

Bruno DALLAPICCOLA – Giuseppe NOVELLI

Genetica Medica




Edizioni Scientifiche Falco

Sani per scelta o malati per caso: a che punto è la ricerca?

Giuseppe Novelli



Università degli Studi di Roma «Tor Vergata»



Fondazione Lorenzini, Milano



University of Nevada, Reno, USA



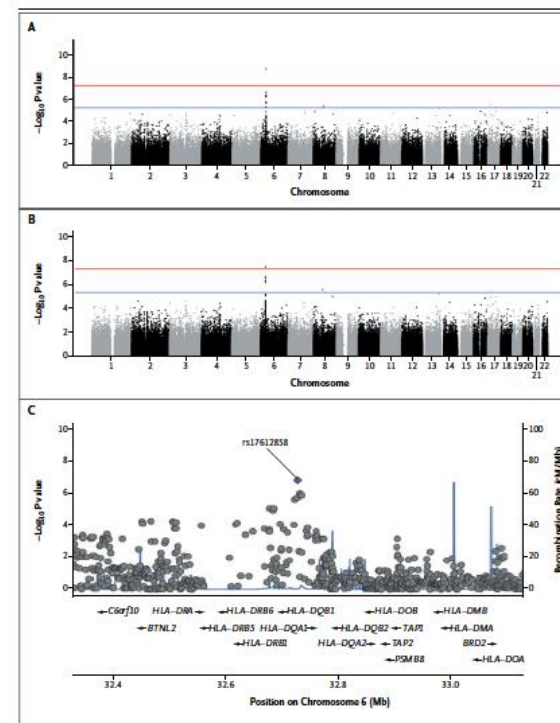
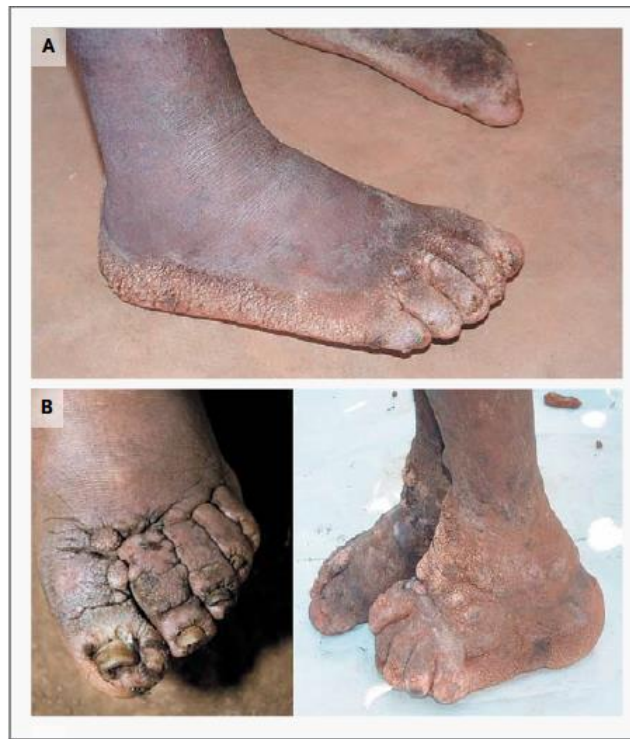


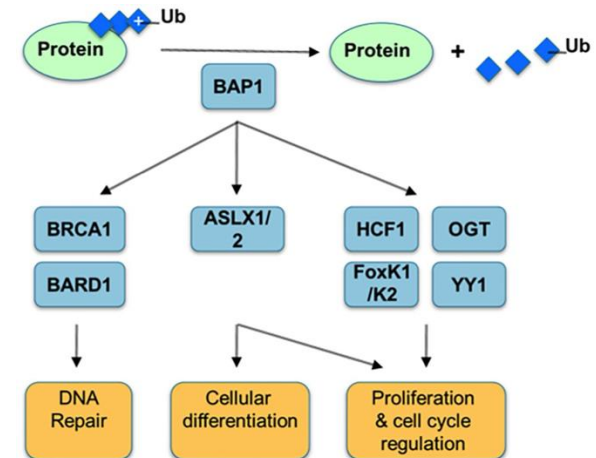
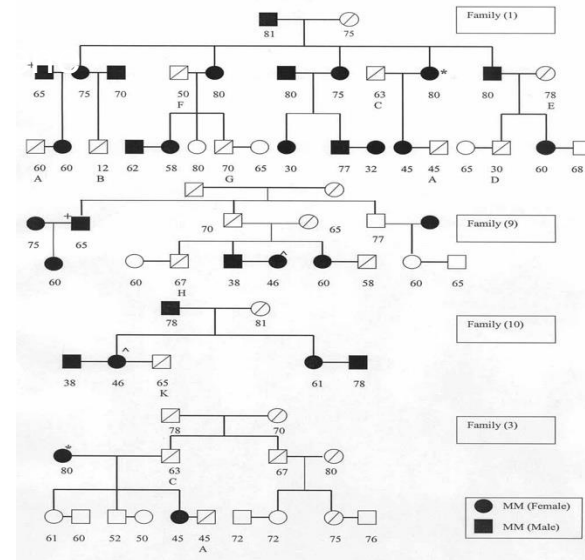
Wolayta

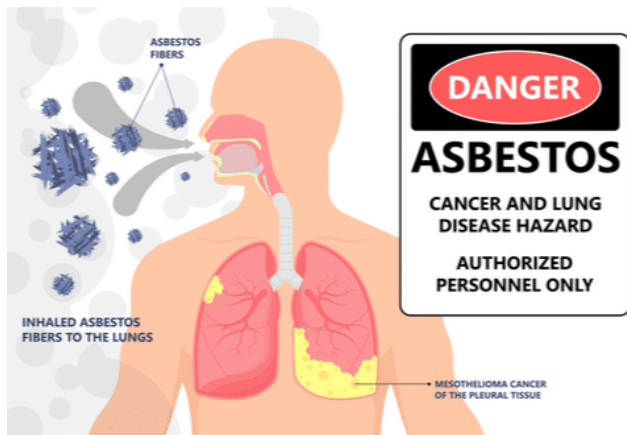
a causa di siccità,
carestie e scarsità di
acqua potabile, soffrono
la fame e la sete, e dove
un agricoltore su 20 si
ammala di podoconiosi



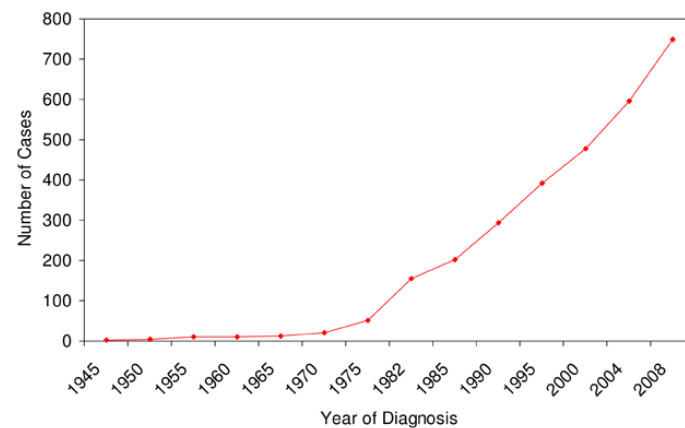
HLA Class II Locus and Susceptibility to Podoconiosis







Incidence of Mesothelioma 1945 to 2008



Vo', dove tutto ebbe inizio. Un anno fa la prima vittima del Coronavirus

NORDEST > PADOVA

Venerdì 19 Febbraio 2021 di Angela Pederiva



...“we found out that 43% of the positive for virus showed no sign of infection..... An enormity”....

Article

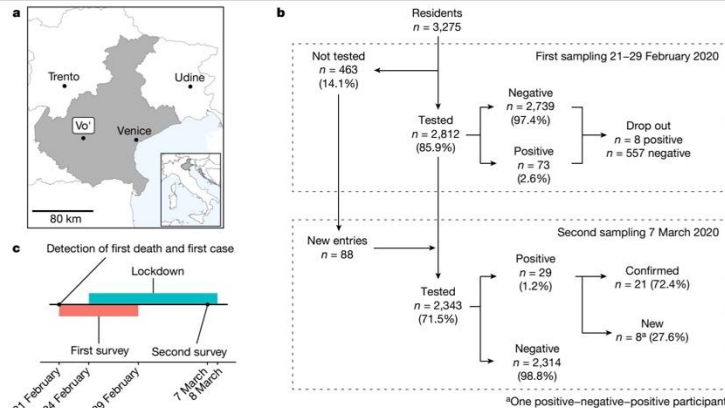
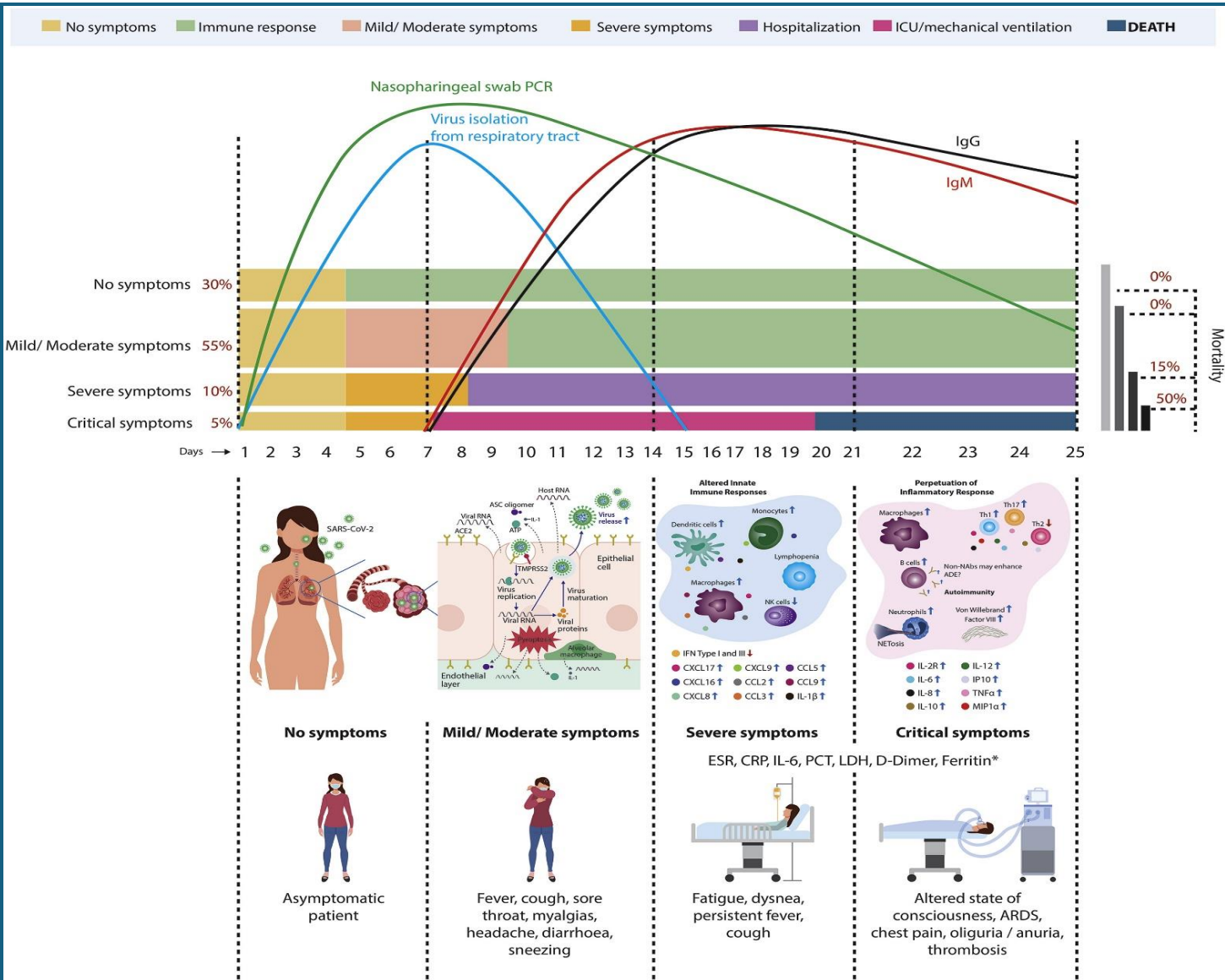


Fig. 1 | Study description. **a**, Map showing the location of Vo' and the Veneto region (grey area) within Italy, produced using shapefiles from GADM (<https://gadm.org/>) and Italian National Institute of Statistics (ISTAT; <https://www.istat.it/it/archivio/222527> and <https://www.istat.it/it/archivio/104317#accord>

ions). **b**, Flow chart summarizing the key statistics on the two sequential nasopharyngeal swab surveys conducted in Vo' to assess the transmission of SARS-CoV-2 before and after the implementation of interventions. **c**, Summary of the key events in the study period.

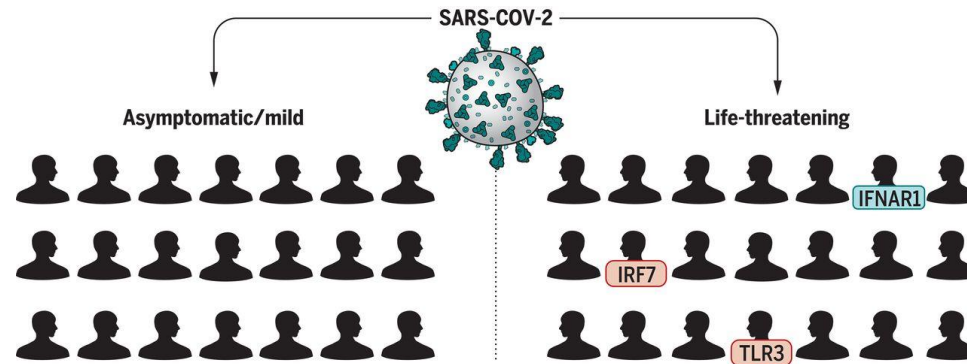
- Nature, 2020 A. Crisanti



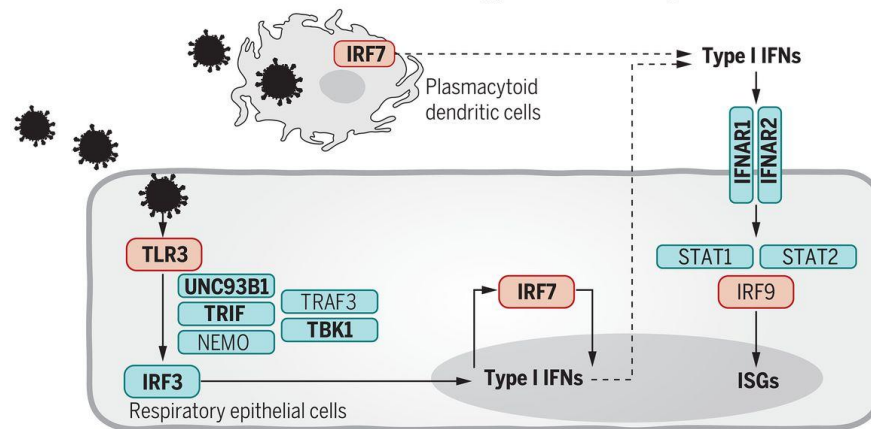
Zyrin Foots, 10,
was taken off
life support on
Wednesday
after a two-
week battle
with COVID-19
and other
complications
from the virus.

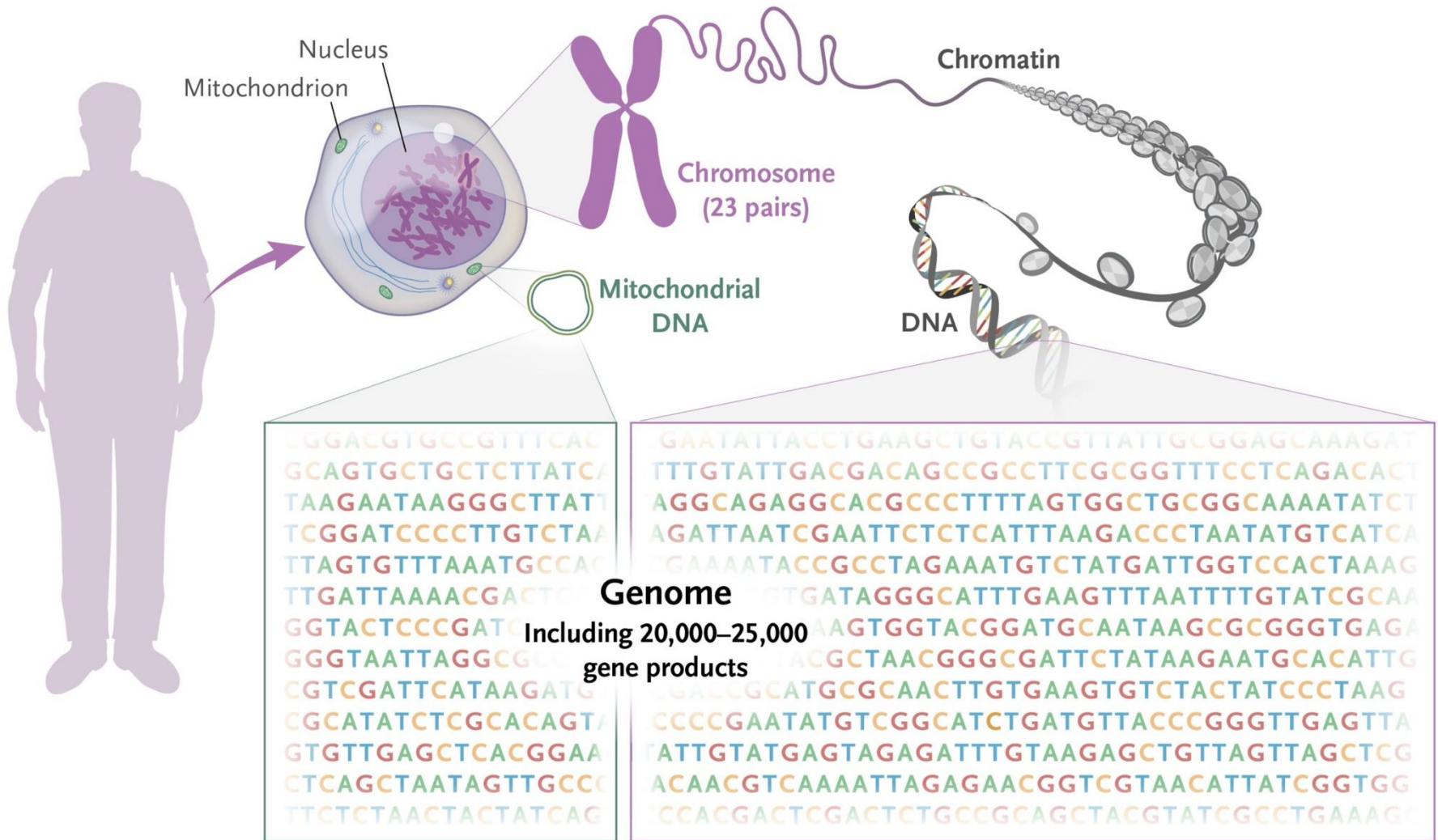


Inborn errors of TLR3- and IRF7-dependent type I IFN production and amplification underlie life-threatening COVID-19 pneumonia.



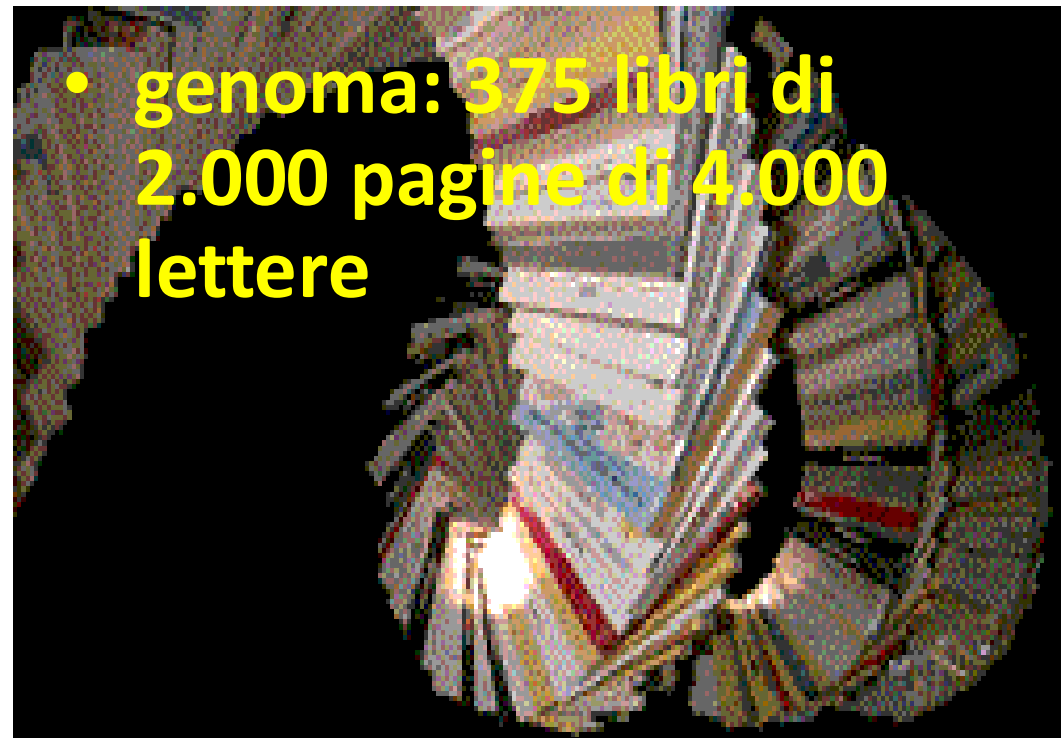
Inborn errors of type I IFN immunity





Il genoma umano come una enciclopedia

- Genoma umano: 3.5 miliardi di basi
- una base come una lettera dell'alfabeto



- genoma: 375 libri di 2.000 pagine di 4.000 lettere

The DNA contribute to the capture of the Sicily's invisible man

NATURE | 405 | 20 February 2003

NEWS FEATURE

GHOST BUSTER

An Italian scientist revived the hunt for the mafia's boss of bosses. Declan Butler reports.

Bernardo Provenzano, Italy's most wanted man, was on the run for more than 40 years. Moving from one safe house to another, he became the godfather of the Sicilian Mafia in 1993, running the huge organization without ever using a telephone, communicating instead through tiny typed notes, pizze, passed back and forth through a labyrinth of secret relay.

Over time, many outside the Mafia had begun to believe the rumours, that he was dead. That was until an Italian scientist used DNA to confirm that Provenzano was still alive, relaunching the manhunt that led to his capture on 11 April last year.

Provenzano had risen up the ranks of the Mafia by moving people down, earning him the nickname 'the tractor'. He was a member of the Corleone clan, which took control of the Sicilian Mafia after a power struggle in the early 1980s that left hundreds dead. Provenzano was the right-hand man, and natural heir, of Salvatore Riina, who was the Corleone boss and Sicilian godfather until his arrest in 1993.

The invisible enemy

The prosecutor who was most responsible for Riina's arrest, Giovanni Falcone, was assassinated in 1992, and Provenzano was implicated in the crime. Pietro Grasso, who is now Italy's national prosecutor against organized crime, vowed to find Falcone's killer. But, as Grasso acknowledges, all the police had to go on was a photograph of Provenzano taken in 1959, and a computer-generated 'identikit' of what he might look like now — his invisibility led to another nickname, the ghost of Corleone. With few leads, there followed a decade of fruitless searching.

But Grasso never gave up. In 2003, he asked Giuseppe Novelli, head of the medical genetics lab at Tor Vergata University in Rome, to help identify Provenzano. "I was taken aback at first," says Novelli, a specialist in genetic fingerprinting. "I mean, how can you identify someone who you have no information about?"

But Grasso had a lead from a Mafia informant, or piovito, arrested in 2003. In 2002,



Wanted! Bernardo Provenzano in 1959; in 'identikit'; and on his capture last April.

the source said, Provenzano had gone to Marseille in France under a false name to be treated for a prostate tumour. A police raid at the clinic found a case history for a man named Gaspare Troia, who had never been admitted to the hospital. The patient's description matched Provenzano.

Novelli extracted DNA from hospital tissue samples and ran a DNA profile of both mitochondrial and Y-chromosome DNA. He then compared the DNA with that taken from blood samples of Provenzano's brother, stored in a Palermo hospital where he had been admitted for surgery.

The results came in November that year. "It showed that they shared the same mother and father — they were brothers," says Novelli. "The lead was the right one, they knew they had the right man." "Novelli's group did a terrific job," says Grasso. "You cannot even imagine my enthusiasm when I had the proof of the complete match between the profiles." The result gave prosecutors and police the strength to carry on looking for Provenzano, adds Paolo Di Simone, head of the Italian Scientific Police's Forensic DNA Unit in Palermo.

Knowing that Provenzano was alive, the investigators focused their attention on busting the ring of people who had provided the logistics of Provenzano's trip and hideout in Marseille. Last April, by tracking a packet of laundry sent by his wife, police captured Provenzano in an isolated farmhouse just a mile from his birthplace in Corleone.

At the hideout, Di Simone collected DNA from false teeth, glasses and an electric razor to confirm Provenzano's identity. She also hoped to find DNA in the house pointing to the benchmark, but the only DNA was his. "Being in the den just after his capture was very emotional," she says.

Code of silence

Novelli told no one what he was working on, except his lab collaborator Ruggiero Mango, who also worked on the case. Grasso advised secrecy to protect the scientists and their families. Novelli admits to having worried for his safety. "I spent one year

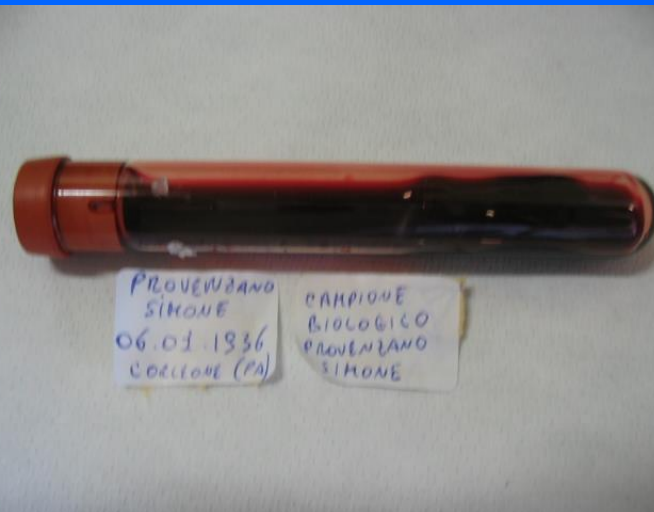
in a dangerous situation," he says, recalling flying once to Palermo to meet Grasso and being whisked away from the steps of the aircraft in a car.

"I didn't even tell my wife," says Novelli. "She learnt it from the TV after Provenzano had been captured." But he now speaks openly about the work and says that he is no longer concerned for his safety. "If I finished, he is in prison. I think it is over — I kept on."

Provenzano was convicted in absentia in 1993 to life imprisonment for his involvement in the bombings that killed Falcone and another prosecutor, Paolo Borsellino, in 1992. He now faces further trials on other charges of murder and blackmail.

His capture also marked the end of an obsession for Grasso, who says he is overjoyed to have fulfilled the promise I made on the grave of Falcone, that for the rest of my life I would pursue a sole objective: capturing all those responsible for his death."

Declan Butler is a senior reporter for Nature based in Paris.



The comparison between a profile obtained from a brother of BP and a profile obtained from a biopsy of BP showed a Probability of 99,87% that two subject are brothers.

Maternal and paternal lineage was confirmed by mtDNA and Chromosome Y analysis.

Yara, il ruolo decisivo della genetica



Il corpo di Yara Come è stato trovato sabato nel campo di Chignolo d'Isola

LA POSIZIONE
Disteso sulla schiena con le braccia all'indietro oltre il capo

LE MANI
Parzialmente coperte dalle maniche del giubbotto

I TAGLI SUL CORPO
Sulla schiena, all'altezza dei reni
Alla gola
Sul petto

LO STATO
In avanzatissimo stato di decomposizione, a tratti quasi mummificato.
In alcuni punti scarnificato

IN TASCA
1 sim card di un cellulare
le chiavi di casa
la batteria di un cellulare
un i-pod

L'APPARECCHIO
L'apparecchio per la correzione dei denti ha permesso di identificarla

giubbotto nero felpe azzurra leggings neri
guanti

BREMBATE DI SOPRA
Bergamo
CHIGNOLO D'ISOLA
Milano

ANSA-CENTIMETRI





PROGERIA - HGPS



10 months



14 yr

Hutchinson, Medicochirurgical Trans 1886;69:473

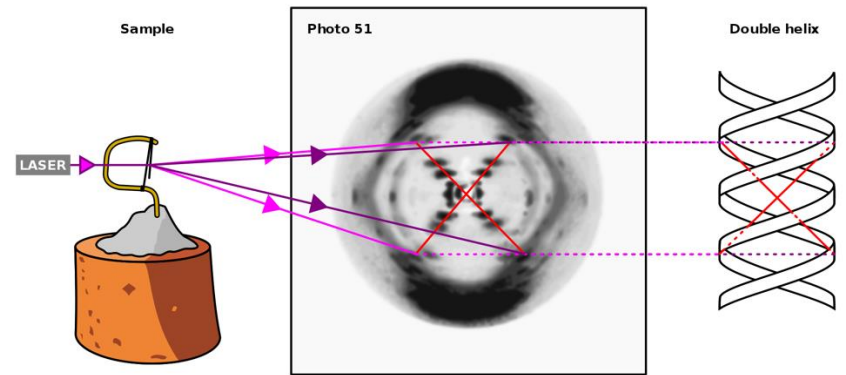
Gilford, Practitioner 1904;73:188

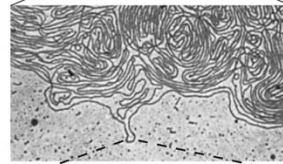
«.....come può il DNA, una molecola così semplice, accumulare un'enorme varietà di informazioni genetiche e fare in modo che queste siano poi utilizzate per la sintesi proteica, alla base di tutte le reazioni che determinano la vita stessa delle cellule degli organismi viventi? C'è solo un modo per stabilirlo, ovvero scoprire la struttura del DNA.»

John Turton Randall



da: Dallapiccola-Novelli 2024, Ed. Falco





Double Helix

5'...GGATTTCTAGGTAAGTCAGTCGA... 3'
 3'...CCTAAAGATCCATTGAGTCAGCT... 5'

Reference Sequence ...GGATTTCTAGGTAAGTCAGTCGA...

Individual 1	...GGATTTCTAGGTAAGTCAGTCGA...
Individual 2	...GGATTTCTAGGTAAGTCAGTCGA...
Individual 3	...GGATTTCTAGGTAAGTCAGTCGA...
Individual 4	...GGATTTCTAGGTAAGTCAGTCGA...
Individual 5	...GGATTTCTAGGTAAGTCAGTCGA...

Conoscere il DNA per capire:



- **Perchè alcuni individui si ammalano mentre altri no?**
- **Perchè solo su alcuni individui i farmaci producono effetti avversi molto gravi e risultano tossici invece che efficaci?**
- **Perchè alcune terapie sono efficaci sono su alcuni e non su tutti?**

“Gli esseri umani sono molto più diversi tra loro di quello che avremmo mai potuto pensare”

- Più di 4.1 milioni di varianti di DNA
- Il 44% dei geni sono eterozigoti per una o più varianti
- Circa 70 diverse mutazioni trasmissibili dai genitori

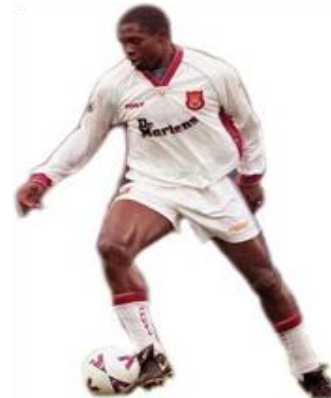


HCM

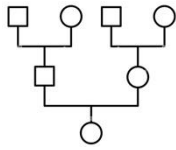
- ☑ Sport giovanile e morte improvvisa è un'eventualità che più volte ci colpisce dalla cronaca.
- ☑ La morte improvvisa di un atleta, soprattutto se di alto livello, viene accettata con molta difficoltà

Marc-Vivien Foe

Cameroon midfielder 28 y.o. Expires in 72nd minute in soccer match vs. Columbia in Lyon, France in 6/2003



Genetic/Familial

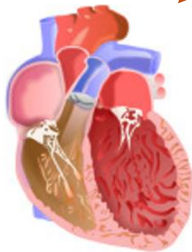


**Non-familial/Non-genetic
Idiopathic or Acquired**

NORMAL HEART



**Hypertrophic
Cardiomyopathy
(HCM)**



**Dilated Cardiomyopathy
(DCM)**



**Arrhythmogenic Cardiomyopathy
(ACM)**



**Restrictive Cardiomyopathy
(RCM)**



**Left-Ventricular
Non-compaction
(LVNC)**

Mai più morti in campo, ora c'è il test del dna

La scomparsa di Morosini ha stimolato la ricerca per evitare altre tragedie. Con la tecnologia sarà possibile scoprire prima chi sono gli atleti più a rischio di malattie cardiovascolari

04 DICEMBRE 2013 - MILANO



Mai più morti in campo. La cosiddetta morte improvvisa, il black out del cuore che ha portato a drammi come quello di Piermario Morosini, può essere prevenuta, prima ancora che curata con l'utilizzo - in caso di estremo bisogno - del defibrillatore. In Portogallo è stata messa a punto una nuova tecnologia, la HeartGenetics, che scova a livello genetico le patologie asintomatiche che portano alla morte improvvisa, causata in oltre il 60% dei casi proprio da difetti del dna. Il dna microchip riconosce, anche in soggetti giovani e apparentemente sani, con una accuratezza del 99% le principali anomalie genetiche, tra cui la cardiomiopatia ipertrofica, la cardiomiopatia dilatativa, la cardiomiopatia aritmogena del ventricolo destro, le sindromi congenite del QT lungo e la sindrome di Brugada. In parole più semplici: Morosini, con questo test, sarebbe stato fermato molto prima della fatale partita di Pescara. E infatti club come Real Madrid e Barcellona, ma anche Milan, Inter e Juventus, si sono dimostrate estremamente interessate al dna microchip, pianificando a partire dal settore giovanile.

IL CONVEGNO — Di questo e di tanto altro si parlerà oggi a Pavia (alla sala del Broletto) al convegno organizzato dall'Associazione prevenzione malattie genetiche, presieduta dal professor Richichi, già direttore del reparto cardiologia San Matteo. Un luminare della cardiologia, il professor Schwartz, terrà una *lectio magistralis* sulla morte improvvisa, che ogni anno causa la morte di 70mila persone in Italia e che ha un'incidenza di una persona su 500. In una tavola rotonda su genetica e sport, sarà presentato il "Progetto Pavia '93", ovvero la mappatura genetica di tutti i nati a Pavia nel 1993. "Un progetto lodevole e avveniristico, un segnale importante destinato a rivoluzionare l'approccio culturale al fenomeno: non attendere che il problema si manifesti ma anticipare i tempi", ha scritto Giovanni Malagò, presidente del Coni, in una lettera agli organizzatori del convegno. Morosini, Bovolenta, Puerta, Curi. Lo sport ha già pagato un prezzo molto alto. Ora i conti si possono chiudere.

Alex Frosio

APPROFONDIMENTI [PIÙ LETTI](#) [PIÙ COMMENTI](#)



Caso Morosini, l'udienza i



Muore a 14 anni durante la



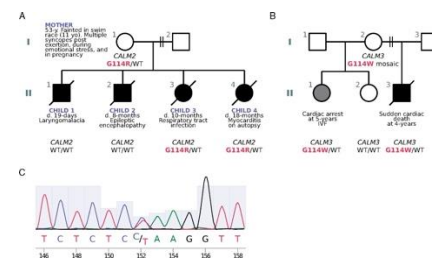
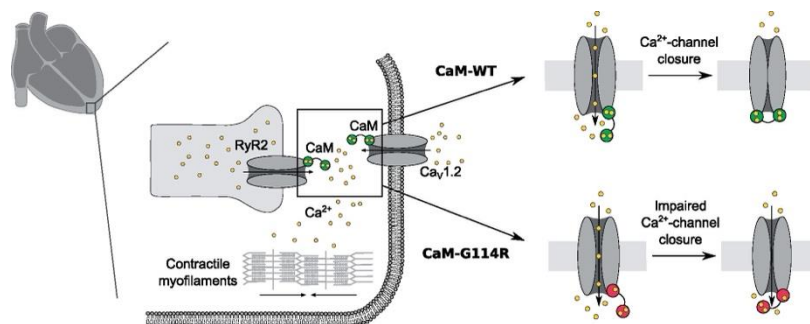
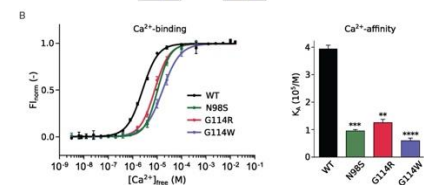
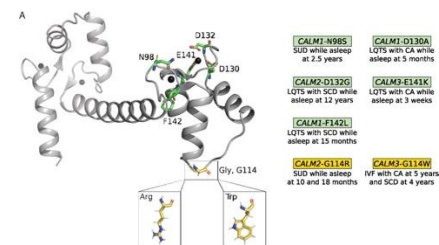
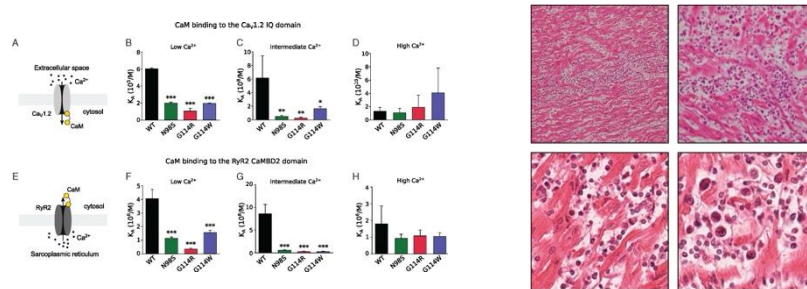
Pettinari: "Il cuore mi ha t

Australia, la mamma in carcere da vent'anni aspetta la grazia



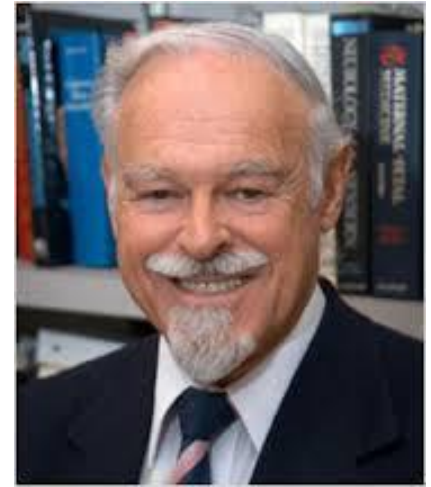
«Uccise i 4 figli»: ora un gene la scagiona

Kathleen Folbigg, 56 anni, in carcere da venti. A fianco i quattro figli (foto EPA) Evangelisti a pag. 9

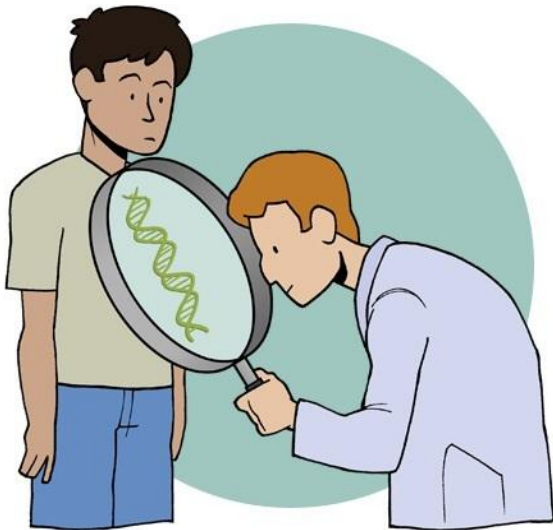


Your Genetic Destiny

Aubrey Milunsky



*"...by knowing
your genes,
you can save your
life"*





Fagot et al, 2001

Il rash può iniziare con macule che poi si sviluppano in papule, vescicole, bolle, piaghe urticarie o eritema confluyente.

**La reazione compare generalmente entro le prime 6 settimane dall'inizio della terapia antiretrovirale .
È possibile un'evoluzione verso la Necrosi Epidermica Tossica (TEN).
La frequenza della reazione è di circa 1/1000 nei pazienti con HIV**



REAZIONI AVVERSE AI FARMACI (ADR)

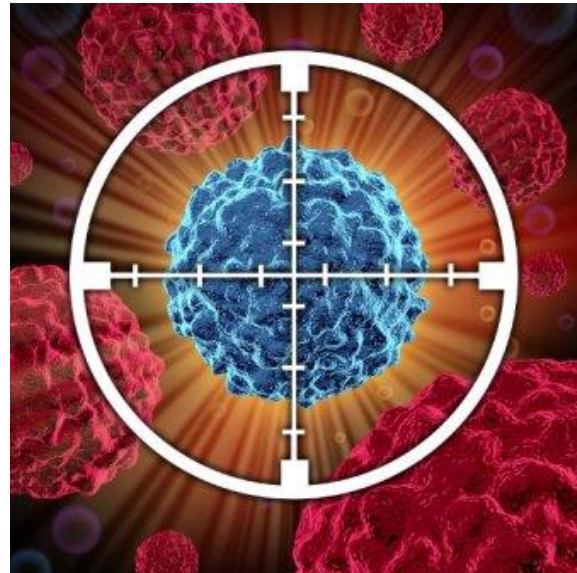
- 2 milioni di ADR all'anno degli Stati Uniti, 100.000 letali
- Costo stimato:
 - 1 miliardo di sterline all'anno nel Regno Unito
 - 4 miliardi di dollari all'anno negli Stati Uniti

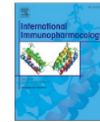
Rischio ritiro dal commercio di molecole attive

CARCINOMA POLMONARE: MUTAZIONI EGFR

Standard terapeutico nel trattamento dei pazienti con mutazione del gene EGFR: Gefitinib, Erlotinib e Afatinib

Molecole in grado di bloccare e contrastare la crescita delle cellule tumorali.





Study of lncRNAs expression profile in the response to biological drugs in Psoriatic Arthritis: MEG3 could be a potential genomic biomarker of therapy efficacy

Giada De Benedittis^a, Arianna D'Antonio^b, Andrea Latini^{a,*}, Chiara Morgante^a, Paola Conigliaro^b, Paola Triggianese^b, Alberto Bergamini^b, Giuseppe Novelli^{a,c,d}, Cinzia Ciccacci^e, Maria Sole Chimenti^{b,1}, Paola Borgiani^{a,1}

MEG3

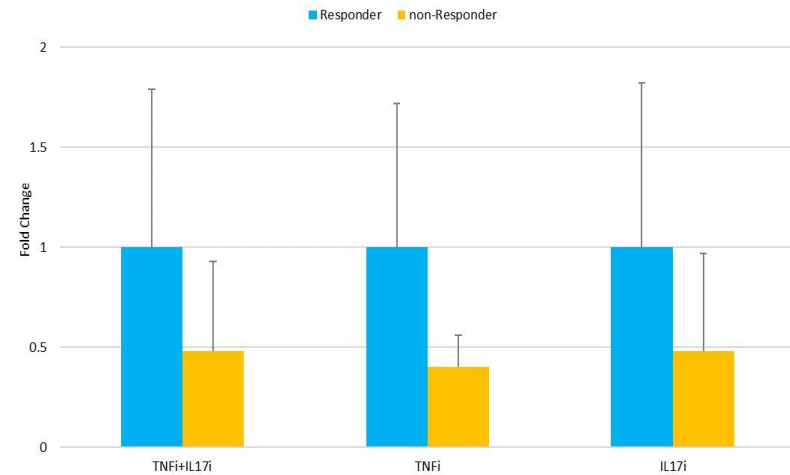


Figure 2. VALIDATION ANALYSES RESULTS.

MEG3 relative expression levels in Responder and non-Responder patients, in the whole cohort and in the single groups of patients treated with TNFi and IL17i

THE PRECISION MEDICINE INITIATIVE



PRECISION MEDICINE INITIATIVE PRINCIPLES STORIES

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"Doctors have always recognized that every patient is unique, and doctors have always tried to tailor their treatments as best they can to individuals. You can match a blood transfusion to a blood type — that was an important discovery. What if matching a cancer cure to our genetic code was just as easy, just as standard? What if figuring out the right dose of medicine was as simple as taking our temperature?"

- President Obama, January 30, 2015

The goal of precision medicine is to target the right treatments to the right patients at the right time.



«They said I'd go blind. Now gene therapy has changed that»

[The Guardian](#), Jan 20, 2019



**nature
medicine**

LETTERS

<https://doi.org/10.1038/s41591-018-0185-5>

**Beneficial effects on vision in patients undergoing
retinal gene therapy for choroideremia**

First evidence in humans

The New York Times

Gene Therapy Allows an 11-Year-Old Boy to Hear for the First Time

The genetic treatment targeted a particular kind of congenital deafness and will soon be tried in children who are younger.

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Some deaf children in China can hear after gene therapy treatment

After deafness treatment, Yiyi can hear her mother and dance to the music. But



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Experimental Gene Therapy Enables Hearing in Five Children Born Deaf

Study co-led by HMS scientist corrects gene mutation involved in inner ear function

By ALVIN POWELL | Harvard Gazette | January 25, 2024 | Research

Sickle Cell Anemia, a Molecular Disease¹

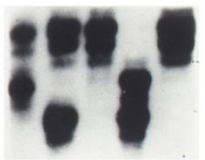
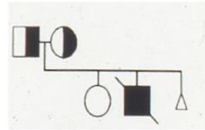
Linus Pauling, Harvey A. Itano,² S. J. Singer,² and Ibert C. Wells³

*Gates and Crellin Laboratories of Chemistry,
California Institute of Technology, Pasadena, California⁴*

THE ERYTHROCYTES of certain individuals possess the capacity to undergo reversible changes in shape in response to changes in the partial pressure of oxygen. When the oxygen that form from normal erythrocytes. In this condition they are termed promesococytes. The hemoglobin appears to be uniformly distributed and randomly oriented within normal cells and promesoc-



Victoria Gray, who underwent a landmark treatment for sickle cell disease last year, has been at home in Forest, Miss., with her three kids, Jadasia Wash (left), Jamarius Wash (second from left) and Jaden Wash



Regular Article

Survival Motor-Neuron Gene Transcript Analysis in Muscles from Spinal Muscular-Atrophy Patients

Gennarelli M., Lucarelli M., Capon F., Pizzuti A., Merlini L., Angelini C., Novelli G., Dallapiccola B.

[Show more](#) ✓



Spinal Muscular Atrophy



2020

CRISPR/Cas9 applications

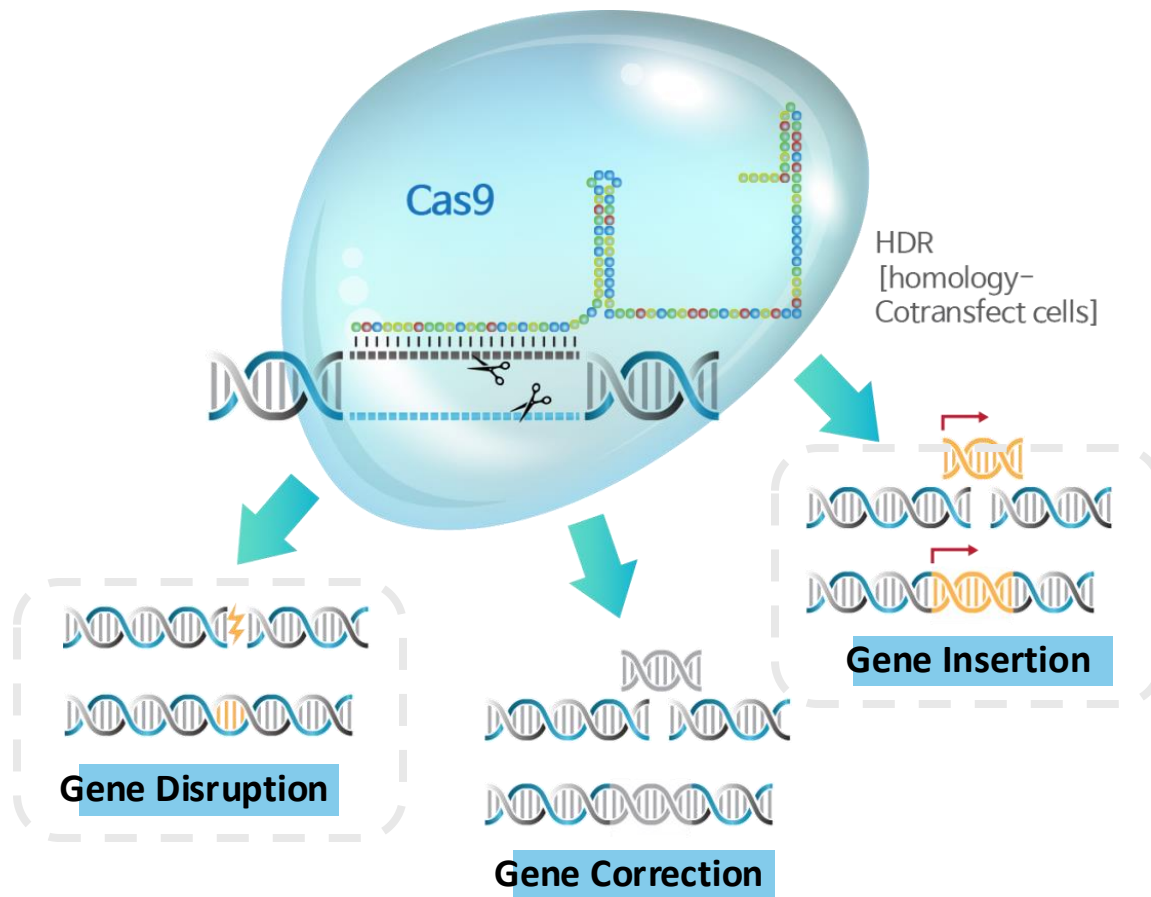
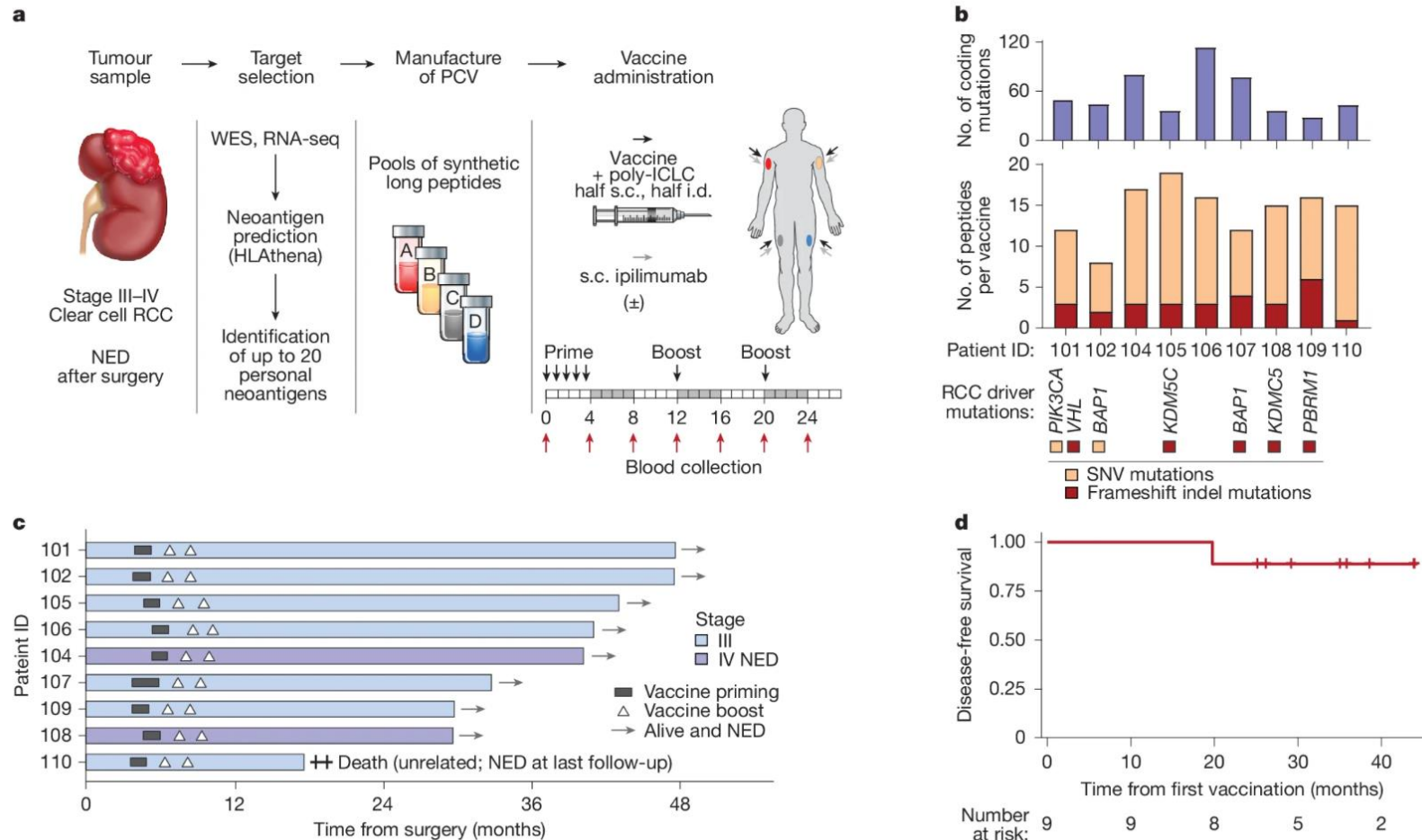


Fig. 1: Vaccine manufacturing process and clinical outcomes.

From: [A neoantigen vaccine generates antitumour immunity in renal cell carcinoma](#)



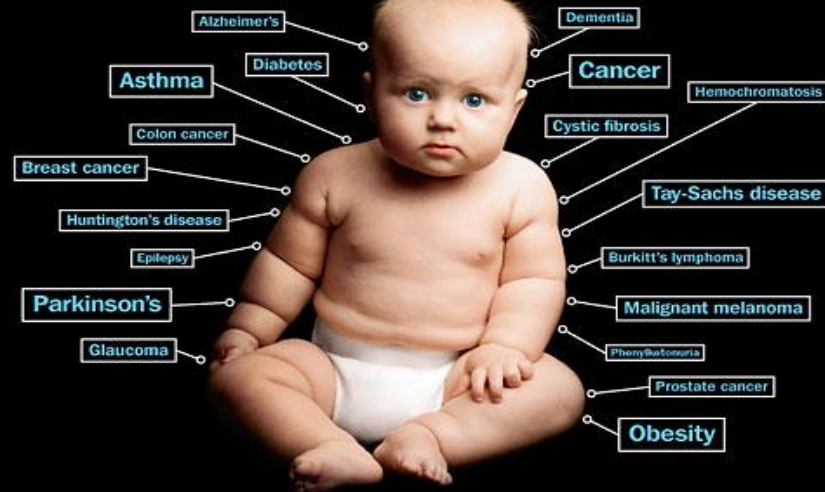
DECEMBER 24, 2012

Egypt Divided / Pot's Big Moment / Best of 2012

Movies, Music,
Books & More

TIME

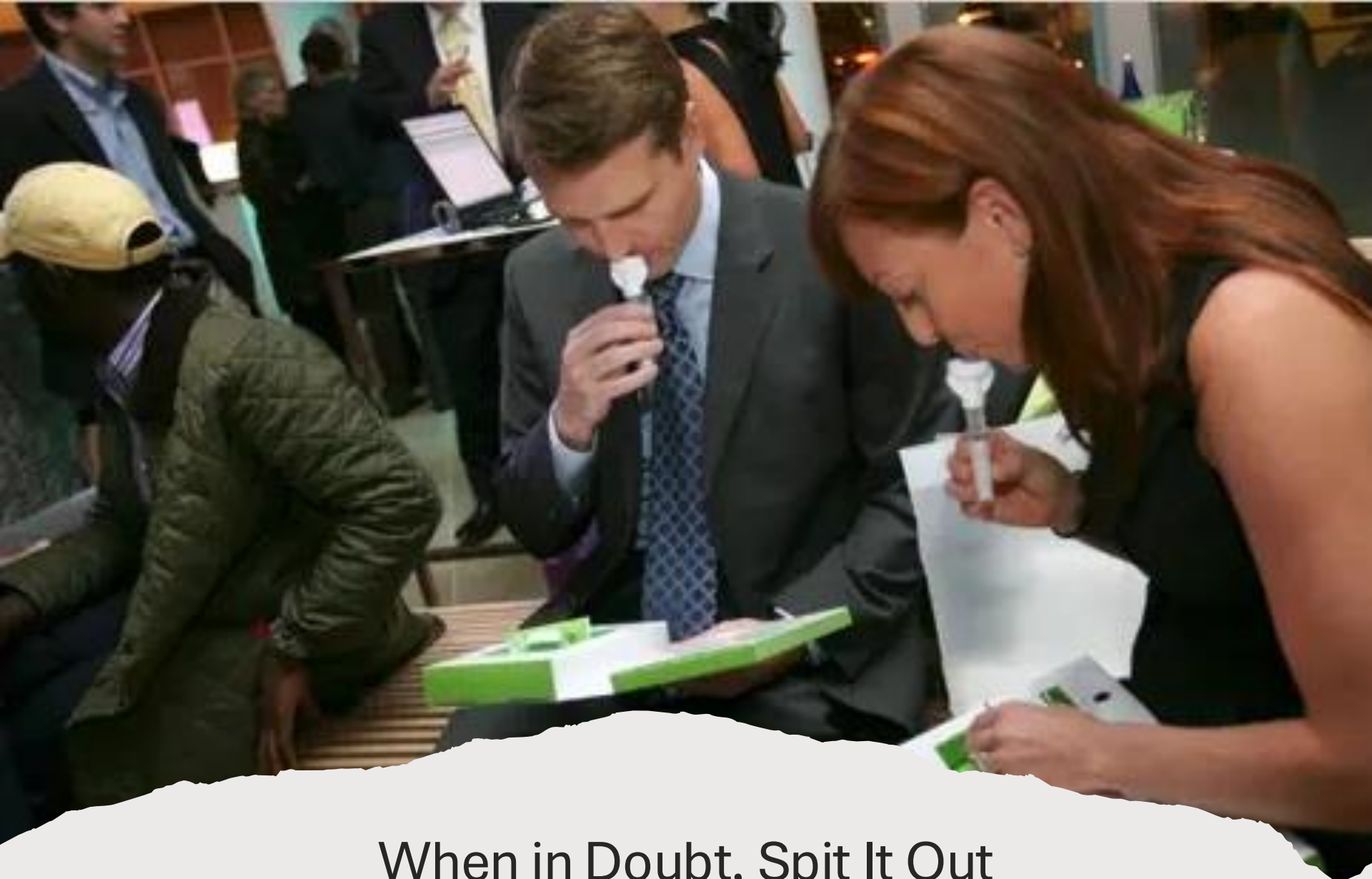
Want to Know My Future?



New genetic tests can point to risks—
but not always a cure

BY BONNIE ROCHMAN

www.time.com



When in Doubt, Spit It Out

The New York Times, Sept. 12, 2008



23andMe analyses DNA in saliva provided by customers to produce genealogy information and health-risk predictions. Credit: Tiffany Hagler-Geard/Bloomberg via Getty

MAY 21, 2013

TIME

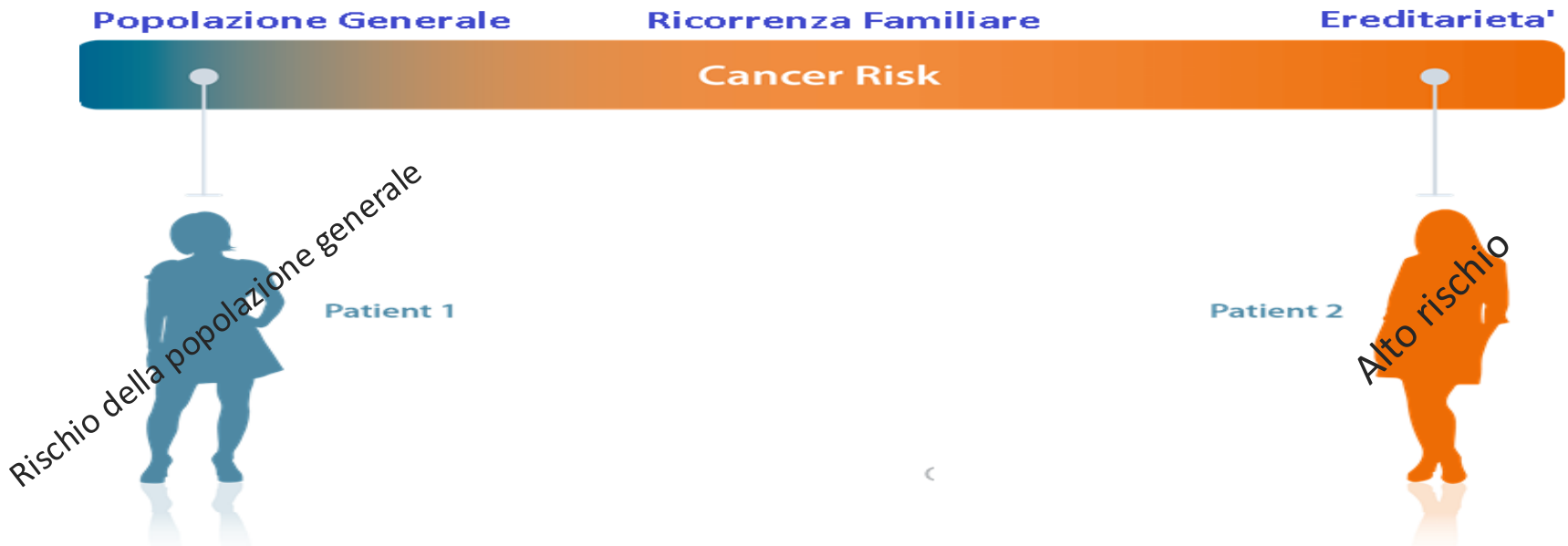
THE ANGELINA EFFECT

Angelina Jolie's double mastectomy puts genetic testing in the spotlight. What her choice reveals about calculating risk, cost and peace of mind

BY JEFFREY KLUGER & ALICE PARK

time.com

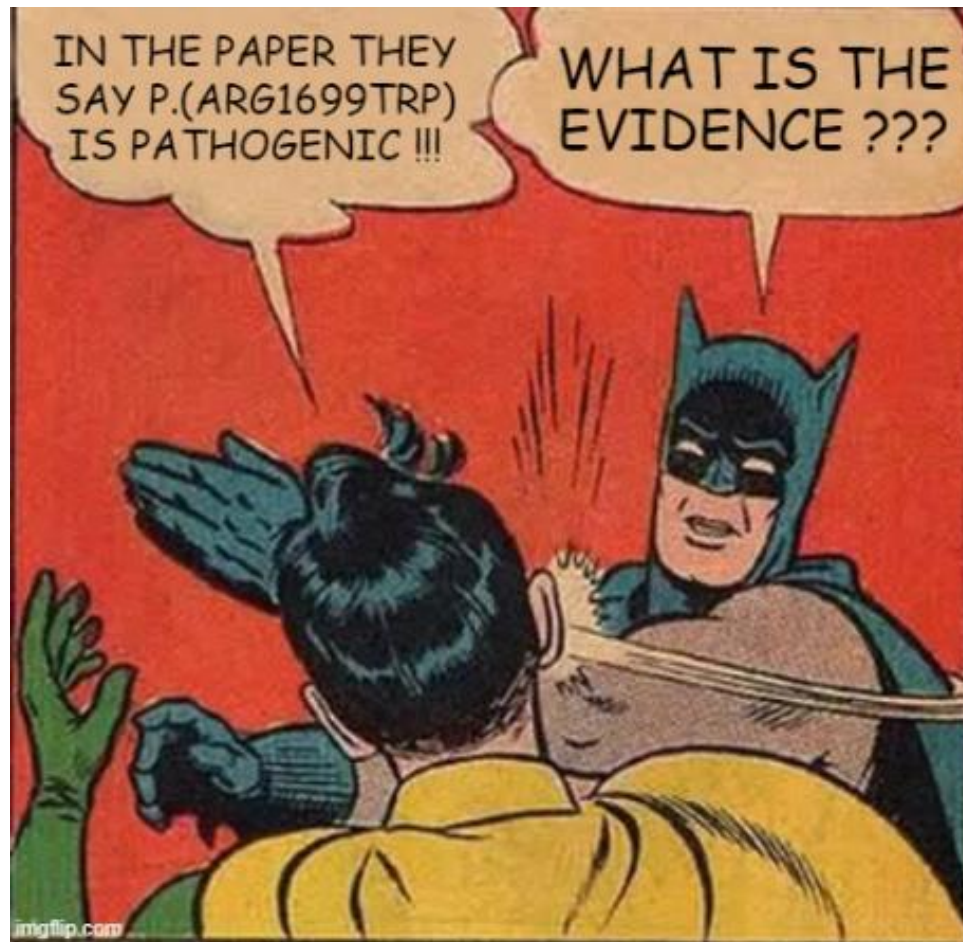
Tumore della mammella – Il rischio





"BUT IF YOU WANT THE REAL LOWDOWN, WE'LL
NEED SOME OF YOUR DNA."

The “First Rule” in Variant Interpretation?





Camilleri:

«Quando uno nasce, gli viene dato un ticket con malattie e gioie»

