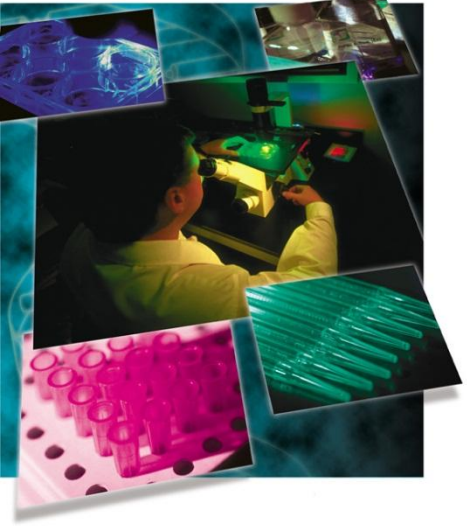
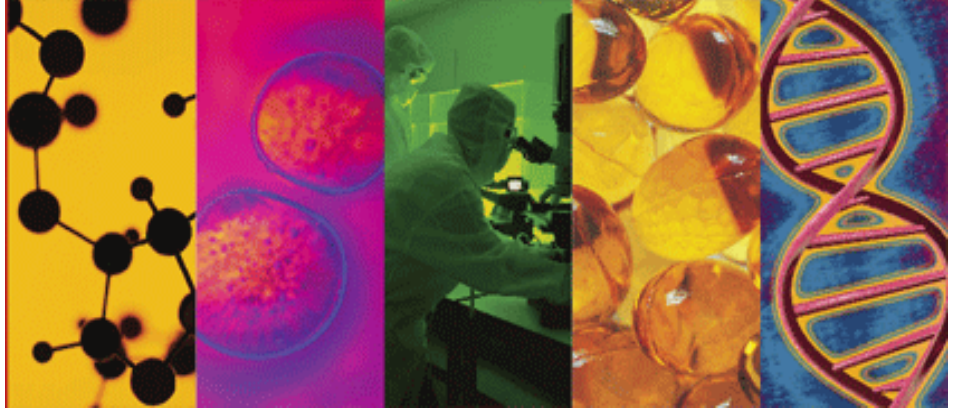


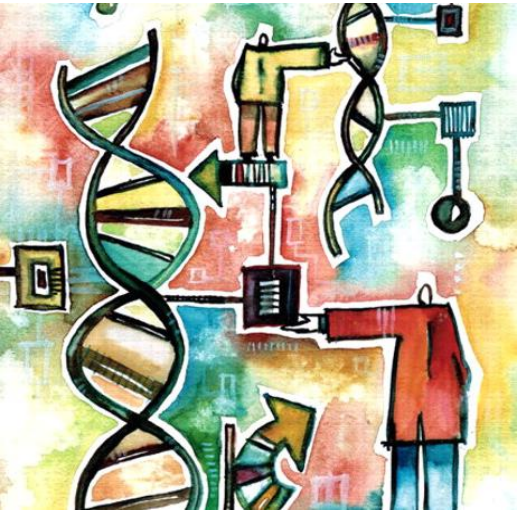


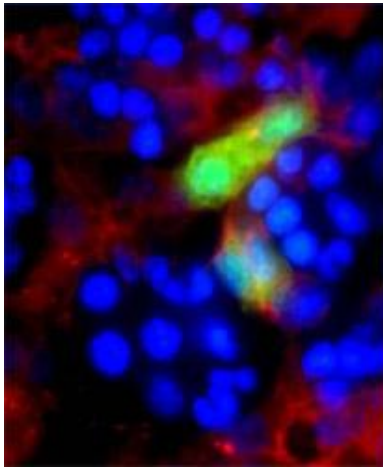
Genes, Gene Therapy, and Gene Patents

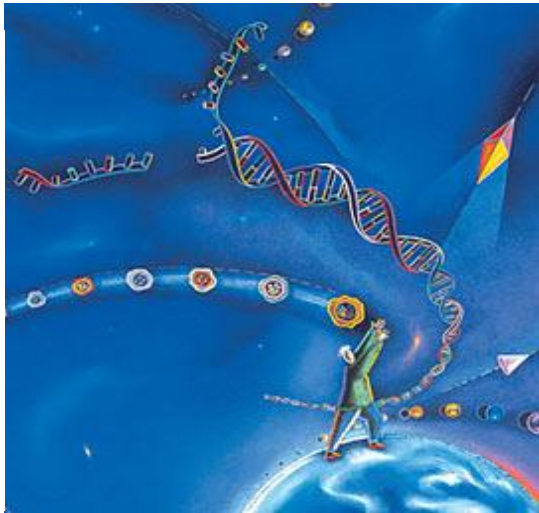
TE WHARE WĀNANGA O TE ŪPOKO O TE IKA A MĀUI
VICTORIA
UNIVERSITY OF WELLINGTON

SCHOOL OF BIOLOGICAL SCIENCES
Te Kura Mātauranga Koiora

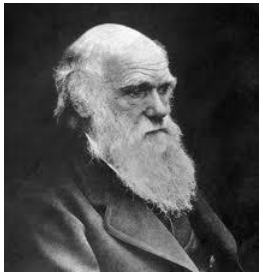
Professor David Ackerley, Biotechnology Programme Director, Victoria University of Wellington





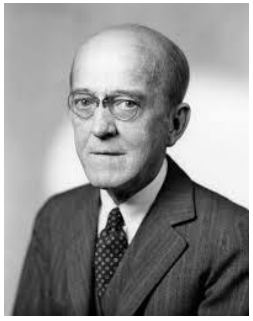


Background: What IS a gene?



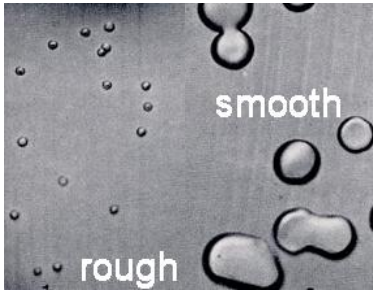
Charles Darwin
"Vive l'Evolution"
1859

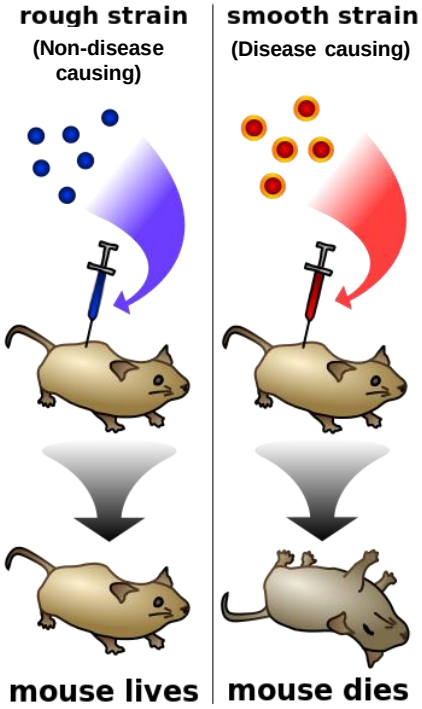
Frederick Griffith
"Mouse-hater"
1928



Oswald Avery
"DNA is the business"
1944

Gregor Mendel
"Units of inheritance"
1866





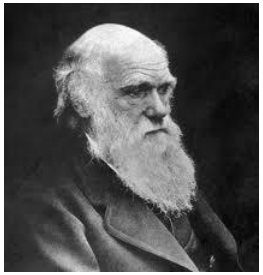
grading enzyme

grading enzyme

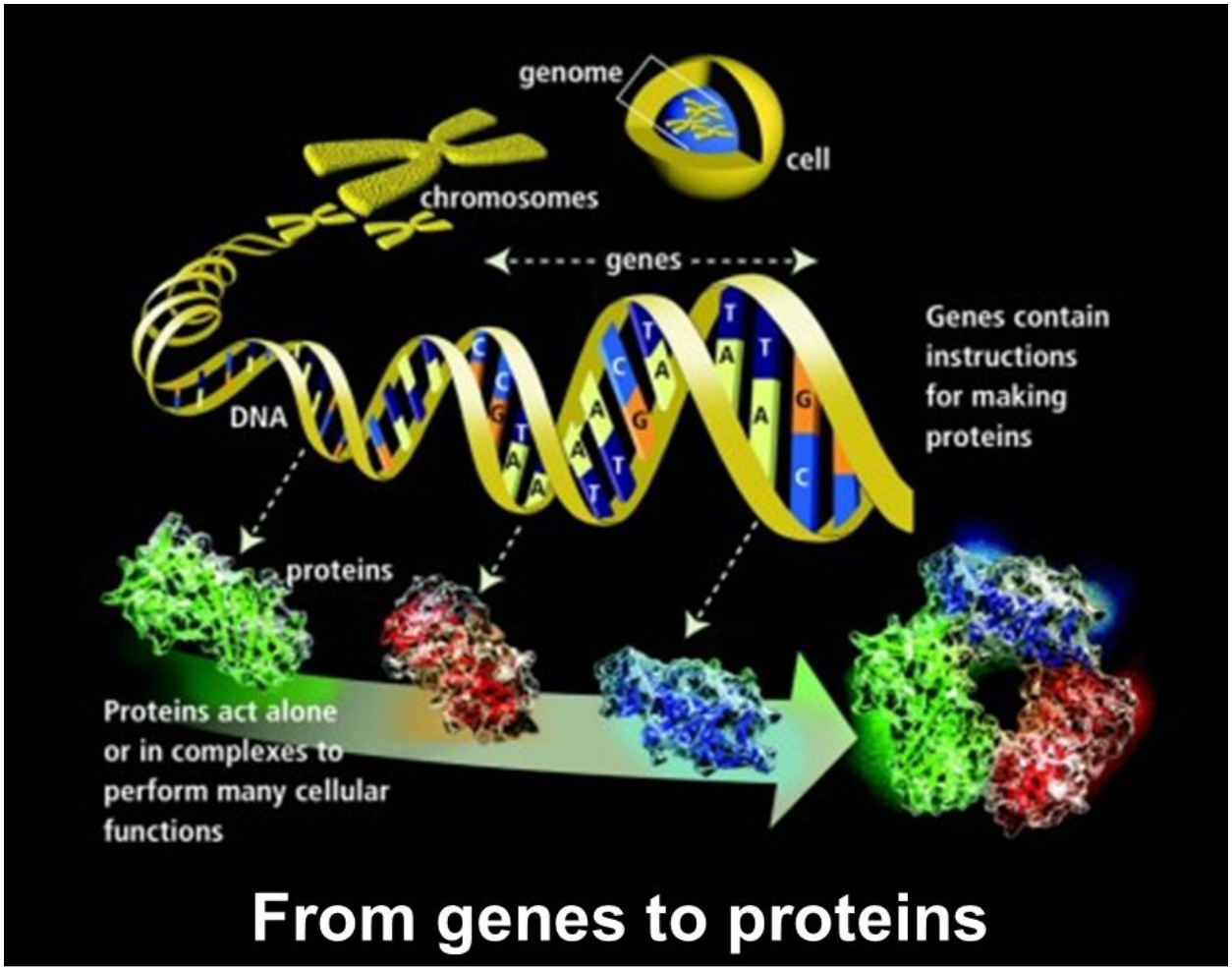
degrading
zyme

formation"

Genes: blueprints for proteins

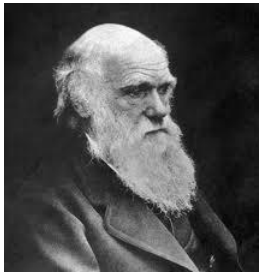


Charles Darwin
"Vive l'Evolution"
1859



Gregor Mendel
"Units of inheritance"
1866

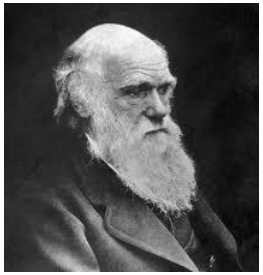
Genes: blueprints for proteins



Charles Darwin
"Vive l'Evolution"
1859

Gregor Mendel
"Units of inheritance"
1866

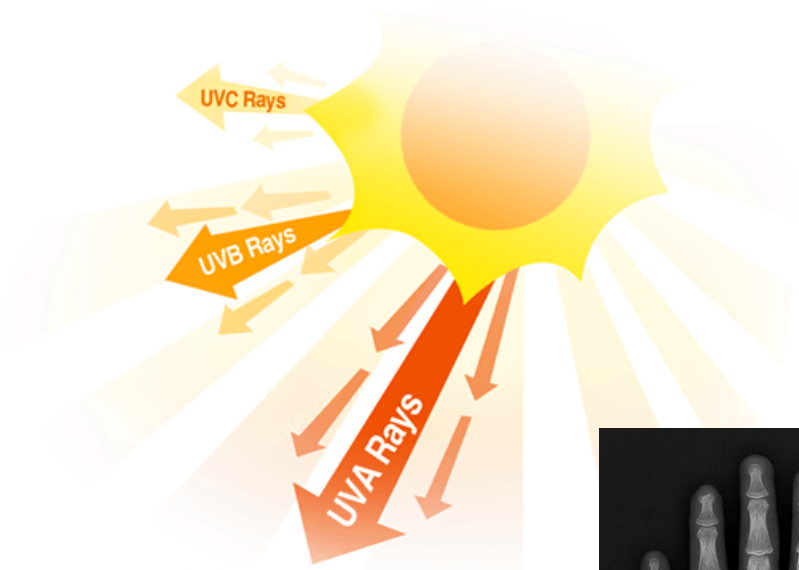
Effects of genetic mutation

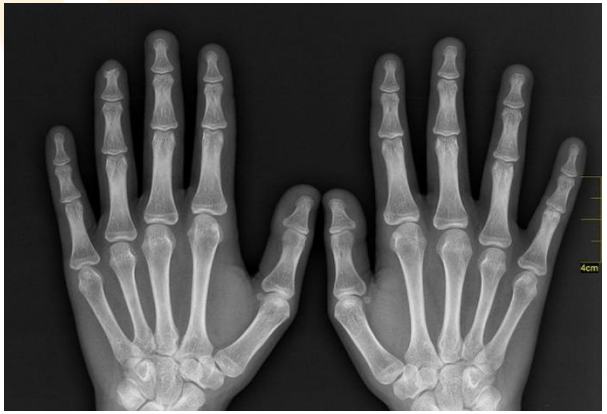


Charles Darwin
"Vive l'Evolution"
1859

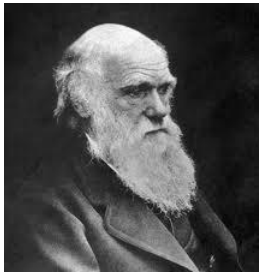
Changes in the genetic code can lead to changes in a protein

Gregor Mendel
"Units of inheritance"
1866



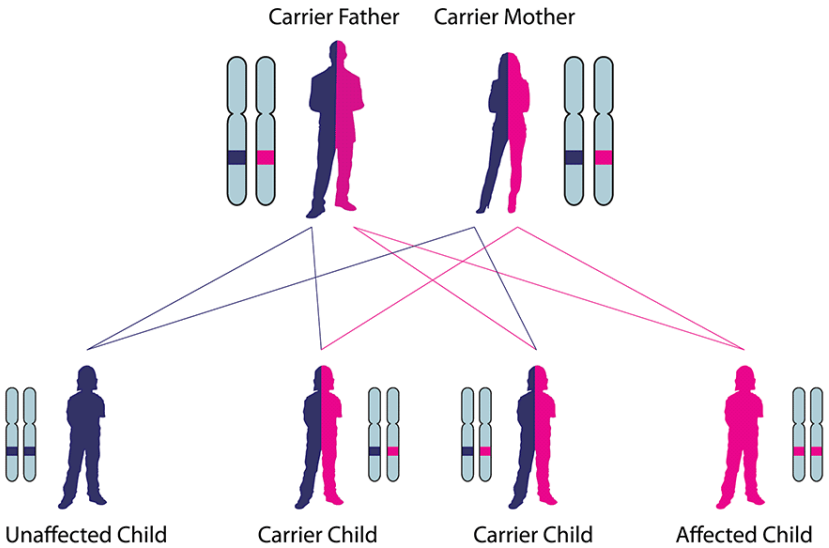


Effects of genetic mutation



Charles Darwin
"Vive l'Evolution"
1859

Changes in the genetic code can lead to changes in a protein



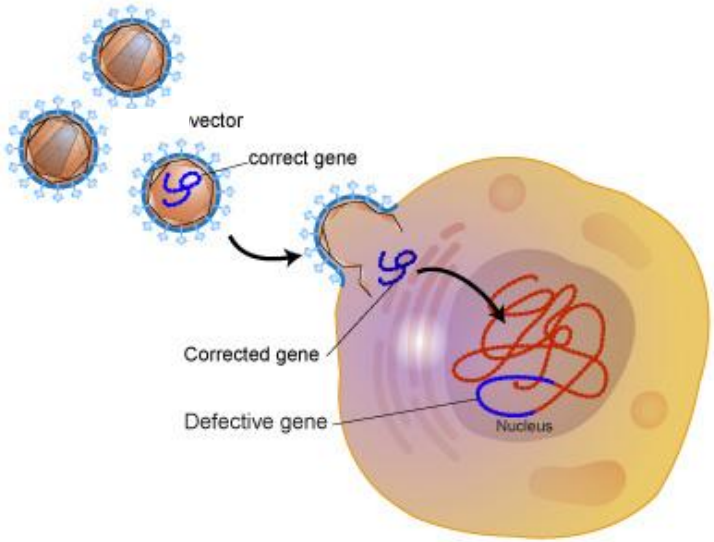
Gregor Mendel
"Units of inheritance"
1866

Gene Therapy



1964: Tatum, Lederberg, Kornberg suggested that the future of genetic disease therapy would be in curing disorders by replacing defective genes with functional ones

→ singled out cystic fibrosis, muscular dystrophy, multiple sclerosis



“required tools do not currently exist”

The SCID Story

- Severe Combined Immunodeficiency Disorder - patients cannot form an ‘acquired’ immune system

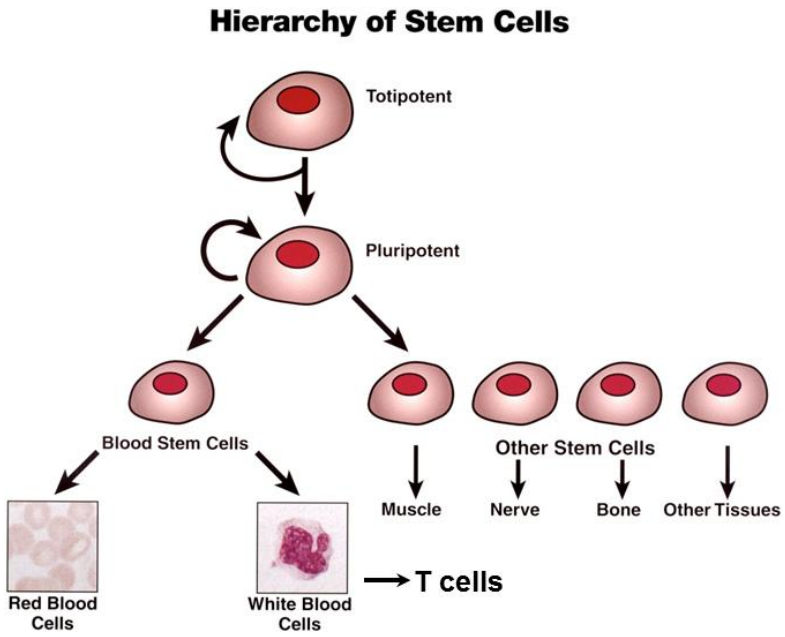
- Large number of genetic defects can give rise to disorder

- Usually fatal

Treatment Options

1) Bone marrow transplant

- Requires high level match - even siblings may differ



Treatment Options

2) Raise child in sterile environment

→ famous example: David, “the bubble boy” 1971-1984

Treatment Options

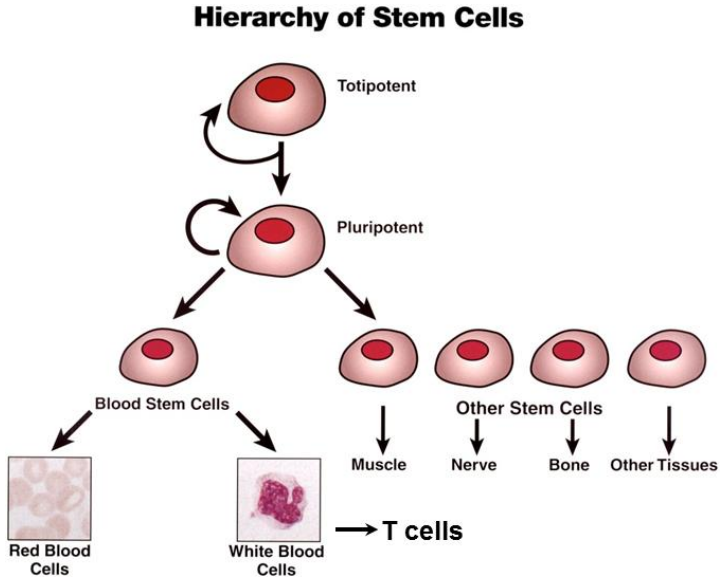
3) Gene Therapy

- Ideal candidate for first human gene therapy trial (1990)

  → monogenic, genetic basis well characterised, gene cloned

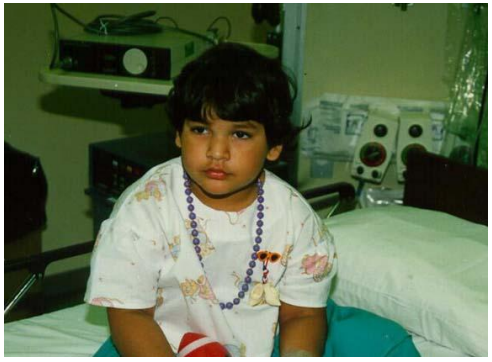
  → lethal, for many forms there is no alternative treatment

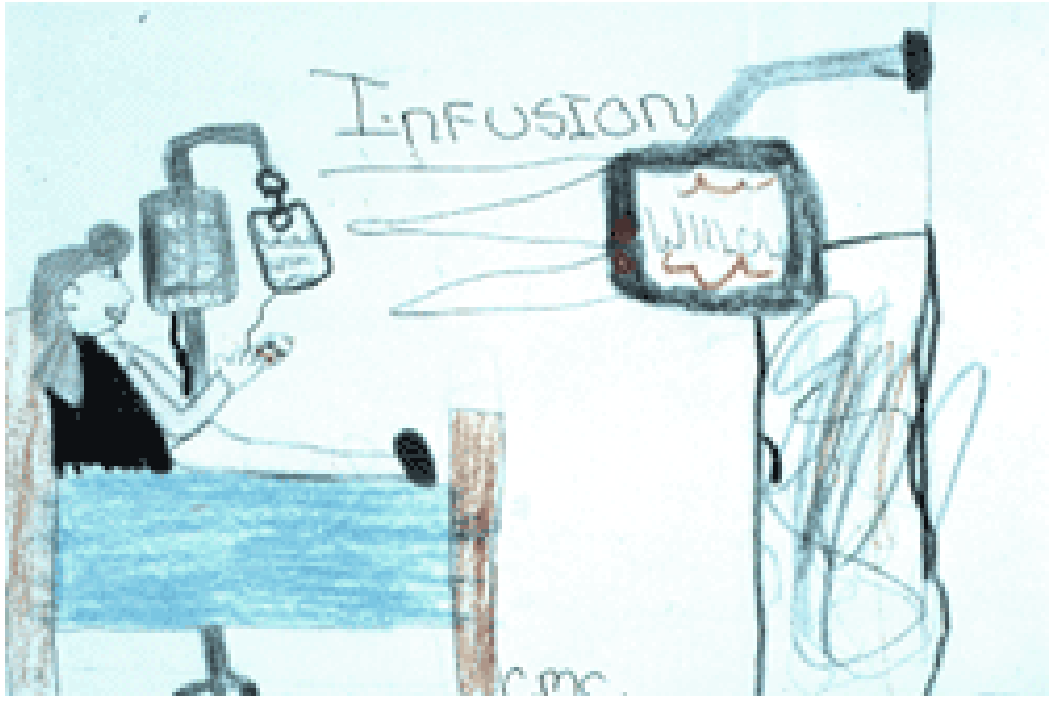
  → variable gene expression levels well tolerated



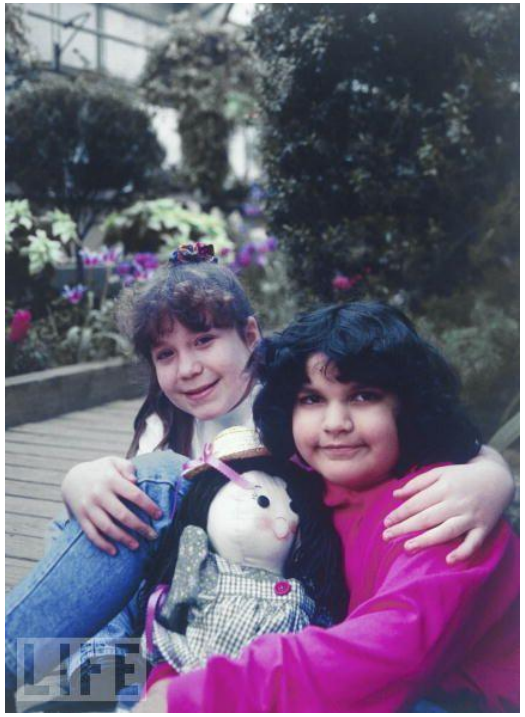
First human gene therapy trial initiated 1990

Ashanti de Silva, 4 year old SCID patient





Cynthia Cutshall, 9 years old, 1991



Not an unqualified success – but pretty good!

Immune Deficiency Foundation

Search..

Ask IDF

Home | About IDF | Learn About Primary Immunodeficiencies | Living with Primary Immunodeficiencies | Take Action | Resources | Connect | Donate

First Gene Therapy Patients Attend IDF 2013 National Conference

2 OCT 2013

DATE: 02 OCT 2013 / POSTED BY: KMORAN / LEAVE A COMMENT

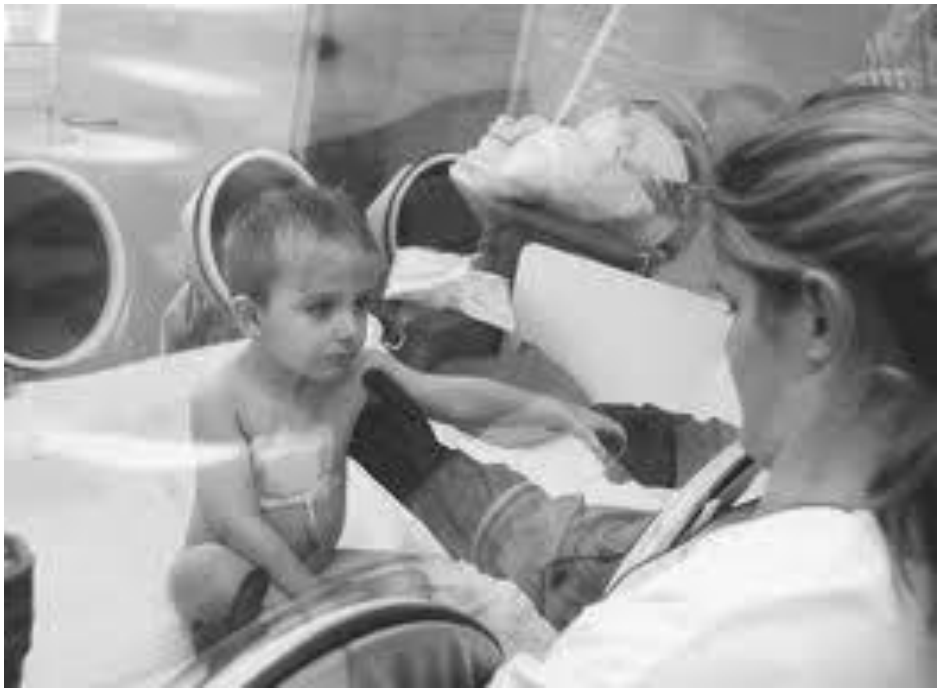
RETURN TO IDF BLOG HOME PAGE

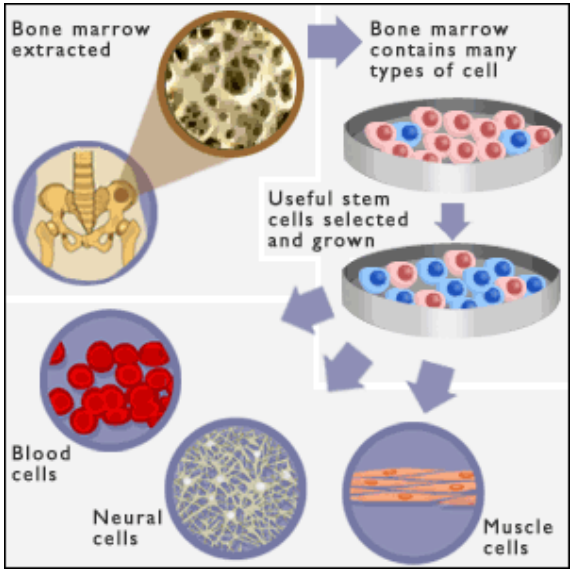
Ashanthi DeSilva and Cindy Kisik were born with ADA-SCID, a type of Severe Combined Immune Deficiency (SCID) with mutations in a gene that encodes an enzyme called adenosine deaminase (ADA). On September 14, 1990, Ashanthi, only 4 years old, underwent the first human gene therapy, and four months later 10-

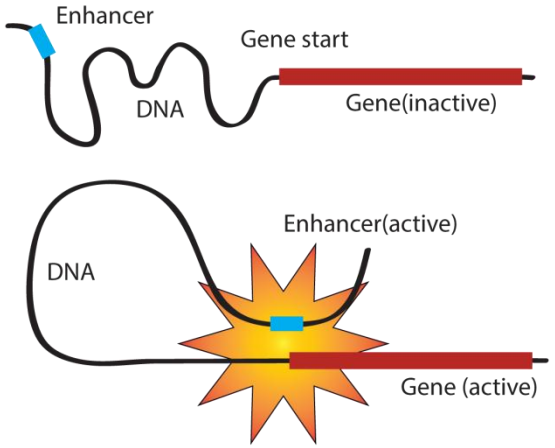
What risks are acceptable for a total cure?

France, 11 boys with X-linked SCID diagnosed *in utero* and treated at stem cell level

→ Great success! Initially…





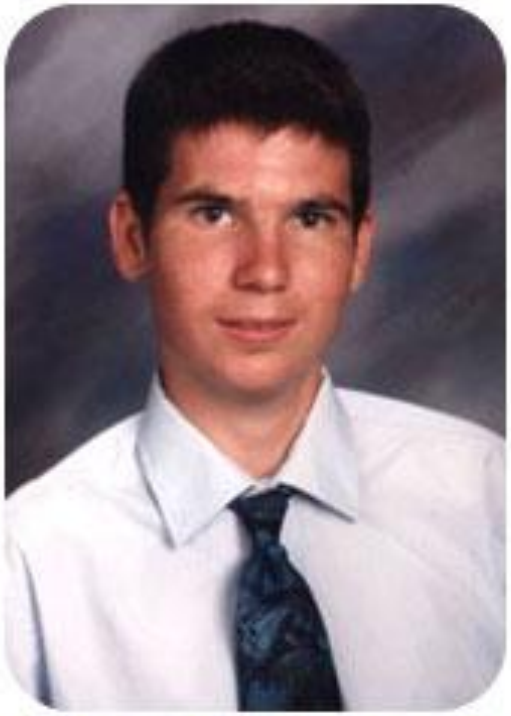


→ 3 of the 11 boys subsequently developed leukaemia

What risks are acceptable for a total cure?

France, 11 boys with X-linked SCID diagnosed
in utero and treated at stem cell level

→ Great success! Initially…



Jesse Gelsinger's death from a gene therapy clinical trial in 1999 raised many questions concerning the safety of experimental gene therapy treatments.

→ 3 of the 11 boys subsequently developed leukaemia

What risks are acceptable for a total cure?

The Seattle Times | Business / Techn

Home Local Nation/World Business/Tech Sports Entertainment Living

Quick links: Traffic | Movies | Restaurants | Today's events | Video | Photos | Blogs

Use search engine marketing to grow your smal

Originally published November 10, 2007 at 12:00 AM | Page modified November 10, 2007 at 2

E-mail article Print view

Gene therapy unlikely cause in death

Recent tests run by University of Chicago scientists point to the innocence of Targeted Gene arthritis...

By Ángel González
Seattle Times business reporter

Recent tests run by University of Chicago scientists point to the innocence of Targeted Genetics' gene therapy for inflammatory arthritis in last summer's death of an Illinois woman in a clinical trial, one of the university researchers said.

Related

- Archive | Health p
  Targeted Genetics

The results suggest that the Seattle-based company's experimental therapy didn't greatly amplify the immune suppression of a commercial arthritis drug the patient was already taking. A breakdown of 36-year-old Jolee Mohr's immune system led to the massive fungal infection that killed her in July.

There's "no real 'smoking gun' here," said Dr. Kyle Hogarth, the University of Chicago who treated Mohr at the intensive-care unit where she died.

Woman's death calls gene therapy into question

Jolee Mohr died three weeks after experimental treatment using a virus

Courtesy Mohr Family / ASSOCIATED PRESS

Jolee Mohr (top right) died in a Chicago hospital in July, three weeks after taking an experimental treatment for rheumatoid arthritis. The cause of her death is being investigated. Also pictured are Robb Mohr and their daughter Toree.

washingtonpost.com > Nation > Science

More From the Science & Medicine Desk

Science News | Environment Headlines | Health News | Tech Frontiers | Live Web Q&As

Fungus Infected Woman Who Died After Gene Therapy

By Rick Weiss
Washington Post Staff Writer
Friday, August 17, 2007; Page A10

Finally making the clinic!

Human Gene Therapy, Vol. 28, No. 11 | Review Articles

Full Access

Twenty-Five Years of Gene Therapy for ADA-SCID: From *Bubble Babies* to an Approved Drug

Francesca Ferrua and Alessandro Aiuti

Published Online: 1 Nov 2017 | https://doi.org/10.1089/hum.2017.175

SCIENTIFIC AMERICAN

By Heidi Ledford, Nature magazine on April 18, 2019

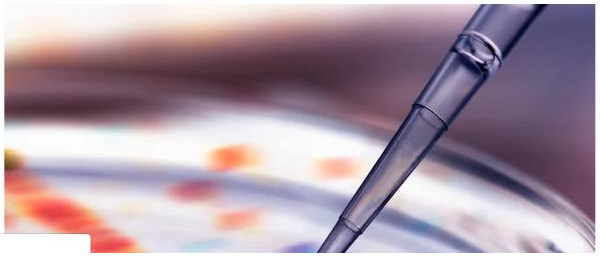
nature

MEDICAL & BIOTECH

Experimental Gene Therapy Frees "Bubble-boy" Babies from a Life of Isolation

Treatment restores immune-system function in young children with severe disorder

By Heidi Ledford, Nature magazine on April 18, 2019

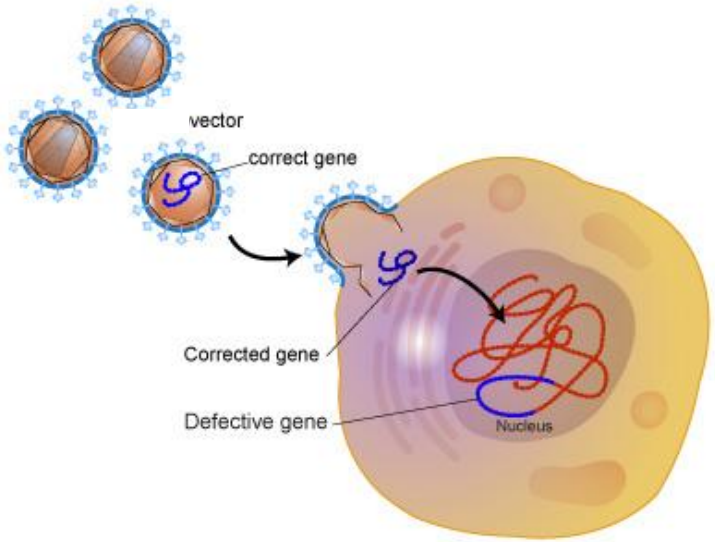


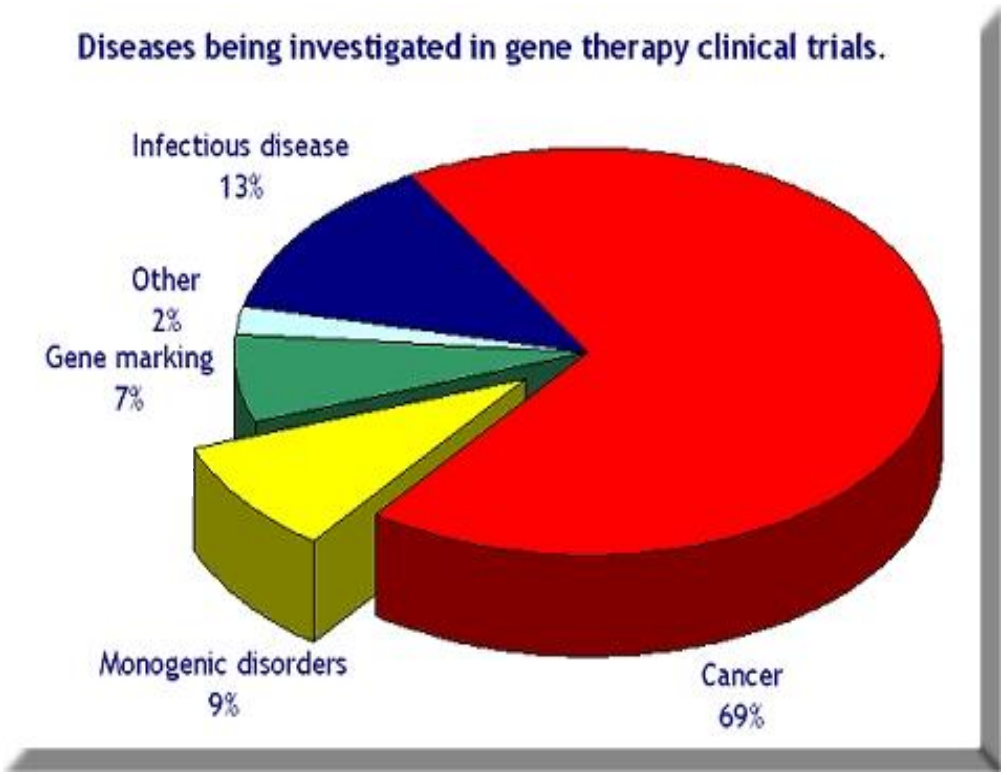
LATEST NEWS

Brain-Controlled Hearing Aids Could Cut through Crowd Noise

From the Lunar Far Side,

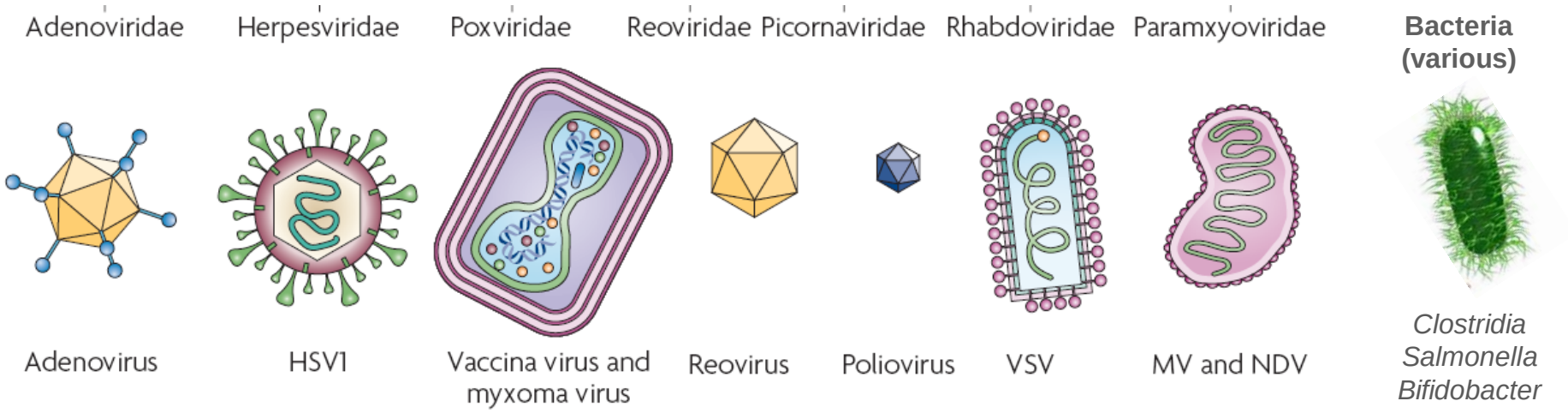
Emergence of cancer as a target





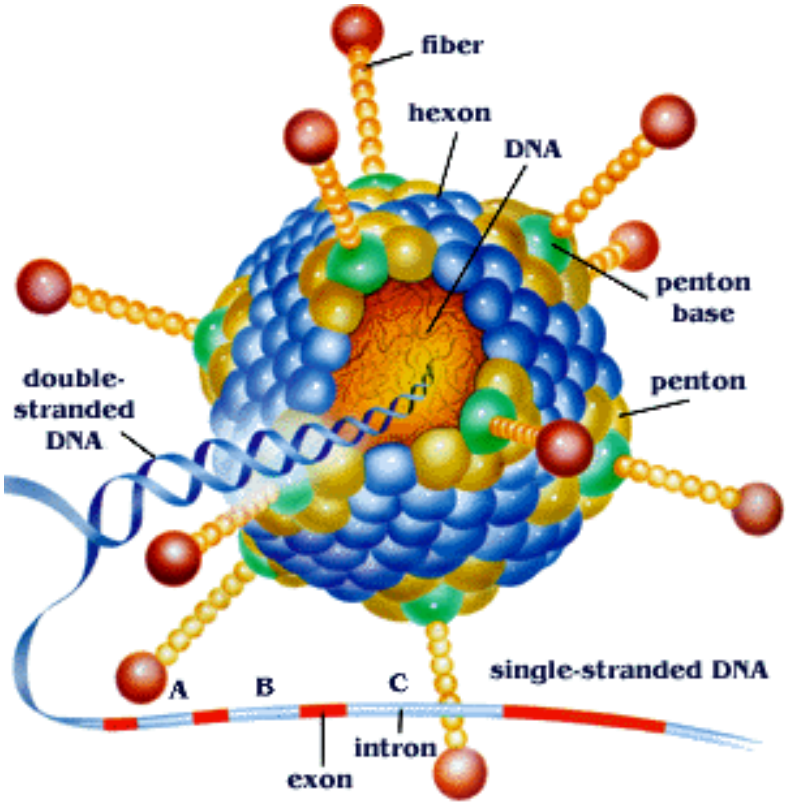
Biological agents for cancer therapy

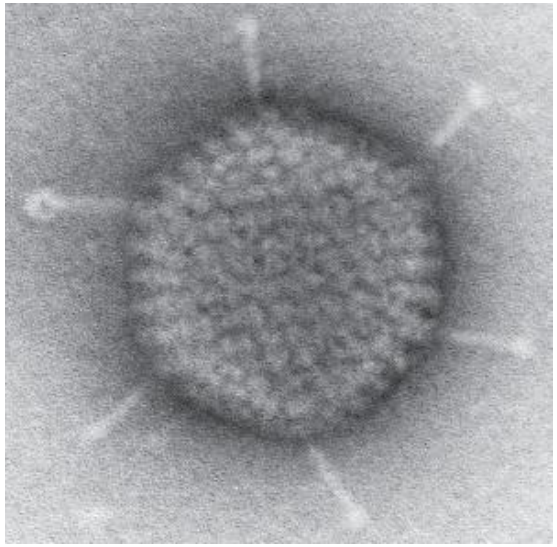
Tumour-targeting microbes:



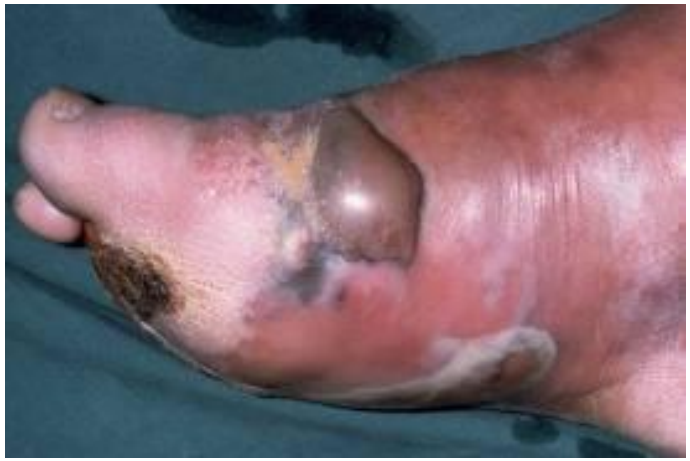
- Synergise with chemo and radiotherapies
- Can be engineered for heightened tumour selectivity
- Can be engineered for enhanced potency

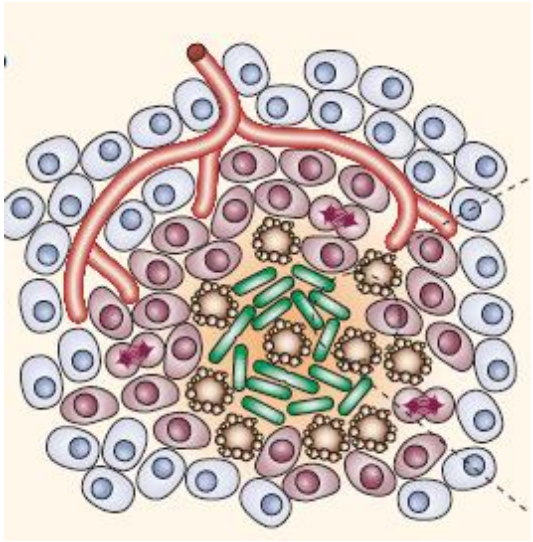
Adenovirus


fiber
hexon
DNA
penton base
penton
double-stranded DNA
single-stranded DNA
A
B
C
intron
exon



Clostridium





Biological agents for cancer therapy

DEAL WATCH Nature Reviews Drug Discovery (March 2011)

Amgen buys oncolytic virus company

In a deal worth up to a possible US$1 billion, Amgen has acquired the biotechnology company BioVex. BioVex's lead product OncoVEX^{GM-CSF} (herpes virus JS1/34.5-/47-/ granulocyte–macrophage colony stimulating factor (GM-CSF)) is an oncolytic virus that caused tumour regression and increased survival in patients with metastatic melanoma in a Phase II trial, and is also being investigated in head and neck cancer.

Oncolytic viruses get a boost with first FDA-approval recommendation

The future of cancer-killing viruses lies in their potential to augment cell and antibody immunotherapies.

Elie Dolgin

A virus engineered to infect and destroy tumour cells stands on the cusp of regulatory approval by the US Food and Drug Administration (FDA). On 29 April, members of an expanded advisory committee to the agency voted 22 to 1 in favour of allowing sales of talimogene laherparepvec (T-VEC) — a version of the herpes simplex virus that both attacks cancer cells and enhances antitumour immune responses — for the treatment of unresectable and recurrent melanoma.

If approved, T-VEC will become the first tumour-targeted viral agent to reach pharmaceutical shelves outside of China. Such a stamp of approval could usher in a long-awaited era of viral therapies for cancer and provide a powerful tool for enhancing the efficacy of the latest immune-stimulating antibodies and cell therapies. "It's an exciting time for our patients," says Howard Kaufman, Chief Surgical Officer at the Rutgers Cancer Institute of New Jersey, New Brunswick, New Jersey, USA, who led the T-VEC trials. "This will open up a completely new class of drugs."

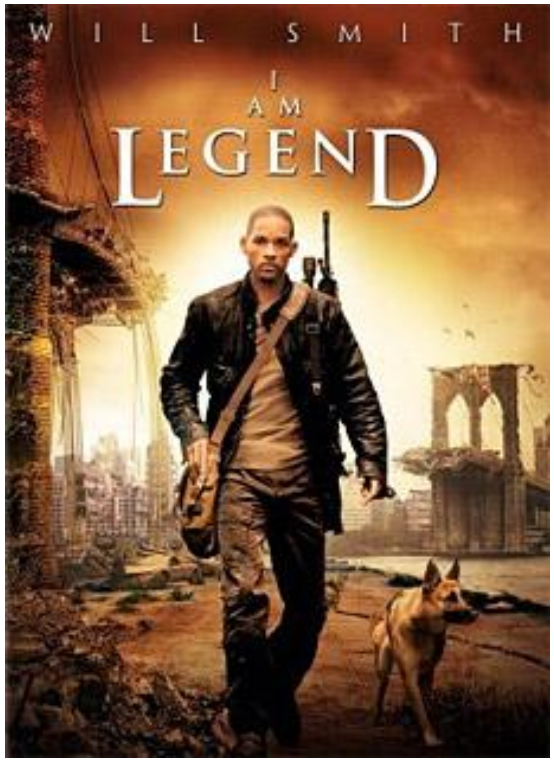
The FDA will make a full licensing decision by 27 October. An evaluation for European marketing authorization is expected before the end of the year.

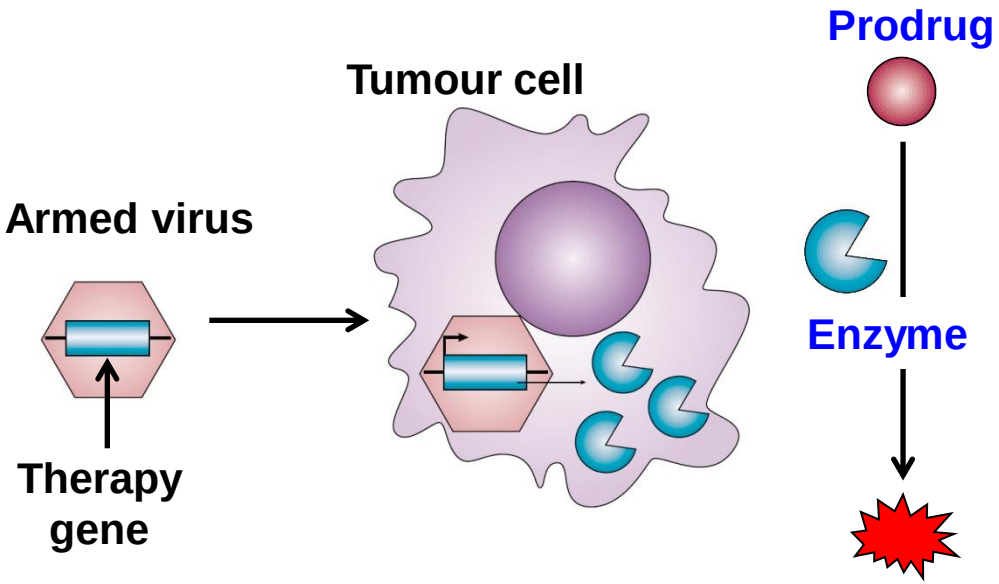
T-VEC is being developed by the biotech giant Amgen, which in 2011 promised to pay up to US$1 billion (including $575 million in milestone commitments) to acquire the product's inventor, BioVex Group. In the therapy's Phase III trial, 16% of the 295 participants who received intralesional doses of T-VEC experienced a durable response — their tumours shrank for at least 6 months — whereas only 2% of the 141 participants who received subcutaneous shots of granulocyte–macrophage colony-stimulating factor (GM-CSF) showed such a response.

Although patients who took T-VEC gained an average of just 4.4 months of life over those who took GM-CSF — with median survival times of 23.3 months and 18.9 months, respectively — 11% of T-VEC recipients showed no signs of cancer after treatment. This complete response rate

Anti-cancer gene therapy

Can enhance the potency of tumour-targeting biological agents by ‘arming’ them with therapeutic genes

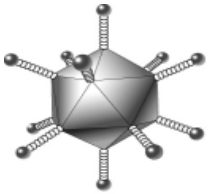




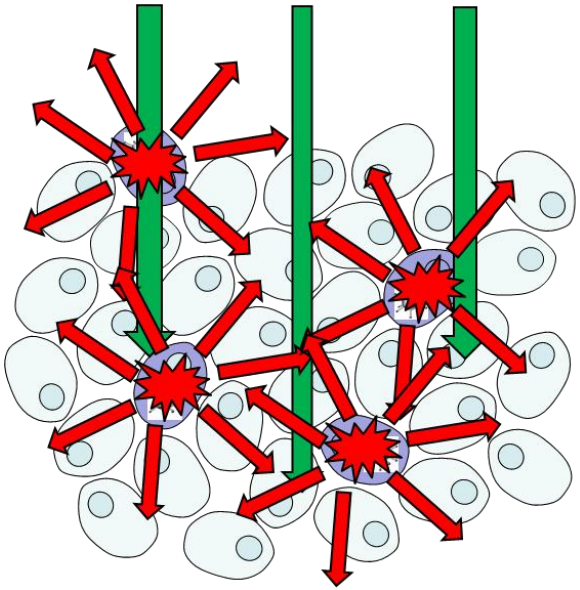
Anti-cancer gene therapy

Historically, gene therapies suffer from the inability to reach more than a small minority of target cells

→ for anti-cancer gene therapy can counter this by using prodrugs that have a good “bystander effect”

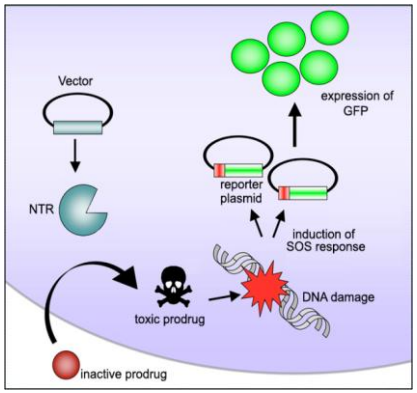


Viral vector

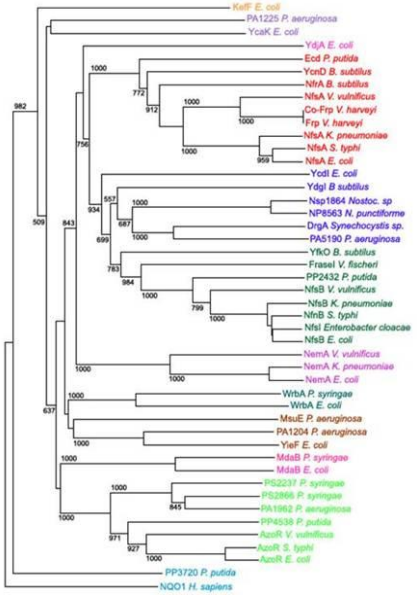


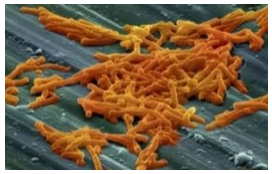
Our research at VUW

Enzyme Engineering

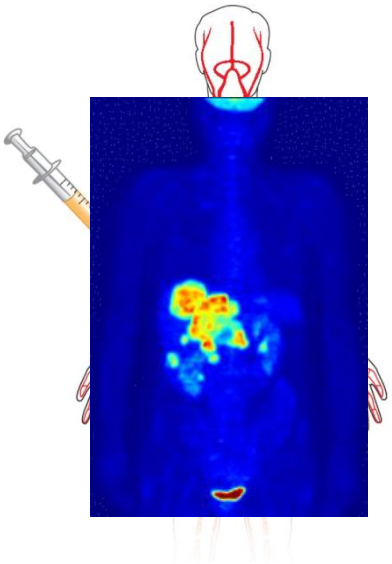


Enzyme Collection

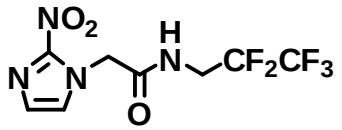




Enzyme 'Armed' Vector

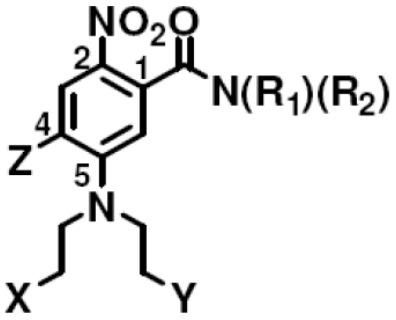


Bio-imaging



^{18}Fluoroetanidazole (EF5)

Bio-therapeutics



Nitrobenzamide mustard prodrugs

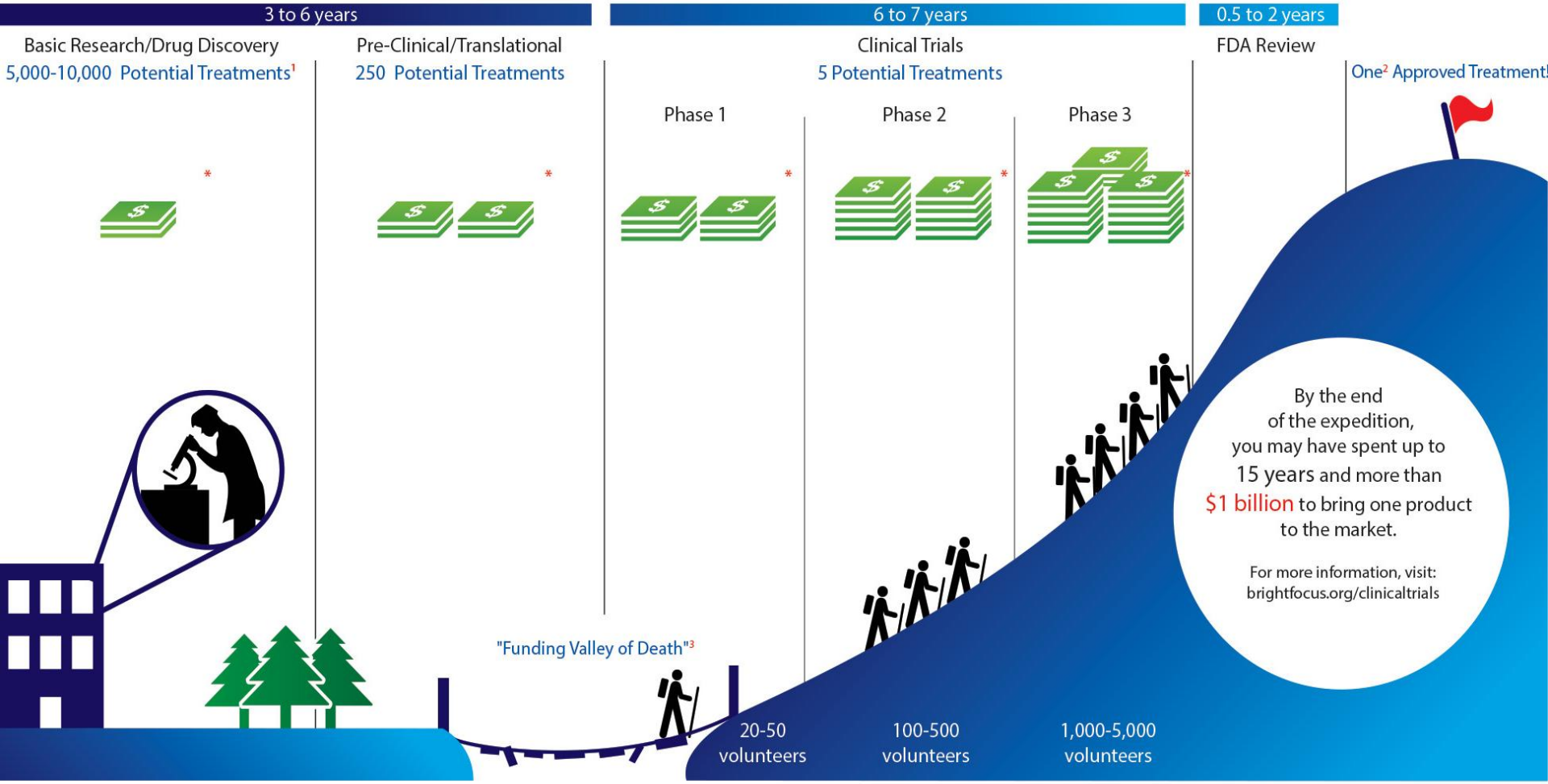
Next move: Clinical trials

Key Step: Raise money!

→ How much needed?

Next move: Clinical trials

From www.brightfocus.org



By comparison: New Zealand's entire Pharmac budget p.a. ~NZ$800 million

Alternatives to rigorous testing

Market highly experimental therapies without testing?

→ numerous examples throughout history of people selling "snake oil" - treatments that don't work, aren't safe, or both!

Sulfanilamide - one of first antibacterials

→ large pills difficult for children, Harold Watkins dissolved in diethylene glycol + raspberry flavour

→ 1937 - 107 deaths reported

Next move: Clinical trials

Key Step: Raise money!

→ How much needed?

→ Approximately $5 million to cover Phase I, possible from government grants (maybe)

→ Thereafter, private venture capital funding will be required

→ Only possible if we can offer a potential return on investment

→ Need to **patent** our therapeutic genes

What is a patent?

A contract with the state (government)

→ Provides the owner of the invention with a monopoly on the idea for 20 years

→ In return, details of the invention must be fully disclosed to the public, so that after 20 years others can implement

→ For new drugs / gene therapies, this typically leaves about 5 years post-trials to recoup investment – after which anyone can copy the idea (**generics**)

Why not just go “open source”?

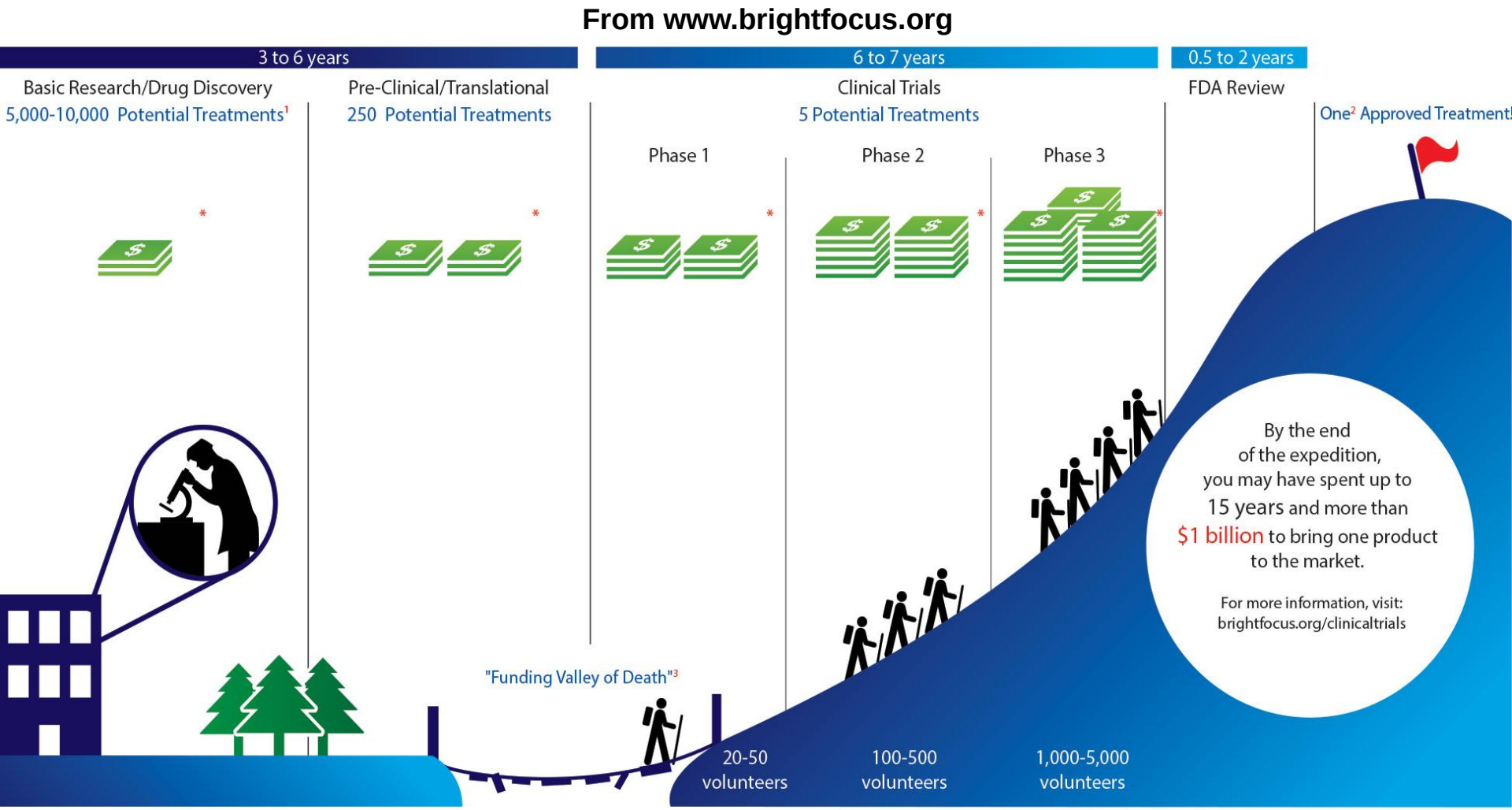
A patent is fundamentally a blocking strategy

→ Having the right to deny someone else access to medical treatment seems **extremely** morally questionable

However, once you disclose your idea publically, **no one** (including you) can patent it

→ it is often argued that any scientist who thinks their work has therapeutic applications has a moral obligation to file a patent!

Why not just go “open source”?



By comparison: New Zealand’s entire Pharmac budget p.a. ~NZ$800 million

Diagnostics: the Dark(er) Side of gene patents

athena diagnostics™ formerly Genica Pharmaceuticals Corporation

Athena Diagnostics, Inc.
Four Biotech Park
377 Plantation Street
Worcester, MA 01605
Tel 508 756 2886 Fax 508 753 5801

March 21, 1997 SECOND NOTICE

RE: U.S. Patent Number 5,508,167

As part of our effort to be at the forefront of developments in diagnostic testing, I would like to advise you that Athena Diagnostics has acquired exclusive rights to certain tests in the diagnosis of late onset Alzheimer's disease. These tests are covered under U.S. Patent number 5,508,167 a copy of which is enclosed.

The patent covers methods of diagnosing for increased risk of late onset Alzheimer's disease by testing for the presence of the ApoE 4 allele.

We understand that University of Pennsylvannia may be offering a diagnostic test covered by this patent. Any such testing would infringe on the above patent under which Athena has exclusively licensed.

This diagnostic testing service is available through Athena's facilities, and it is only by using Athena's facilities that other laboratories can offer this patented diagnostic test without infringing the patent.

If University of Pennsylvannia is interested in continuing to offer this patented testing service to its customers, Athena would be pleased to perform the services on University of Pennsylvannia behalf. Our currently published price is $195 per specimen.

Very truly yours,

Michael A. Boss, Ph.D.
Vice President, Research and Development

MAB/cml

non-recoverable under many US health insurance schemes

From Dr Debra Leonard, University of Pennsylvania Medical Center

Diagnostics: the Dark(er) Side of gene patents

MYRIAD®

US$3,500 to test for mutant BRCA1/BRCA2 alleles

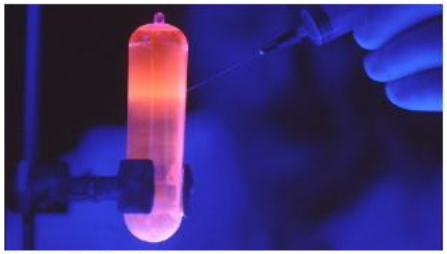
Supreme Court 2013: ACLU *vs.* Myriad Genetics

The Scientist » News & Opinion » Daily News

Gene Patents Decision: Everybody Wins

Last week's Supreme Court decision to invalidate patents on human genes was a win for patients, independent researchers, and even the wider biotech industry.

By Jeffrey M. Perkel | June 18, 2013

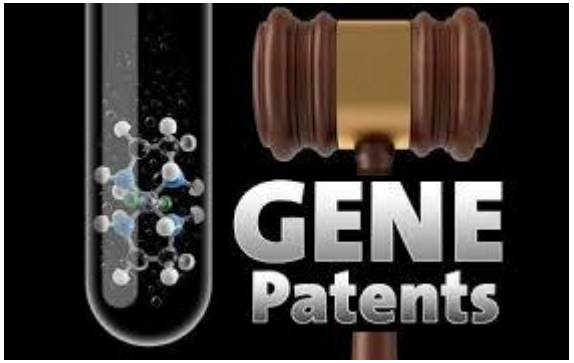


DNA purification
WIKIMEDIA, MIKE MITCHELL FOR THE NATIONAL CANCER INSTITUTE

It's been nearly a week since the US Supreme Court invalidated Myriad Genetics' patents on the *BRCA1* and *BRCA2* genes, and the response from bioethicists, patient advocates, and the research community has been nearly uniformly positive.

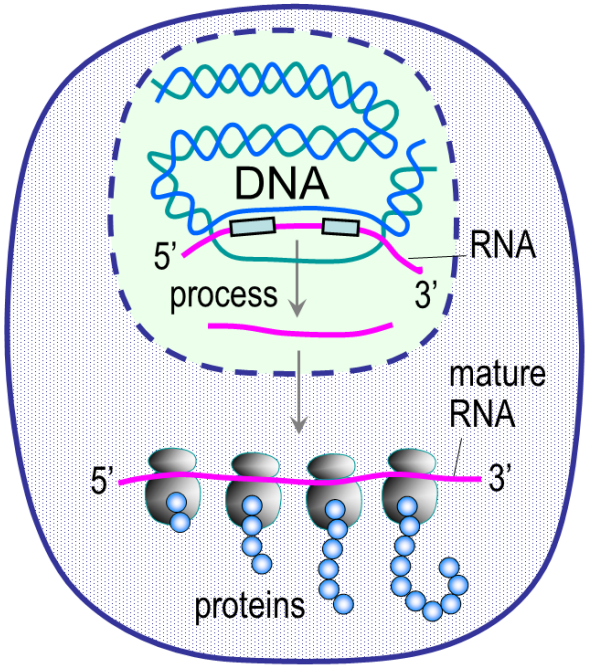
"VICTORY! Supreme Court decides: Our genes belong to us, not companies," declared the American Civil Liberties Union (ACLU), who with the Public Patent Foundation filed the suit.

Mary-Claire King, the pioneer who first established the genetic basis of familial breast cancer and pinpointed the *BRCA1* gene in 1990, told the *New Scientist* two days following the ruling, "I am delighted. This is a fabulous result for patients, physicians, scientists, and common sense."

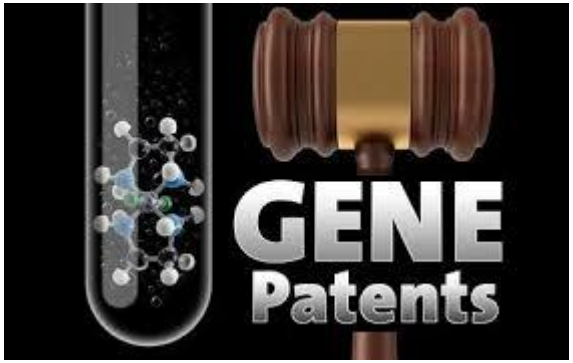


"A naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated"

Supreme Court 2013: ACLU *vs.* Myriad Genetics



Animals



"A naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated"

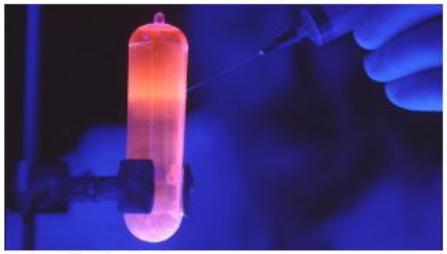
Supreme Court 2013: ACLU *vs.* Myriad Genetics

The Scientist » News & Opinion » Daily News

Gene Patents Decision: Everybody Wins

Last week's Supreme Court decision to invalidate patents on human genes was a win for patients, independent researchers, and even the wider biotech industry.

By Jeffrey M. Perkel | June 18, 2013

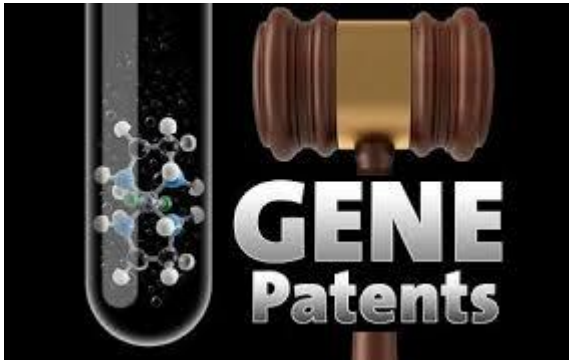


DNA purification
WIKIMEDIA, MIKE MITCHELL FOR THE NATIONAL CANCER INSTITUTE

It's been nearly a week since the US Supreme Court invalidated Myriad Genetics' patents on the *BRCA1* and *BRCA2* genes, and the response from bioethicists, patient advocates, and the research community has been nearly uniformly positive.

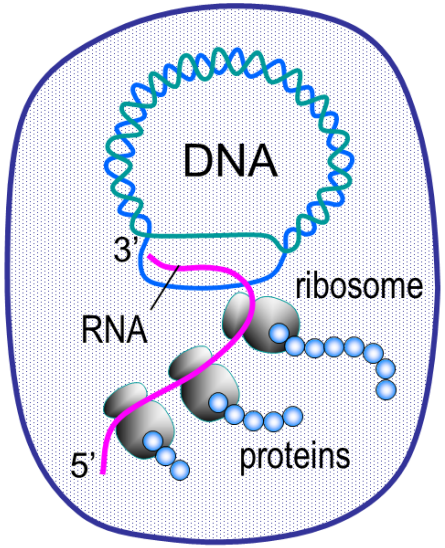
"VICTORY! Supreme Court decides: Our genes belong to us, not companies," declared the American Civil Liberties Union (ACLU), who with the Public Patent Foundation filed the suit.

Mary-Claire King, the pioneer who first established the genetic basis of familial breast cancer and pinpointed the *BRCA1* gene in 1990, told the *New Scientist* two days following the ruling, "I am delighted. This is a fabulous result for patients, physicians, scientists, and common sense."

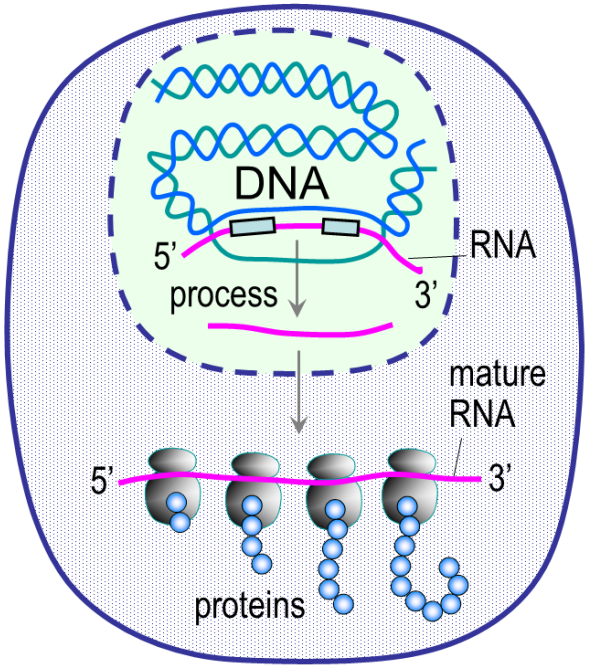


"A naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated"

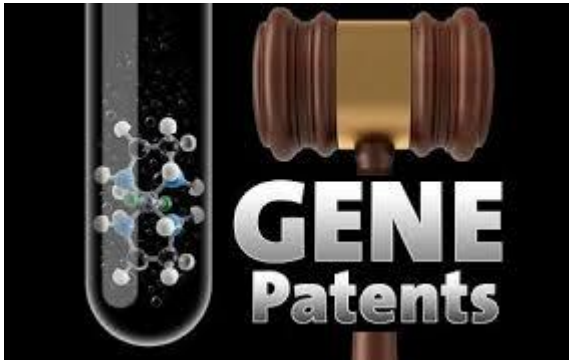
Supreme Court 2013: ACLU *vs.* Myriad Genetics



Bacteria



Animals



"A naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated"

Funding acknowledgements

National Institutes of Health
NZ Lottery Grants Board TE PUNA TAHUA
MARSDEN FUND TE PŪTEA RANGAHAU A MARSDEN
hrc
viclink
MBIE
Cancer Society
genesis oncology trust
MWC

The folk who actually did all the work

Postdocs


Dr Janine Copp


Dr Pearl Swe


Dr Elsie Williams


Dr Jeremy Owen


Dr Katherine Robins


Dr Mark Calcott


Dr Liwei Liu


Dr Michelle Rich


Dr Alistair Brown


Dr Abby Sharrock

PhD students


Dr Jeremy Owen


Dr Gareth Prosser


Dr Laura Green


Dr Claire Horvat


Dr Elsie Williams


Dr Becky Edgar


Dr Mark Calcott


Dr Katherine Robins


Dr Alistair Brown


Dr Michelle Rich

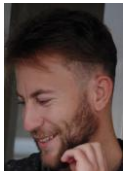

Jasmine Chan-Hyams


Dr Abby Sharrock


Luke Stevenson

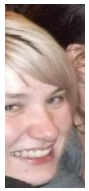

Kelsi Hall

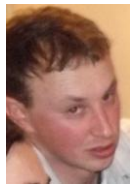

Mathew Storey


Mitch Ganley

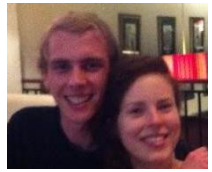

Hannah Lee-Harwood

Masters students

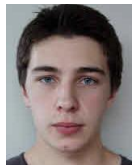

Sarah Condon


Mathew Storey


Rory Little


Jack Sissons


Hannah Lee-Harwood


Vincent Collins


Sarah Messenger


Janine Sharma


Jenni Francis


Geoff Hoggins

Hons and UG students

(not already listed)


Neil Fisher


Dr Nick Milne

Kate Walmsley


Melz Thompson

Dr Kyle Webster

Maddie Parker

Michelle Gramse

The ones who (mostly) put up with me