LEE KUAN YEW
Distinguished Visitors
PROGRAMME

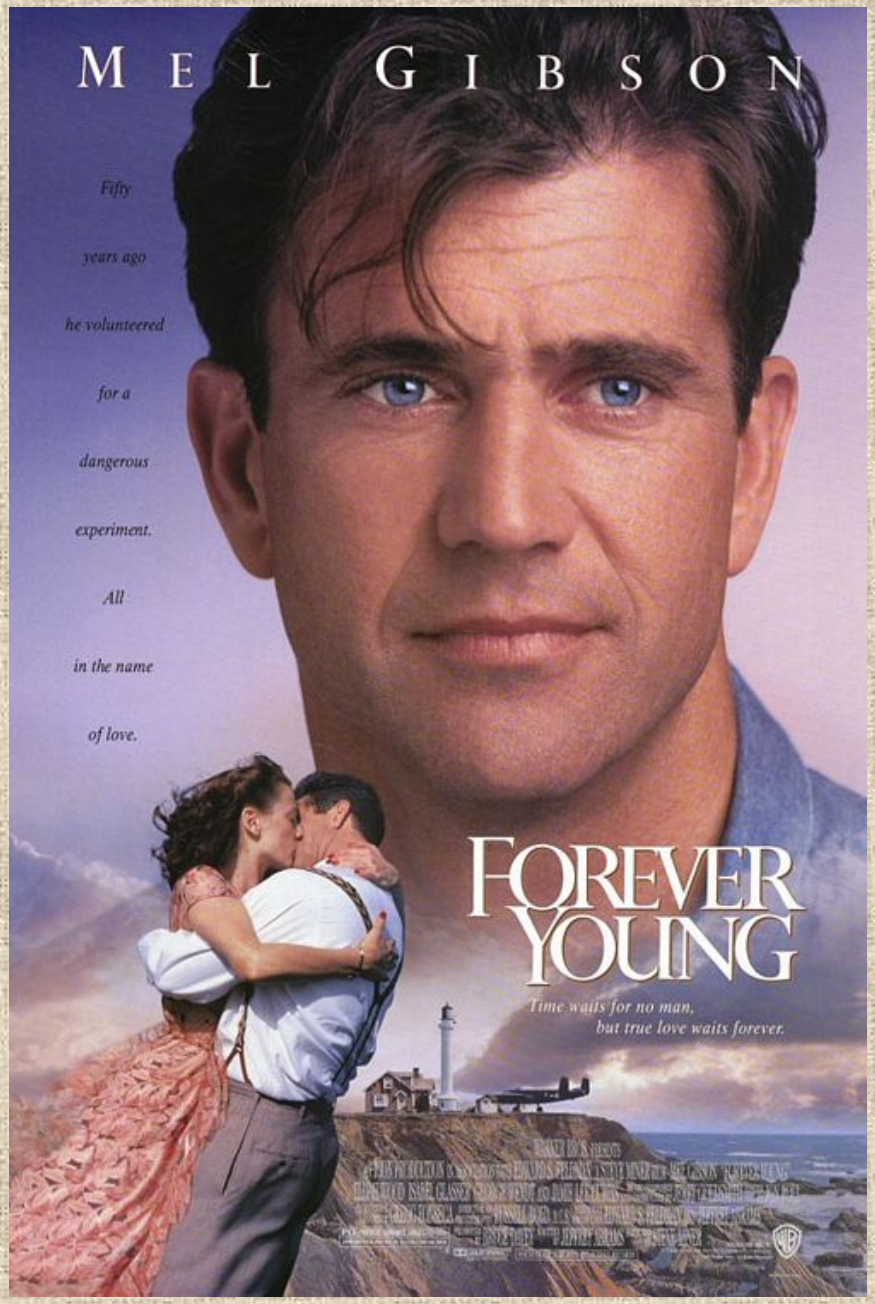
PUBLIC LECTURE SERIES

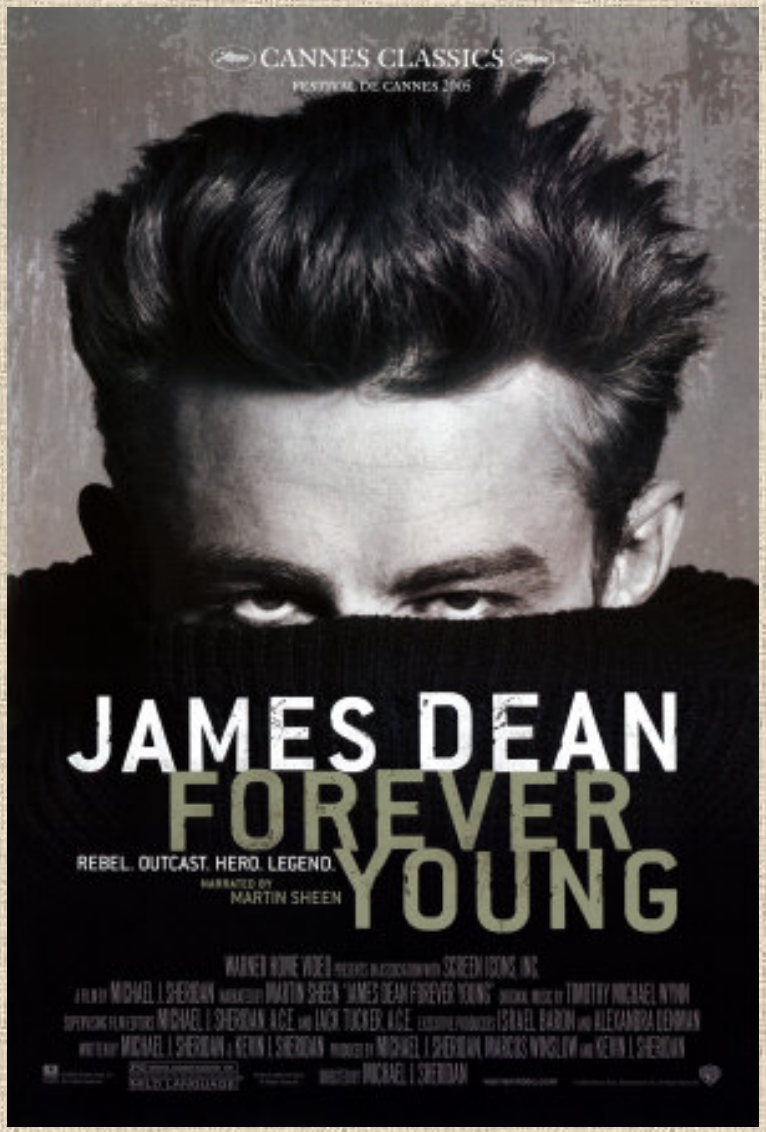
Prof Aaron Ciechanover

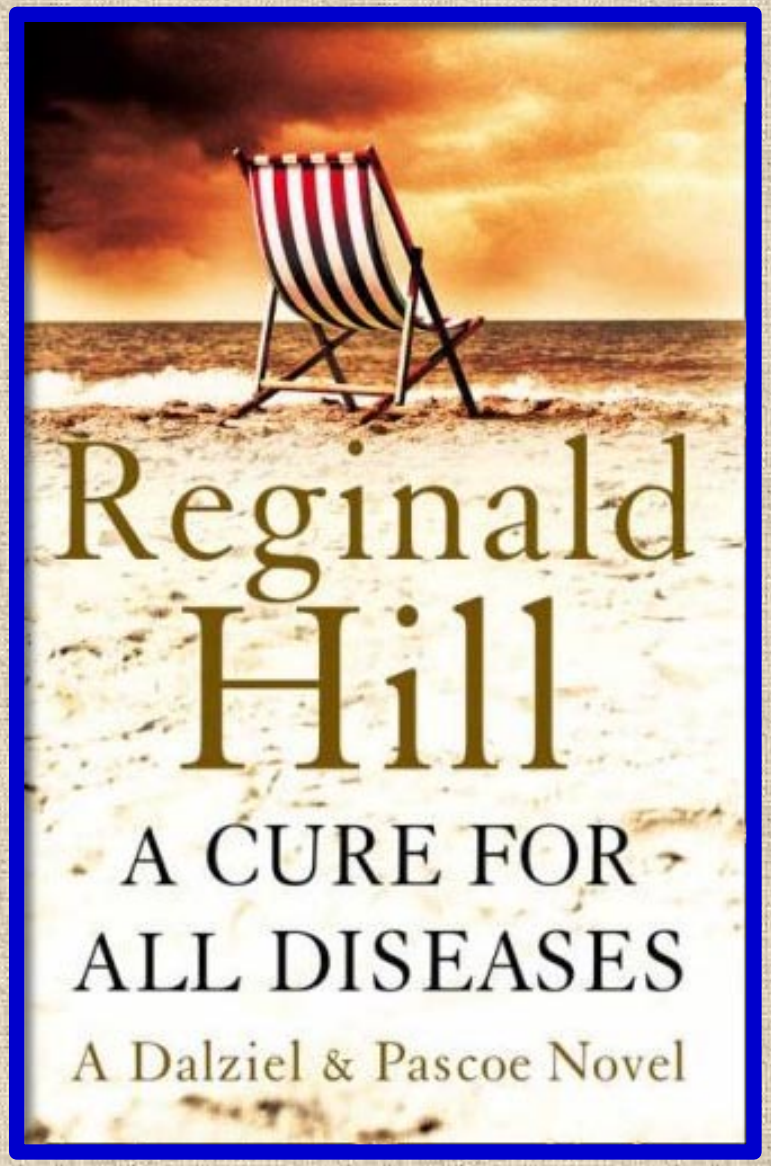
2004 Nobel Laureate in Chemistry
Distinguished Research Professor, Faculty of Medicine
The Technion-Israel Institute of Technology

DRUG DEVELOPMENT IN THE 21ST CENTURY: ARE WE GOING TO CURE ALL DISEASES

NANYANG TECHNOLOGICAL UNIVERSITY

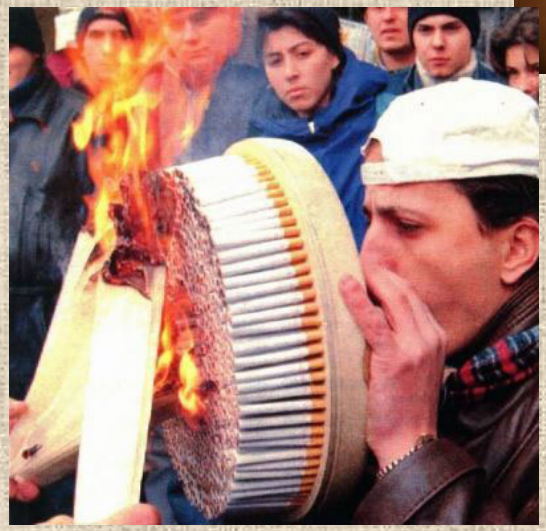

MEL GIBSON
Fifty years ago he volunteered for a dangerous experiment. All in the name of love.
FOREVER YOUNG
Time waits for no man, but true love waits forever.


CANNES CLASSICS
FESTIVAL DE CANNES 2005
JAMES DEAN
FOREVER YOUNG
REBEL. OUTCAST. HERO. LEGEND.
NARRATED BY MARTIN SHEEN


Reginald
Hill
A CURE FOR
ALL DISEASES
A Dalziel & Pascoe Novel

Genetics

Environment



Diseases

Behaviour

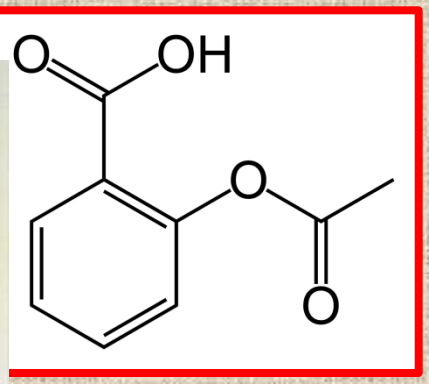
Drug Discovery and BioMedical research in the 21st century?

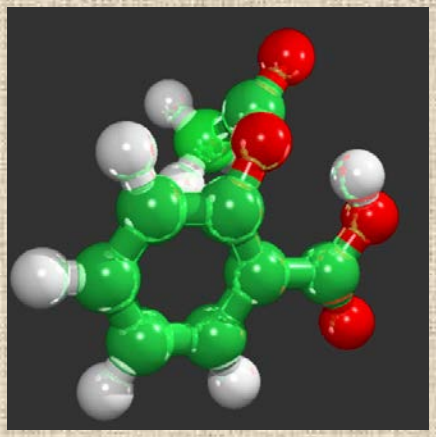
The third revolution

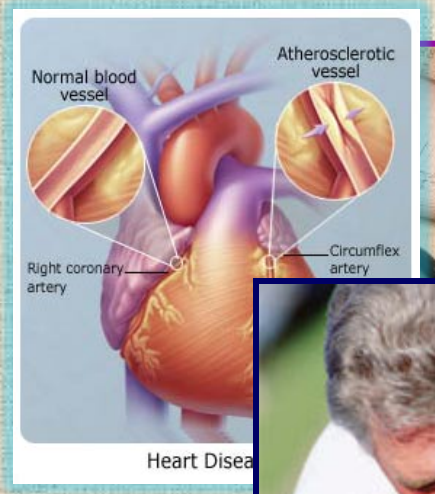
The first revolution:
The era of incidental discoveries
1930s-1960s

Clinical observation
at times dates back to old times
followed by isolation of the active ingredient
and only last –
understanding the mechanism of action

Felix Hoffman



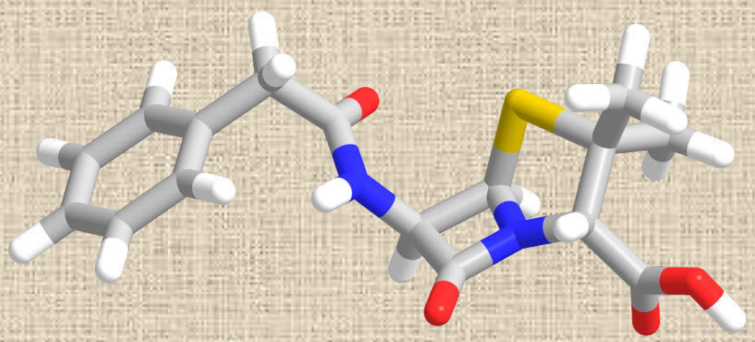


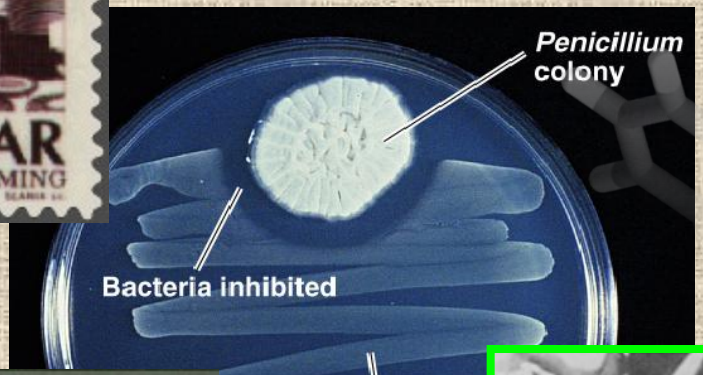


Aspirin

Penicillin

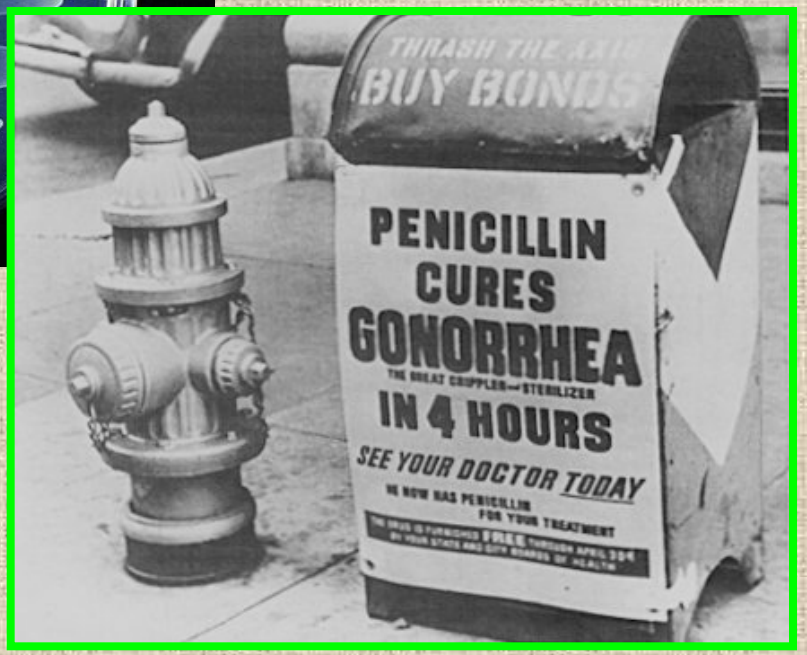

EUROPA
400
FØROYAR
SIR ALEXANDER FLEMING




Penicillium colony
Bacteria inhibited


Bacteria

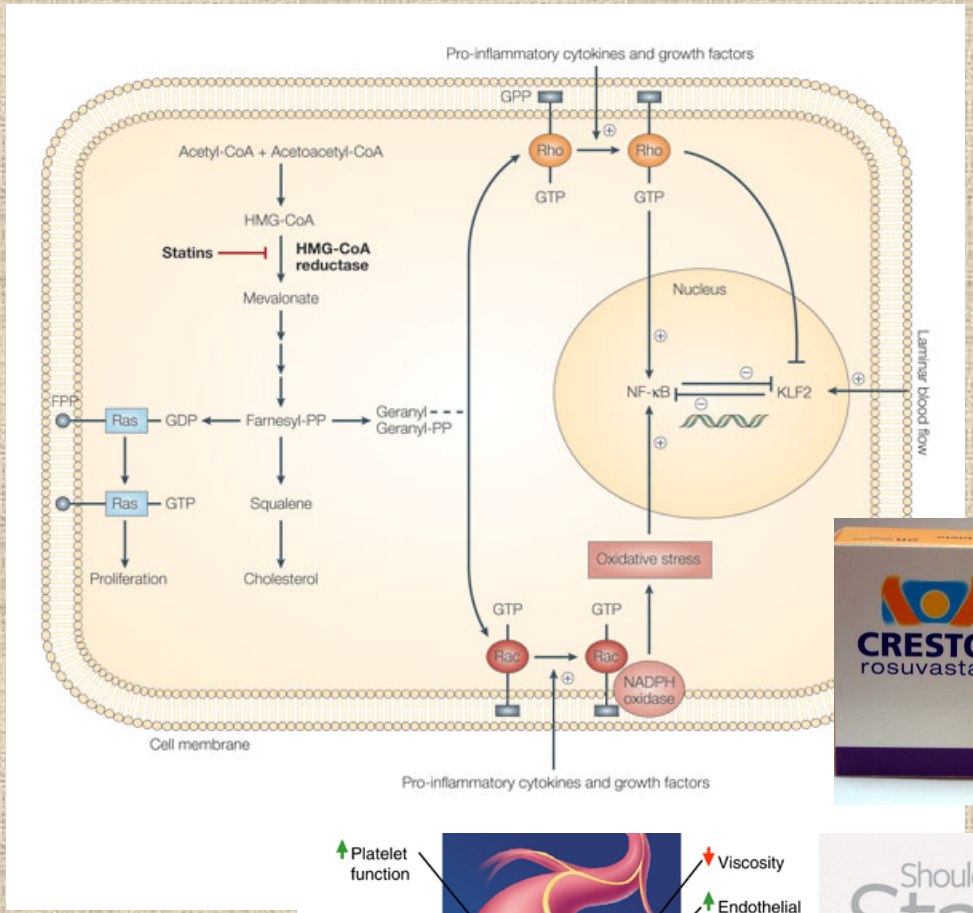

H
N
H
S
O
N
O
COOH

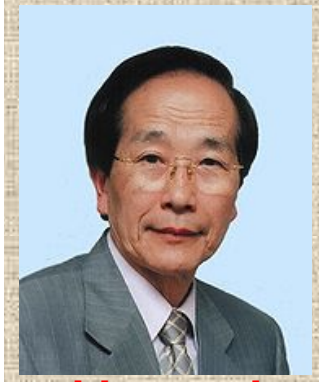

BUY BONDS
PENICILLIN
CURES
GONORRHEA
IN 4 HOURS
SEE YOUR DOCTOR TODAY

The second revolution
1970s-2000s

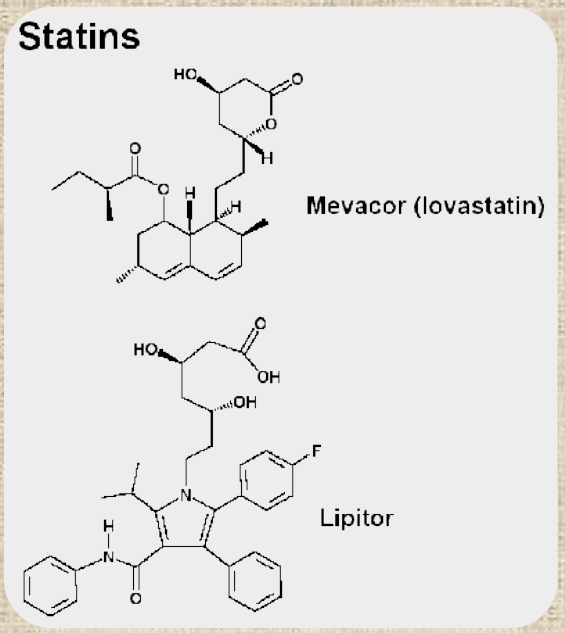
High throughput – brute force screening of large libraries of chemical compounds

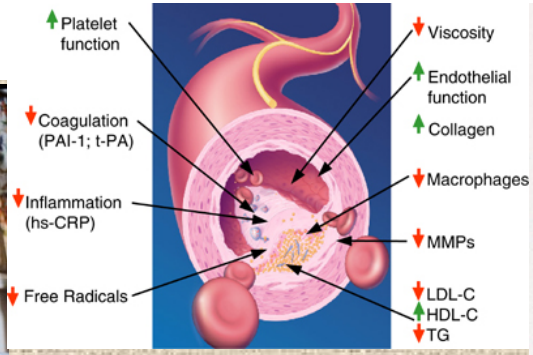
Statins

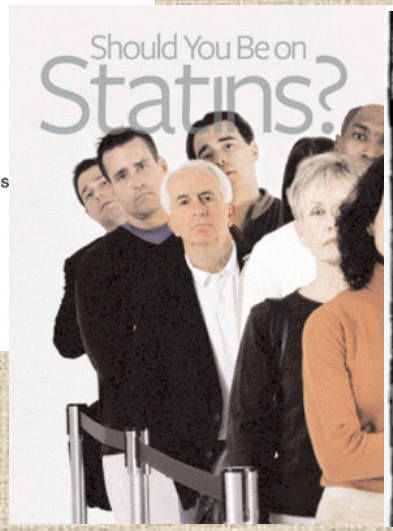




Akira Endo



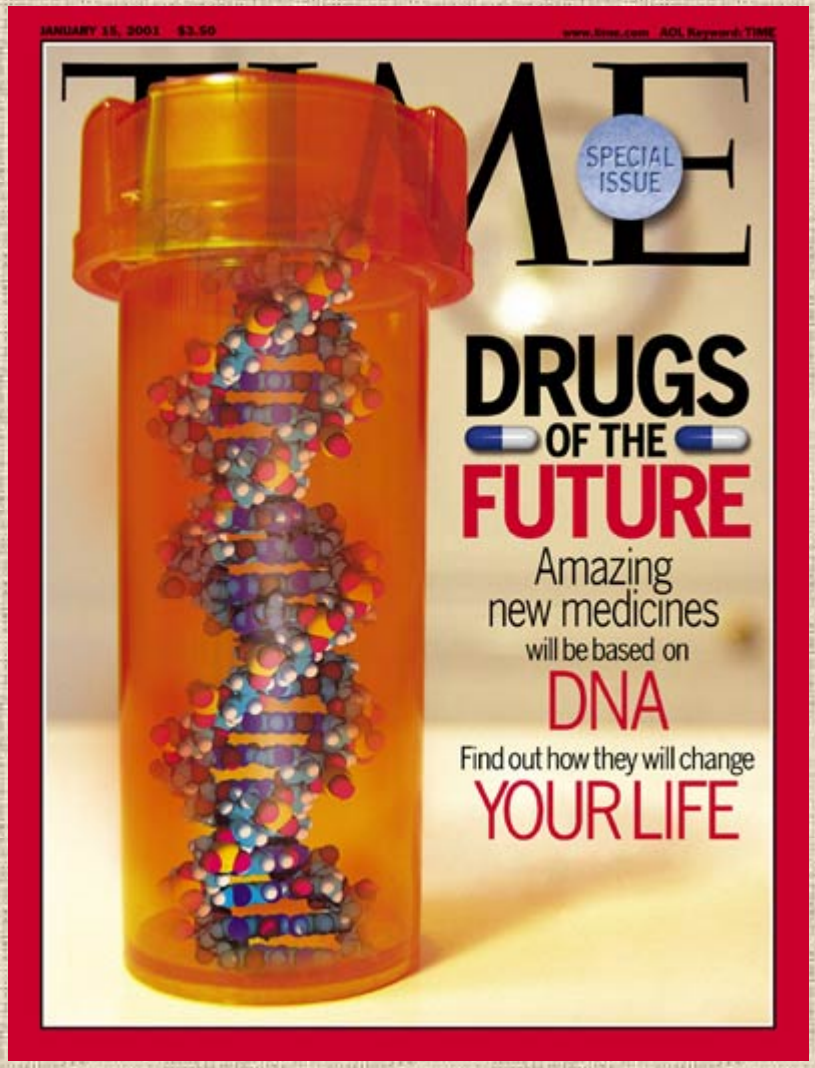




The third revolution:
2000s-

The era of planning -
understanding the mechanisms first, followed by targeted drug design

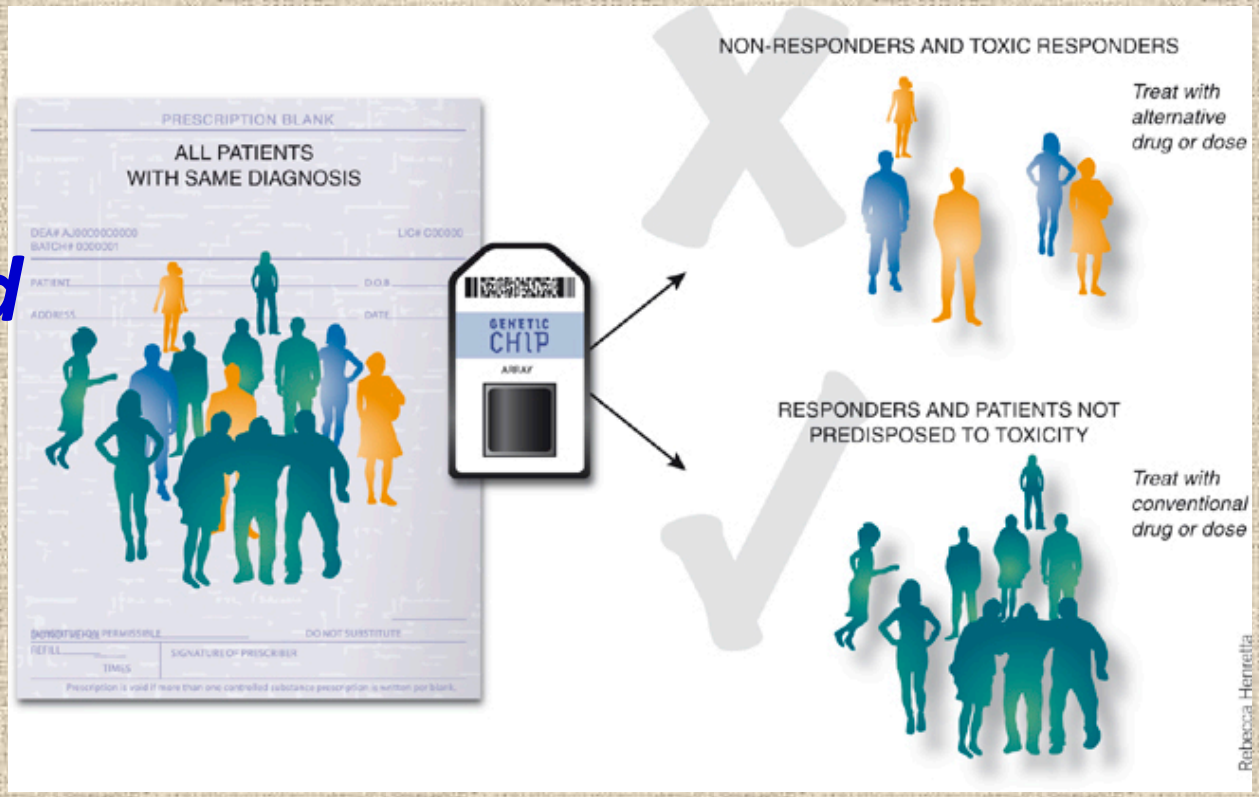

FEBRUARY 17, 2003
COUNTDOWN TO WAR
TIME
SPECIAL REPORT
SOLVING THE MYSTERIES OF
DNA
The 50th Anniversary:
Reliving Watson and Crick's historic discovery
How gene science has changed our lives
Visions of the future
www.time.com AOL Keyword: TIME


JANUARY 15, 2001 $3.50
www.time.com AOL Keyword: TIME
SPECIAL ISSUE
DRUGS
OF THE
FUTURE
Amazing new medicines will be based on
DNA
Find out how they will change
YOUR LIFE

Current medicine –

One size fits all

Future medicine- Targeted and Personally "fitted" and medicine –

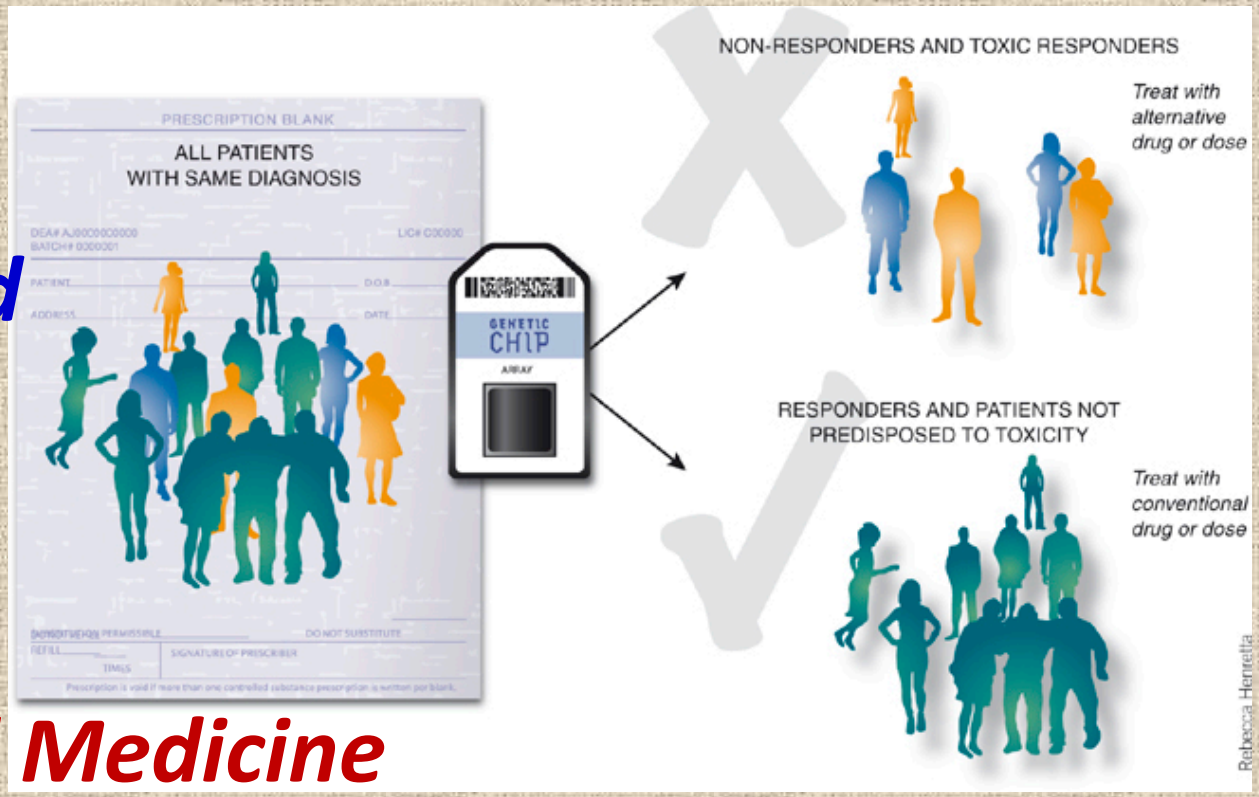


Personalized Medicine

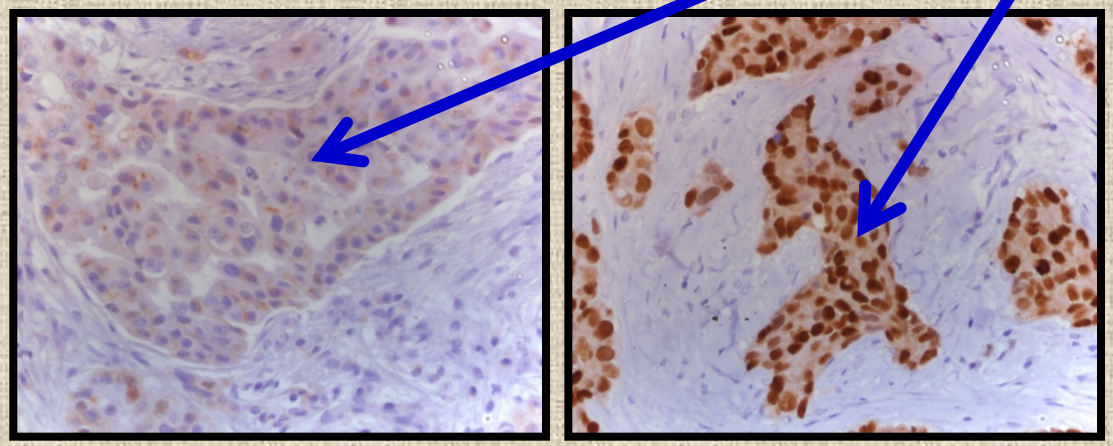
The key element in personalized medicine is to be able to identify new "personal" drug targets - predict the responders and the non-responders, treat the responders and develop new drugs aiming at new targets to the non-responders

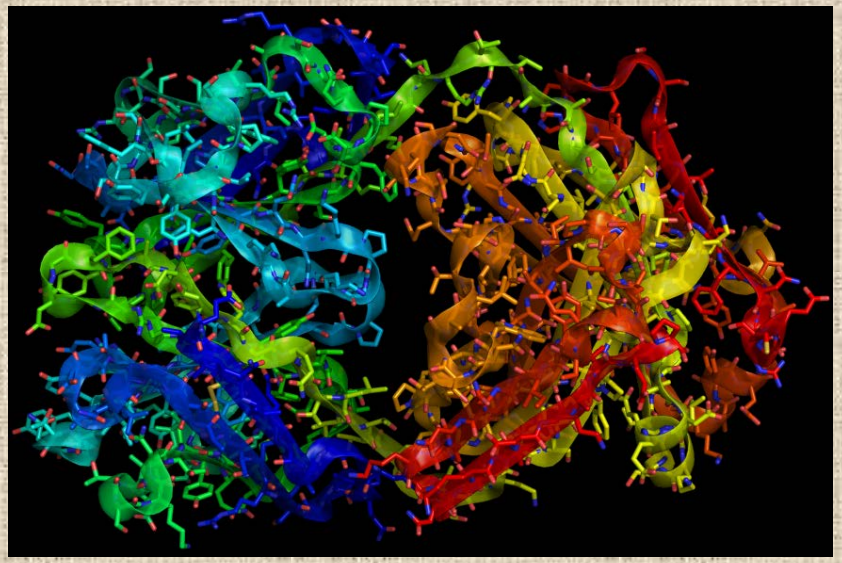

FEBRUARY 18, 2002
www.time.com AOL Keyword: TIME
TIME
THE NEW THINKING ON
BREAST CANCER
The Smartest Drugs
The Gentlest Treatments
The Latest on Mammograms

Future medicine- Targeted and Personally "fitted" and medicine - Personalized Medicine

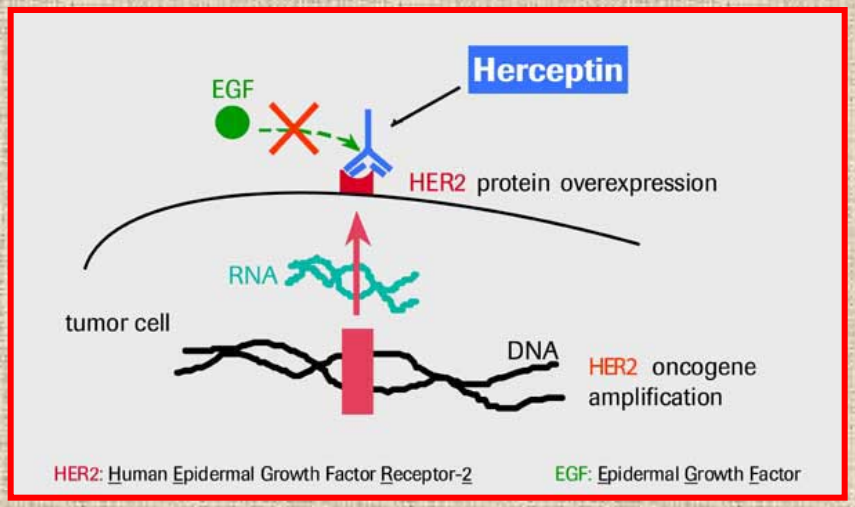


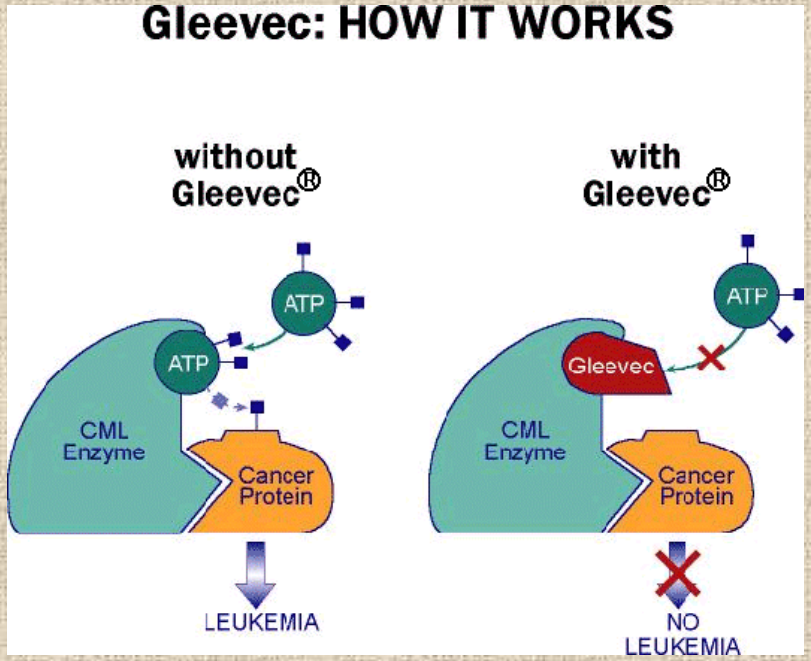
Breast Cancer – Estrogen Receptor Negative and Positive (predicts sensitivity to Tamoxifen)

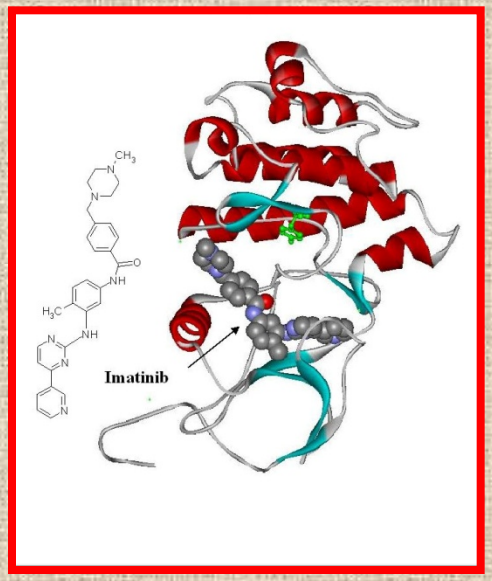


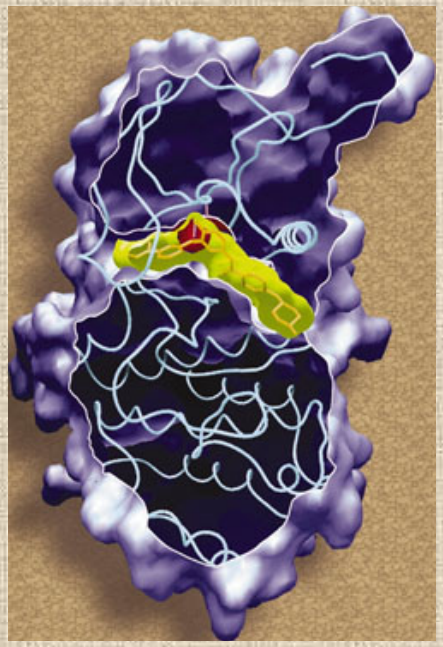


Herceptin *(targeted)*









Gleevec

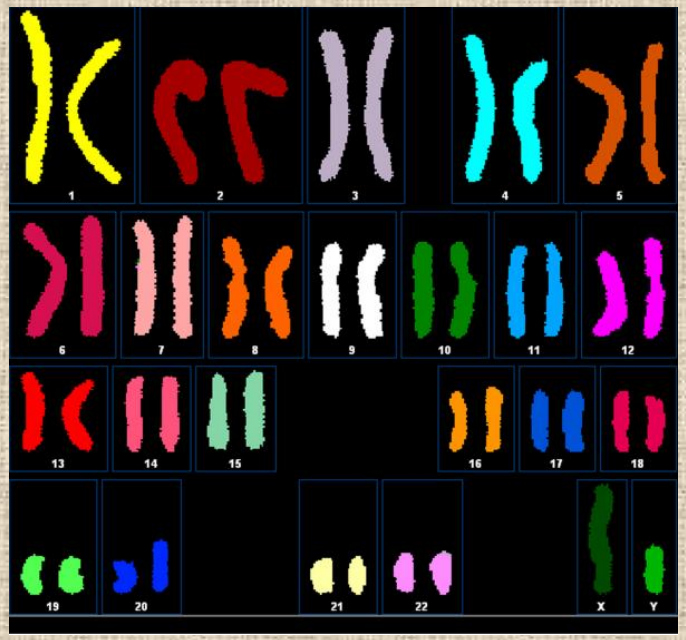
(Imatinib)

Treating CML

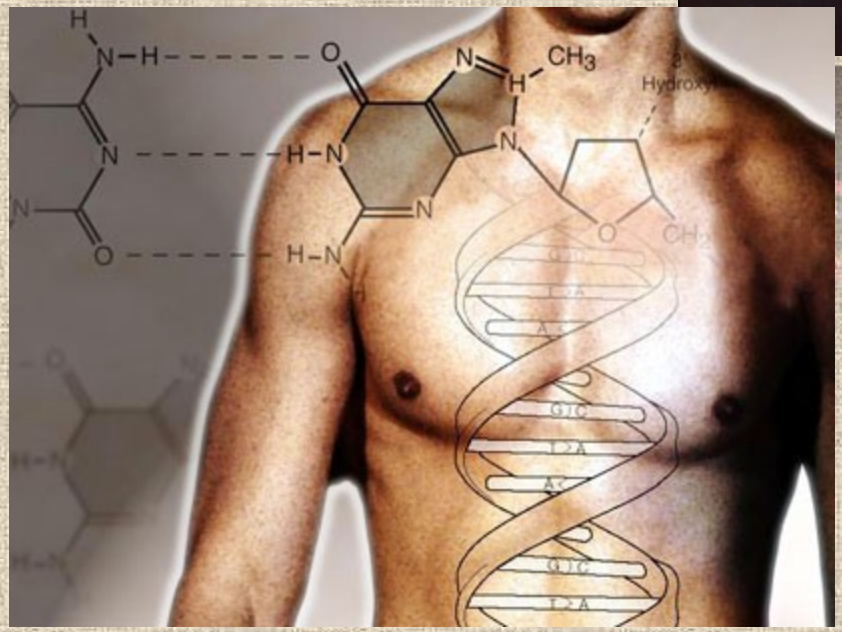
(by inhibiting BCR-ABL)

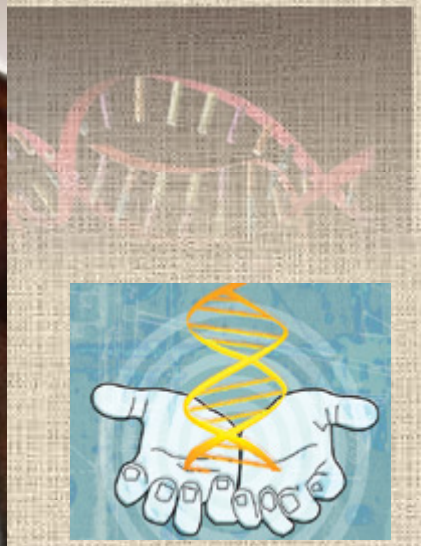
(targeted)

The Human Genome

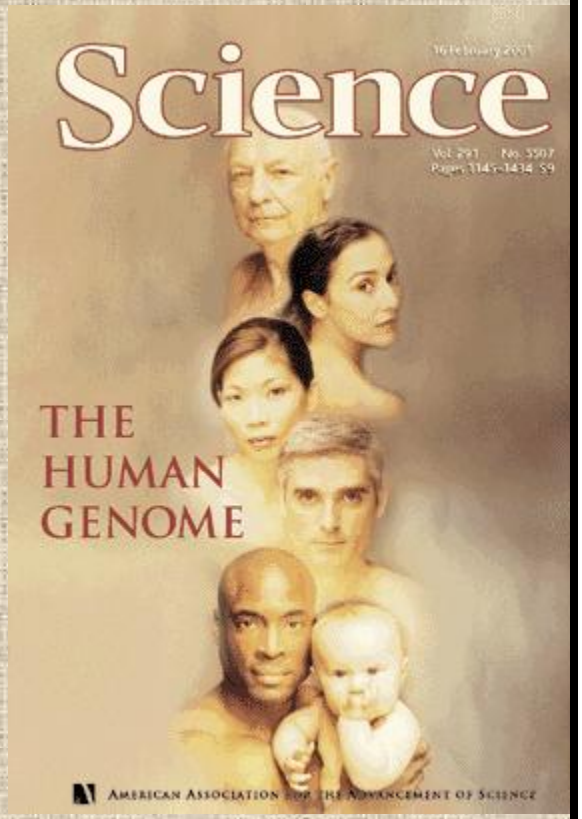


Size of the entire Human Genome = 3 Billion Bases





Sequencing of the individual human genome will be converted into an yet another tool in the Diagnostic, therapeutic, and prognostic toolkit



Number of Sequenced Human Genomes Doubles

Less than a decade ago, it took hundreds of millions of dollars and a large international community to sequence a single human genome. This week, three reports in the 6 November issue of *Nature* describe three more human genomes—the first African, the first Asian, and the first cancer patient to have their entire DNA deciphered. The sequences provide clues about genome variation and disease; they also demonstrate the potential of a relatively new sequencing technique to mass-produce human genomes. "The methods are extremely powerful," says geneticist James Lupski of Baylor College of Medicine in Houston, Texas. "Reading these papers, I think the personal genomes field is moving even faster than I anticipated."

Until now, four human genomes have been published: the reference human genome, derived from sequencing DNA from several anonymous individuals; one by Celera Genomics; and those of genome stars J. Craig Venter and James Watson. Efforts to date to identify differences among individuals have relied not on entire genome sequences but on surveys of single-base changes called SNPs and of structural variations in duplicated pieces of DNA (*Science*, 21 December 2007, p. 1842).

Even the broadest SNP surveys look at just a few million SNPs out of the 3 billion bases in the genome, leaving researchers in the dark about how much individual variation there is and how specific differences correlate with disease risks. Hence the push to drive down the cost of sequencing to $1000 per genome (*Science*, 17 March 2006, p. 1544). The newly published genomes came in with price tags of $250,000 to $500,000 each but would cost half that or less if done today. The three groups all used a technology developed by Solexa, now part of Illumina Inc. in San Diego, California, to speed and slash the cost of sequencing. It generates smaller pieces of sequence faster and cheaper than previous technologies. Such small pieces used to be difficult to stitch together, but this approach can work well now because the reference genome helps guide their assembly.

New genome on the block. The first genome sequence from a Chinese was on display last year at a technology fair in Shenzhen, China.

To explore the genetic underpinnings of cancer, Richard Wilson and colleagues at the Washington University School of Medicine in St. Louis, Missouri, sequenced genomes from both normal skin tissue and tumor tissue of a middle-aged woman who died of acute myelogenous leukemia (AML). They compared the DNA to determine what was different about the cancer cells. About 97% of the 2.65 million SNPs found in the tumor cells also existed in the normal skin cell, suggesting they were not critical to the cancer process. The researchers also eliminated SNPs that had been previously identified elsewhere as well as those that did not change the coding of a gene, ending up with 10 SNPs unique to the tumor cells. "I don't think we missed anything," says Wilson.

Two occurred in genes previously linked to this leukemia. Eight led the researchers to new candidate AML genes, including several tumor suppressor genes and genes possibly linked to cell immortality. By sequencing the whole cancer genome, "we capture what we don't know as well as what we do know [about cancer genes]," says Illumina's David Bentley. "That can really transform our ability to understand cancer."

Bentley and colleagues sequenced the genome of a Yoruba man from Nigeria whose DNA has already been extensively studied, enabling them to check the accuracy of their technology. In the third *Nature* paper, Jiang Wang of the Beijing Genomics Institute in Shenzhen, China, and colleagues sequenced the genome of a Han Chinese male. The Yoruba analysis uncovered almost 4 million SNPs, including 1 million novel ones. The Chinese genome had about 3 million, including 417,000 novel SNPs. As anticipated, the African genome had greater variation per kilobase than either the Chinese or sequenced Caucasian genomes, indicative of its ancestral status.

These new genomes were already significantly cheaper than their predecessors were; next year, Illumina expects the cost to drop to about $10,000. Other companies are promising even lower prices per genome. Nonetheless, geneticist Aravinda Chakravarti of Johns Hopkins University School of Medicine in Baltimore, Maryland, is cautious about how quickly genome sequencing should enter the clinic: "We still don't know how to interpret [the data]," he notes. Bentley agrees. Because of the uncertain applicability and utility of sequence data, "and possibly ethical barriers," he notes, saying the technology is poised to enter the clinic anytime soon is "pushing it."

–ELIZABETH PENNISI

CREDIT: XINHUA/LANDOV

nature news

nature news home | news archive | specials | opinion | features

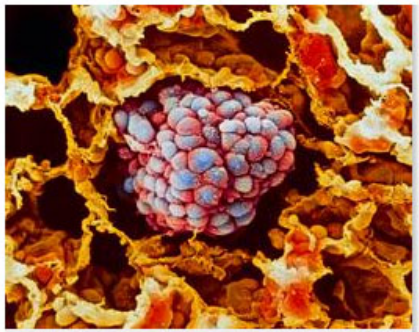
comments on this story

Published online 16 December 2009 | Nature | doi:10.1038/news.2009.1143

Cancer genomes reveal risks of sun and smoke

Sequencing of skin and lung cancers show that many mutations could be prevented.

Brendan Borrell



Sun and smoke leave their fingerprints on cancer genomes.

MOREDUN ANIMAL HEALTH LTD / SCIENCE PHOTO LIBRARY

Researchers have completed the genetic sequences of two types of cancer — skin cancer and small-cell lung cancer — revealing that the genomes bear the hallmarks of their respective carcinogens: sun and smoke. Worldwide, the two diseases kill a total of nearly 250,000 people each year, despite the fact that they are largely preventable.

Tumours develop when a normal cell's DNA is damaged, allowing that cell to proliferate unchecked. By sequencing and cataloguing all the mutations in a single tumour type from multiple individuals, scientists aim to identify the genes that are most susceptible to damage, to understand the processes underlying DNA repair, and to develop drugs that counteract certain types of damage.

Scientists from the Cancer Genome Project at the Wellcome Trust Sanger Institute in Hinxton, near Cambridge, UK, and their collaborators at partner institutions describe the genetic sequences of cell lines derived from patients with small-cell lung cancer[1] or malignant melanoma[2]. The studies are published online today in *Nature*.

> **"Every pack of cigarettes is like a game of Russian roulette."**
>
> *Peter Campbell Wellcome Trust Sanger Institute, Hinxton*

These papers mark the completion of the fourth and fifth cancer-cell genomes to be sequenced, and come just one year after a team from Washington University School of Medicine in St Louis published the first cancer genome, from a patient with leukaemia[3]. The breast-cancer genome was published by a Canadian-led consortium in

The journey into the complexity of life is one of the greatest challenges of our century and will succeed only if we shall collaborate internationally and manage to cross disciplines - all on a large scale