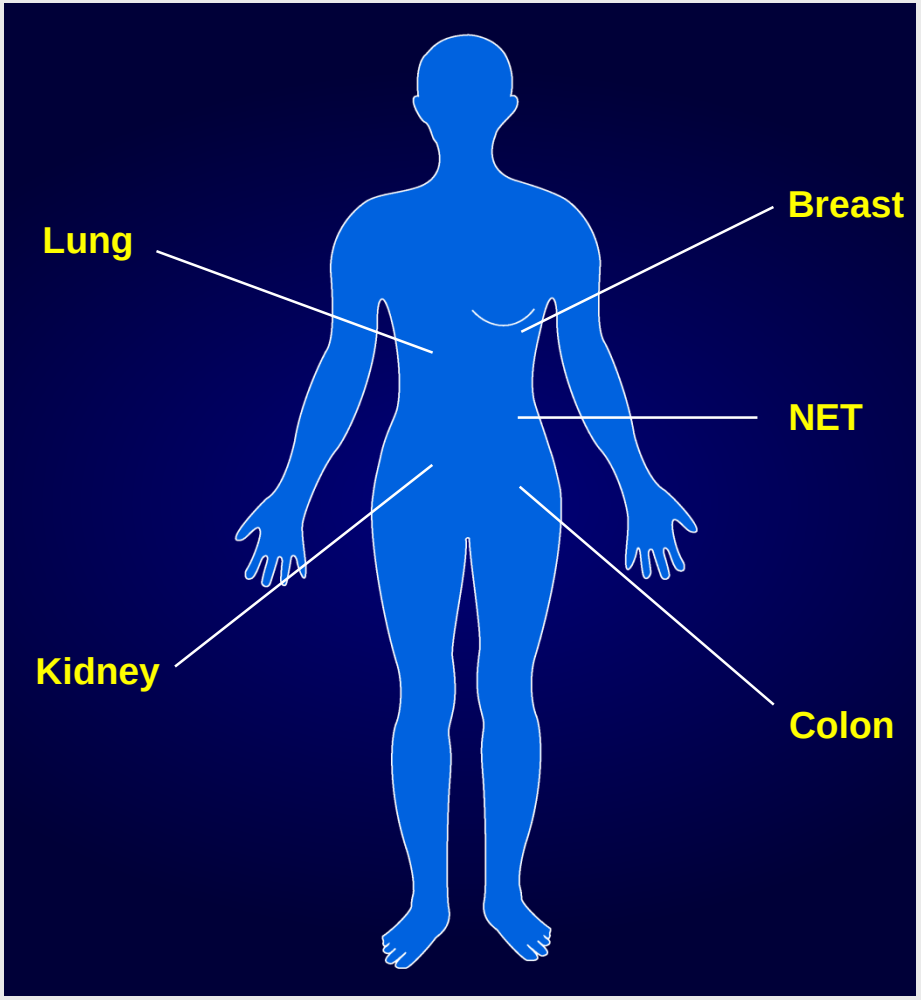


Caratterizzazione Molecolare dei Tumori :

Le stesse Alterazioni Molecolari sono presenti in Tumori Diversi

EGFR, 32%–60%
p-Akt, 23%–50%
Ras, 30%
PTEN, 24%
HER2, 5%
PI3-K, 4%

TGFα/TGFβ1, 60%–100%
VHL, 30%–50%
IGF-1/IGF-IR, 39%-69%
p-Akt, 38%
PTEN, 31%
TSC1/TSC2



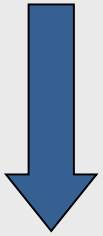
p-Akt, 42%
PTEN, 15%–41%
HER2, 30%–36%
PI3-K, 18%–26%
EGFR, 6%

TSC1/TSC2
IGF-1/IGF-1R
VHL

Ras, 50%
p-Akt, 46%
PTEN, 35%
PI3-K, 20%–32%
EGFR, 8%
HER2, 3%

Caratterizzazione Molecolare dei Tumori

Nuove tecnologie



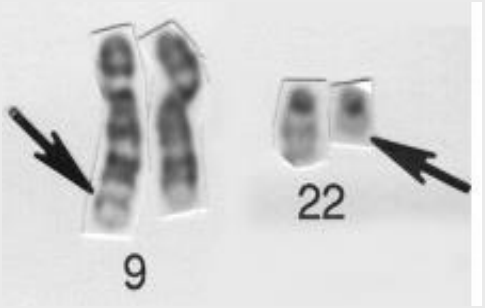
Caratterizzazione molecolare dei tumori

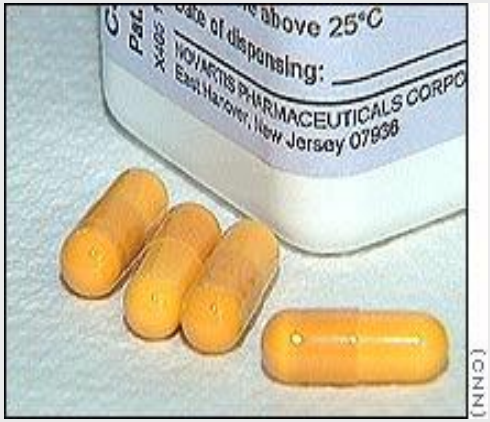
Diagnosi molecolare

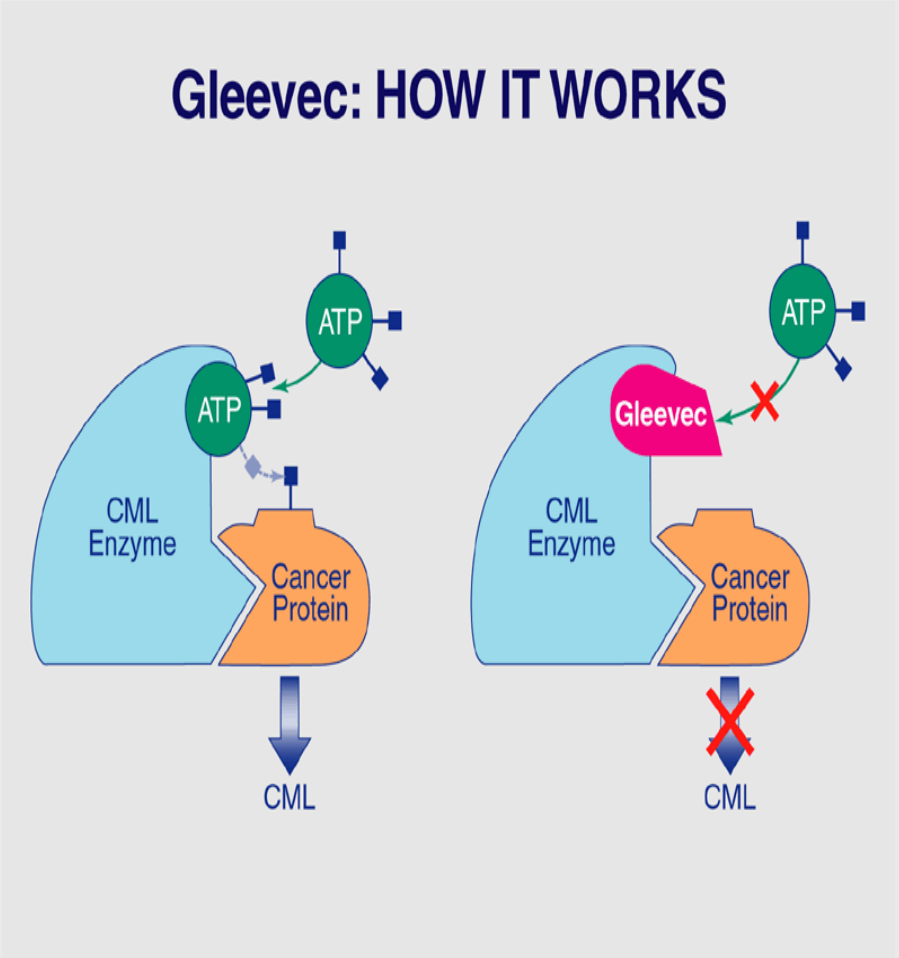
Terapia personalizzata

Gleevec/Imatinib : il primo esempio di farmaco intelligente (targeted therapy)

- BCR/ABL inhibitors and CML therapy





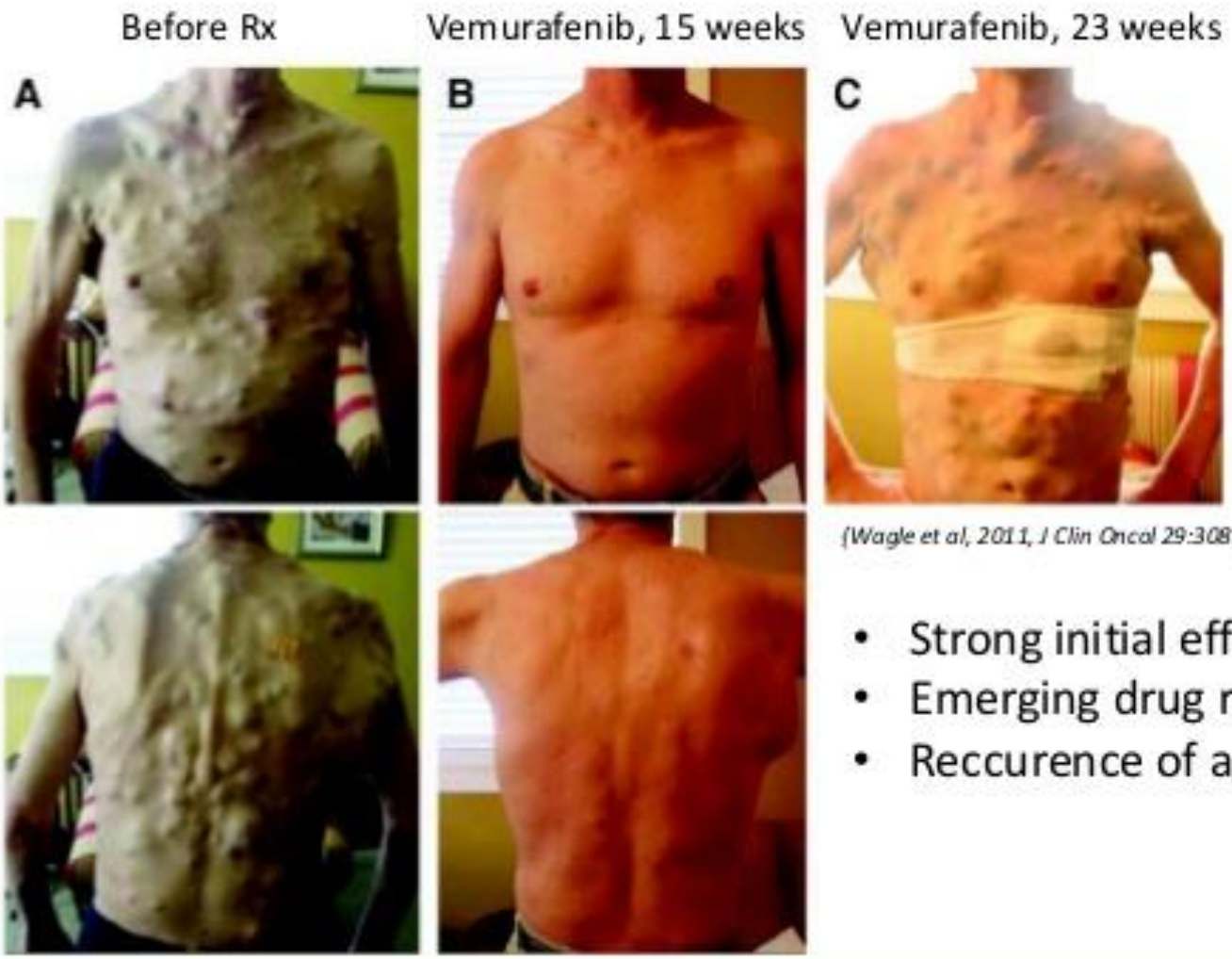


"Il Limite delle Targeted Therapies coi Farmaci Intelligenti"

@ Il farmaco deve essere ,in pratica, continuamente fornito.

@ Quasi inevitabilmente insorgono meccanismi di **Resistenza** con ripresa della malattia.

Clinical efficacy of Vemurafenib



(Wagle et al, 2011, J Clin Oncol 29:3085)

- Strong initial effects vemurafenib
- Emerging drug resistancy
- Reccurence of aggressive tumors

L'Immunoterapia dei Tumori

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 19, 2010 VOL. 363 NO. 8

Improved Survival with Ipilimumab in Patients with Metastatic Melanoma

F. Stephen Hodi, M.D., Steven J. O'Day, M.D., David F. McDermott, M.D., Robert W. Weber, M.D., Jeffrey A. Sosman, M.D., John B. Haanen, M.D., Rene Gonzalez, M.D., Caroline Robert, M.D., Ph.D., Dirk Schadendorf, M.D., Jessica C. Hassel, M.D., Wallace Akerley, M.D., Alfons J.M. van den Eertwegh, M.D., Ph.D., Jose Lutzky, M.D., Paul Lorigan, M.D., Julia M. Vaubel, M.D., Gerald P. Linette, M.D., Ph.D., David Hogg, M.D., Christian H. Ottensmeier, M.D., Ph.D., Celeste Lebbé, M.D., Christian Peschel, M.D., Ian Quirt, M.D., Joseph I. Clark, M.D., Jedd D. Wolchok, M.D., Ph.D., Jeffrey S. Weber, M.D., Ph.D., Jason Tian, Ph.D., Michael J. Yellin, M.D., Geoffrey M. Nichol, M.B., Ch.B., Axel Hoos, M.D., Ph.D., and Walter J. Urba, M.D., Ph.D.


Science
Breakthrough of the Year
Cancer Immunotherapy
T cells on the attack
AAAS

Targeted Therapies: alcuni numeri

Sipleucel-T for metastatic castration-resistant prostate cancer	**$ 93,000 for full course (3 infusions)**
Ipilimumab for metastatic melanoma	$ 120,000 for full course (4 infusions in three months)
Everolimus for renal cell carcinoma and pancreatic cancer	$ 10,000 a month

OncKive The Rising Cost of Cancer Care in the Era of Individualized Therapy: A Q&A With Thomas J. Smith, MD Anna Azvolinsky, PhD May 2012

Diagnosi Molecolare e Terapie Targeted: Un Passo verso la Medicina di Precisione

The Goal of Personalized (Precision) Medicine is:

to provide the right drug

to the right person

at the right dose

IL Cancro
malattia genetica
a livello somatico
e' anche
ereditabile ?

@ SI ma solo nel 5-10% dei casi e si eredita rischio e NON malattia (malati di rischio)

Tutto iniziò nel 1997…

BRCA1 Sequence Analysis in Women at High Risk for Susceptibility Mutations

Risk Factor Analysis and Implications for Genetic Testing

Donna Shattuck-Eidens, PhD; Arnold Oliphant, PhD; Melody McClure; Celeste McBride; Jamila Gupte, MPhil; Todd Rubano, ME; Dmitry Pruss, PhD; Sean V. Tavtigian, PhD; David H.-F. Teng, PhD; Nils Adey, PhD; Mark Staebell, MS; Kathryn Gumpper; Ron Lundstrom, PhD; Mark Hulick; Mark Kelly; John Holmen, PhD; Beth Lingenfelter, MS; Susan Manley, MS; Frank Fujimura, PhD; Michael Luce, PhD; Brian Ward, PhD; Lisa Cannon-Albright, PhD; Linda Steele; Kenneth Offit, MD; Teresa Gilewski, MD; Larry Norton, MD; Karen Brown, MS; Charlene Schulz, MS; Heather Hampel, MS; Alice Schluger, MS; Elena Giulotto, PhD; Wainer Zoli, PhD; Alberto Ravaioli, MD; Heli Nevanlinna, PhD; Seppo Pyrhonen, MD, PhD; Peter Rowley, MD; Starlene Loader; Michael P. Osborne, MD; Mary Daly, MD; Isidore Tepler, MD; Paul L. Weinstein, MD; Jennifer L. Scalia, MS; Richard Michaelson, MD; Rodney J. Scott, PhD; Paolo Radice, PhD; Marco A. Pierotti, PhD; Judy E. Garber, MD; Claudine Isaacs, MD; Beth Peshkin, MS; Marc E. Lippman, MD; Michael H. Dosik, MD; Maria A. Caligo, MD; Robert M. Greenstein, MD; Robert Pilarski; Barbara Weber, MD; Renate Burgemeister, MD; Thomas S. Frank, MD; Mark H. Skolnick, PhD; Alun Thomas, PhD

JAMA, October 15, 1997—Vol 278, No. 15

Context.—A mutation in the *BRCA1* gene may confer substantial risk for breast and/or ovarian cancer. However, knowledge regarding all possible mutations and the relationship between risk factors and mutations is incomplete.

Objectives.—To identify *BRCA1* mutations and to determine factors that best predict presence of a deleterious *BRCA1* mutation in patients with breast and/or ovarian cancer.

Design.— A complete sequence analysis of the *BRCA1* coding sequence and flanking intronic regions was performed in 798 women in a collaborative effort involving institutions from the United States, Italy, Germany, Finland, and Switzerland.

Participants.—Institutions selected 798 persons representing families (1 person for each family) thought to be at elevated a priori risk of *BRCA1* mutation due to potential risk factors, such as multiple cases of breast cancer, early age of breast cancer diagnosis, and cases of ovarian cancer. No participant was from a family in which genetic markers showed linkage to the *BRCA1* locus.

Major Outcome Measures.—Sequence variants detected in this sample are presented along with analyses designed to determine predictive characteristics of those testing positive for *BRCA1* mutations.

Results.—In 102 women (12.8%), clearly deleterious mutations were detected. Fifty new genetic alterations were found including 24 deleterious mutations, 24 variants of unknown significance, and 2 rare polymorphisms. In a subset of 71 Ashkenazi Jewish women, only 2 distinct deleterious mutations were found: 185delAG in 17 cases and 5382insC in 7 cases. A bias in prior reports for mutations in exon 11 was revealed. Characteristics of a patient's specific diagnosis (unilateral or bilateral breast cancer, with or without ovarian cancer), early age at diagnosis, Ashkenazi Jewish ethnicity, and family history of cancer were positively associated with the probability of her carrying a deleterious *BRCA1* mutation.

Conclusions.—Using logistic regression analysis, we provide a method for evaluating the probability of a woman's carrying a deleterious *BRCA1* mutation for a wide range of cases, which can be an important tool for clinicians as they incorporate genetic susceptibility testing into their medical practice.

Il Test Genetico per Mutazioni dei Geni BRCA1 e 2 per Rischio di Cancro Seno/Ovaia.

@ Utilita' clinica dimostrata 1997

@ Riconoscimento SS regionale 2012

1997 – 2012 Test effettuato con Progetto AIRC/FIRC (effettuati circa 15.000 esami gratuitamente a famiglie a rischio e refertate circa 2500 mutazioni)

“Ritorno al futuro”

White House Feb.1, 2016 il Presidente B. Obama lancia la - Cancer Moonshot Task Force -

“Ritorno al Futuro”

(il presente modella il futuro)

@ Medicina di Precisione

Big Data ,IA , Blockchain technologies

Biopsia Liquida (cfDNA)

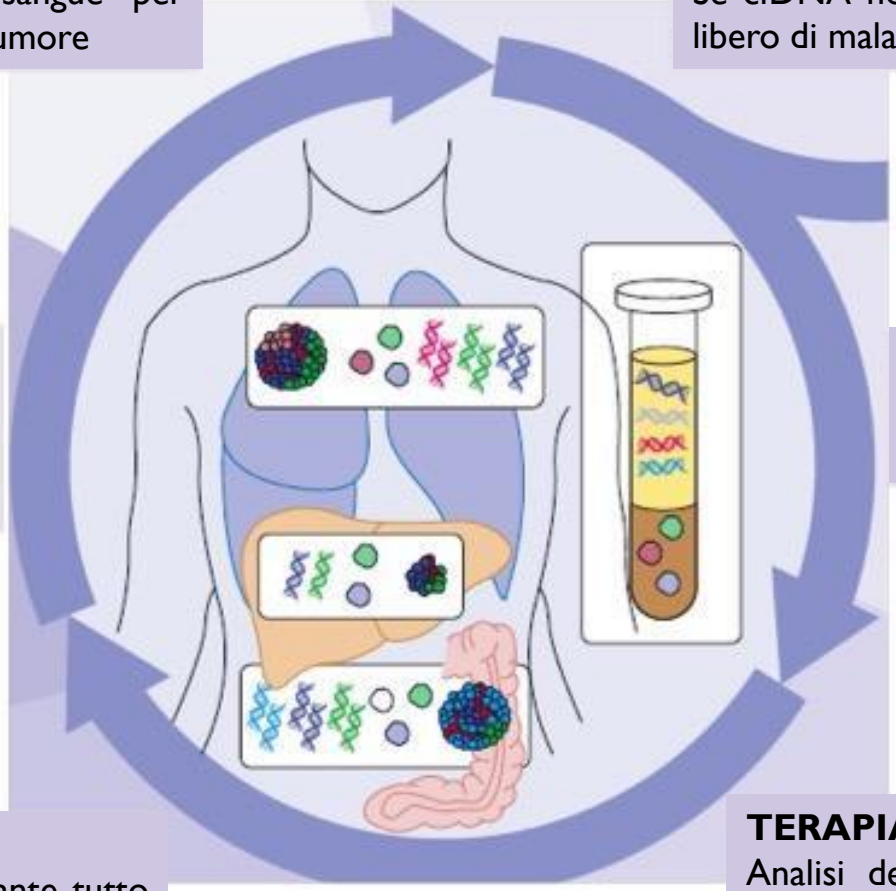
Tailored Therapies

Health Technology Assessments (HTA) = costi/ benefici

“In sangue VERITAS”

DIAGNOSI:
Analisi del cfDNA nel sangue per determinare il profilo del tumore

INTERVENTO:
Se cfDNA non è presente il paziente è libero di malattia



RESISTENZA:
Emergenza di alterazioni genetici associati con la resistenza ai farmaci

MALATTIA MIMIMA RISIDUA:
cfDNA del tumore è ancora presente nel sangue

FOLLOW UP:
Monitoraggio del paziente durante tutto il percorso terapeutico per verificare la risposta e/o resistenza

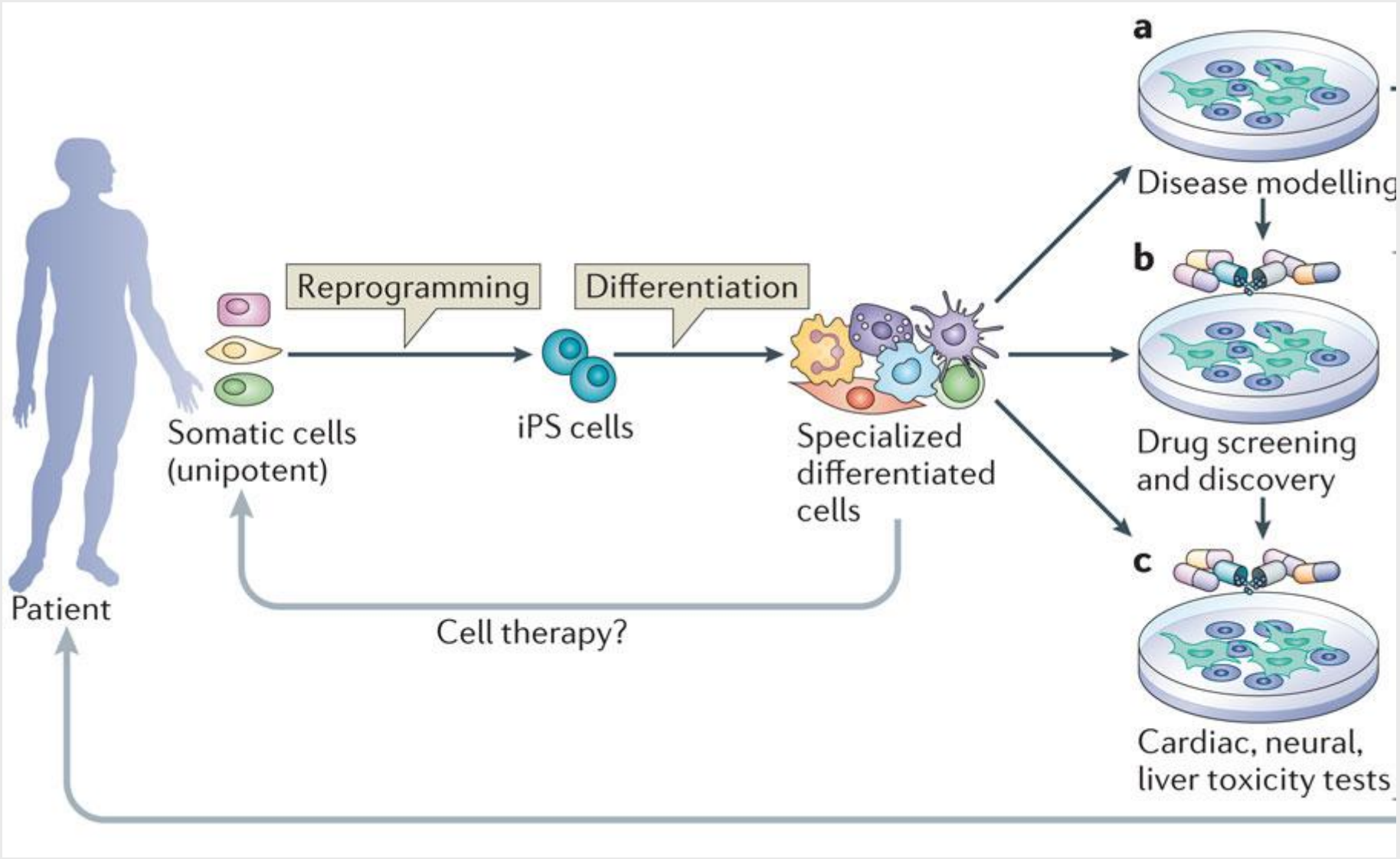
TERAPIA:
Analisi del cfDNA tumorale in tempo reale per monitorare la risposta alla terapia

Adapted from Siravegna and Bardelli, Genome Biology 2014

“Le Tailored Therapies con le cellule staminali indotte pluripotenti”

Embryo

“Le Tailored Therapies con le cellule staminali indotte pluripotenti”



“Medicina di Precisione”

(una voce critica)

“Medicina di precisione”cos’e’?Ben poco, anche se va di gran moda.Per essere precisa la medicina dovrebbe integrare I dati sui primi anni ma anche sulla vita nell’utero e poi educazione,rapporti sociali, biologia genetica, sintomi,dati di laboratorio,dieta,cure. Mi fermo qui, c’e’tantissimo altro, dove abiti per esempio.La medicina di precisione fallira’, scrive il Direttore del “Lancet”,come tutti I tentativi precedenti di mettere etichette alla cura degli ammalati.”

Giuseppe Remuzzi, *Sopra le righe*
Corriere della Sera, 22 aprile 2018

“Ritorno al Futuro”

(il presente modella il futuro)

@ Medicina di Precisione

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@ Farmaci Intelligenti

Combinazione di terapie (e.g. radio-immunoterapia)
Modifica del microambiente tumorale

“Ritorno al Futuro”

(il presente modella il futuro)

@ Medicina di Precisione

Big Data ,IA , Blockchain technologies
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@ Farmaci Intelligenti

Combinazione di terapie (e.g. radio-immunoterapia)
Modifica del microambiente tumorale

@ Genetica

Whole Genome Sequencing (<300 USD) : alla ricerca delle nostre radici e altro……..(medicina predittiva)
Gene editing (CRISPR-Cas9) (modificazione mirata di geni nell’embrione)

“Genetica”

(una voce critica)

“Genomic is only one approach to improving health, and for the most part cannot be used in isolation from other factors or determinants of health and disparities including socioeconomic factors such as housing, education and access to care”

Koury MJ et al, *Genet.Med ,2018*

“Genetica”

(una testimonianza)

“ Ai primi di giugno, ricevetti una email da XXXX(una Company specializzata in test genetici ndr) che mi informava di aver trovato nel mio genoma 172.115 varianti,queste ultime sono cio’ che mi rende differente da 1000 altre persone, teoricamente sane, che erano state usate per stabilire uno standard di normalita’genetica. 15459 di queste varianti sono piuttosto rare e io le condivido con solamente il 5%della popolazione,83 sono molto problematiche, in teoria piu’ che in pratica, sono infatti varianti che indicano una predisposizione (ad una patologia ndr) ma le probabilita’ di ammalarsi veramente sono piuttosto basse…”

G. Remuzzi *Congresso SIC Milano ottobre 2018*

“Conclusioni”

“…Considerate la vostra semenza: fatti non foste per viver come bruti ma per seguir virtute e conoscenza….”

D.A. *Inferno Canto XXVI*