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International Centre for Genetic Engineering and Biotechnology (ICGEB)

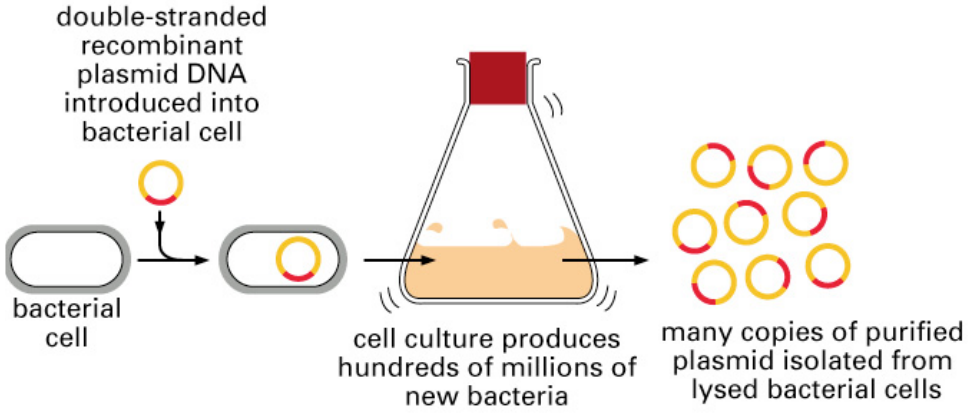
Biotechnologies for global development:the old and the new

Trieste, Italy

Adriatic sea

The Abdus Salam International Centre for Theoretical Physics
50th Anniversary 1964 - 2014

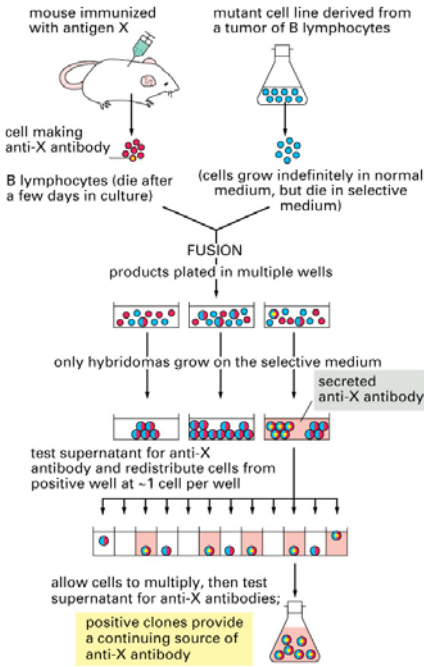
Mid 70's: recombinant DNA and molecular cloning



Biopharmaceutical Products

Product	Year
Insulin	1982
Human Growth Hormone (hGH)	1985
α-Interferon	1986
Hepatitis B Vaccine	1986
Tissue Plasminogen Activator (TPA)	1987
Erythropoietin-α	1989
γ-Interferon	1990
Granulocyte Colony Stimulating Factor (G-CSF)	1991
Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF)	1991
Interleukin 2	1992
Factor VIII	1992
β-Interferon	1993
DNase (Pulmozyme®)	1993
Glucocerebrosidase (Cerezyme®)	1994
ReoPro®	1994

Source: Consulting Resources Corp.



Hybridoma Cell Lines Provide a Permanent Source of Monoclonal Antibodies

Monoclonal antibodies useful for:

- Protein localization
- Protein purification

Cancer therapy using monoclonal antibodies

Table 1 US and EU therapeutic mAb approvals to date

Generic	Company/location	Trade	Description	Therapeutic category	Approval date
Muromonab-CD3	Johnson & Johnson New Brunswick, New Jersey	Orthoclone OKT3	Murine, IgG2a, anti-CD3	Immunological	06/19/86 (US)
Abciximab	Centocor	ReoPro	Chimeric, IgG1, anti-GPIIb/IIIa; Fab	Hemostasis	12/22/94 (US)
Rituximab	Genentech	Rituxan	Chimeric, IgG1κ, anti-CD20	Oncological	11/26/97 (US) 06/02/98 (EU)
Daclizumab	Hoffmann-La Roche Basel	Zenapax	Humanized, IgG1κ, anti-CD25	Immunological	12/10/97 (US) 02/26/99 (EU)
Basiliximab	Novartis Basel	Simulect	Chimeric, IgG1κ, anti-CD25	Immunological	05/12/98 (US) 10/09/98 (EU)
Palivizumab	MedImmune Gaithersburg, Maryland	Synagis	Humanized, IgG1κ, anti-respiratory syncytial virus	Anti-infective	06/19/98 (US) 08/13/99 (EU)
Infliximab	Centocor	Remicade	Chimeric, IgG1κ, anti-tumor necrosis factor (TNFα)	Immunological	08/24/98 (US) 08/13/99 (EU)
Trastuzumab	Genentech	Herceptin	Humanized, IgG1κ, anti-HER2	Oncological	09/25/98 (US) 08/28/00 (EU)
Gemtuzumab ozogamicin	Wyeth Madison, New Jersey	Mylotarg	Humanized, IgG4κ, anti-CD33; immunotoxin	Oncological	05/17/00 (US)
Alemtuzumab	Genzyme Cambridge, Massachusetts	Campath-1H	Humanized, IgG1κ, anti-CD52	Oncological	05/07/01 (US) 07/06/01 (EU)
Ibritumomab tiuxetan	Biogen Idec	Zevalin	Murine, IgG1κ, anti-CD20; radiolabeled (Yttrium 90)	Oncological	02/19/02 (US) 01/16/04 (EU)
Adalimumab	Abbott Deerfield Park, Illinois	Humira	Human, IgG1κ, anti-TNFα	Immunological	12/31/02 (US) 09/1/03 (EU)
Omalizumab	Genentech	Xolair	Humanized, IgG1κ, anti-IgE	Immunological	06/20/03 (US)
Tositumomab-I131	Corixa Seattle	Bexxar	Murine, IgG2aλ, anti-CD20; radiolabeled (Iodine 131)	Oncological	06/27/03 (US)
Efalizumab	Genentech	Raptiva	Humanized, IgG1κ, anti-CD11a	Immunological	10/27/03 (US) 09/20/04 (EU)
Cetuximab	Imclone Systems New York	Erbitux	Chimeric, IgG1κ, anti-Epidermal growth factor receptor	Oncological	02/12/04 (US) 06/29/04 (EU)
Bevacizumab	Genentech	Avastin	Humanized, IgG1, anti-vascular endothelial growth factor	Oncological	02/26/04 (US) 01/12/05 (EU)
Natalizumab[a]	Biogen Idec	Tysabri	Humanized, IgG4κ, anti-α4-integrin	Immunological	11/23/04 (US)

See **Box 1** for methodology.
[a]Voluntary suspension of natalizumab marketing announced February 28, 2005.

World's 10 bestselling prescription drugs made $75bn last year

Majority of bestsellers are created by biological processes rather than chemically synthesised and several are used as cancer medicines

Rank in 2013 (in 2012)	Product	Company	Therapeutic category	2013 sales ($US m)	2012 sales ($US m)
1 (1)	Humira	AbbVie	Other anti-rheumatics	10,659	9,616
2 (2)	Enbrel	Pfizer/Amgen	Other anti-rheumatics	8,776	8,496
3 (4)	Remicade	Johnson & Johnson/ Merck & Co	Other anti-rheumatics	8,386	7,990
4 (3)	Seretide/Advair	GlaxoSmithKline	Other bronchodilators	8,251	7,634
5 (6)	Lantus	Sanofi	Anti-diabetics	7,592	7,155
6 (5)	Rituxan	Roche	Anti-neoplastic MAbs	7,503	6,377
7 (9)	Avastin	Roche	Anti-neoplastic MAbs	6,751	6,282
8 (7)	Herceptin	Roche	Anti-neoplastic MAbs	6,562	6,253
9 (8)	Crestor	AstraZeneca	Anti-hyperlipidaemics	5,622	6,149
10 (10)	Abilify	Otsuka Holdings	Anti-psychotics	5,500	5,304

Humira (adalimumab) – Monoclonal antibody against TNFalpha

Enbrel (etanercept) – Fusion between the p75 TNFalpha receptor and an Ig

Remicade (infliximab) – Monoclonal antibody against TNFalpha

Seretide/Advair – Salmeterol and fluticasone

Lantus – insulin glargine

Rituxan (rituximab) – monoclonal antibody against B cell CD20

Avastin - monoclonal antibody against VEGF-A

Herceptin (trastuzumab) – monoclonal antibody against HER2/neu

Crestor (rosuvastatina) - statin

Abilifty (aripiprazolo) – schizophrenia and bipolar disorders

EP vantage
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The early days in ICGEB history

Late '70s and early '80s: Very successful biotech companies are born in the US (Genentech, 1976; Biogen, 1978; Amgen, 1980; Immunex, 1981; Chiron, 1981; Genzyme 1981)

early '80s: UNIDO functionaries in Vienna conceive the idea of a biotech Centre for developing countries

1982: First meeting organized by UNIDO in Belgrade, Serbia

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1983: Foundation meeting in Madrid, Spain; Italy puts forward its candidature to host the Centre

1987: ICGEB is founded with two seats, one in Trieste, Italy and one in New Delhi, India

Biotechnology for development

Health
Biopharmaceuticals
Vaccines
Diagnostics for viral and genetic disease
Protection against sexually-transmitted diseases

Agriculture
Enhance productivity
- Pest protection
- Herbicide tolerance
- Environmental adaptation

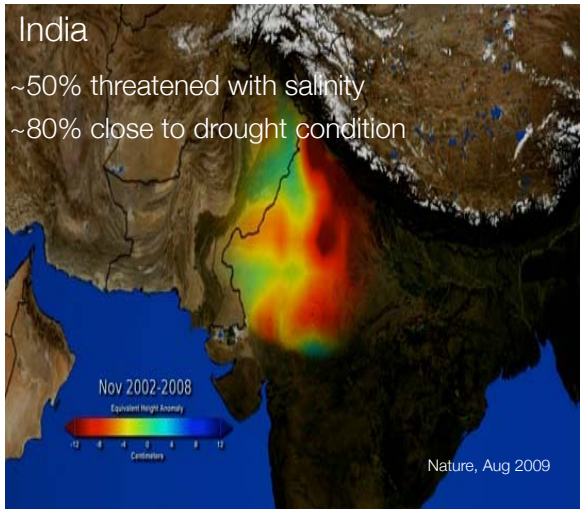
Improve nutritional composition of foods
Reduce allergenicity

Environment
Sanitation
Clean water
Bioremediation

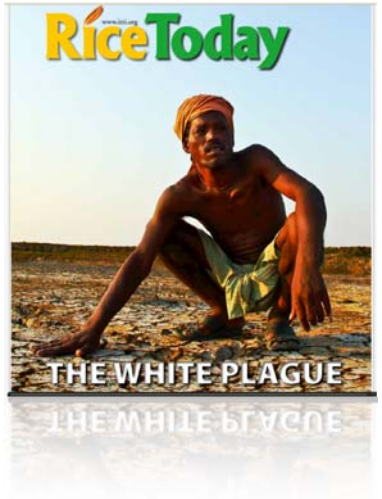
Energy
Biofuels

Salinity and drought: two serious threats to agricultural yield

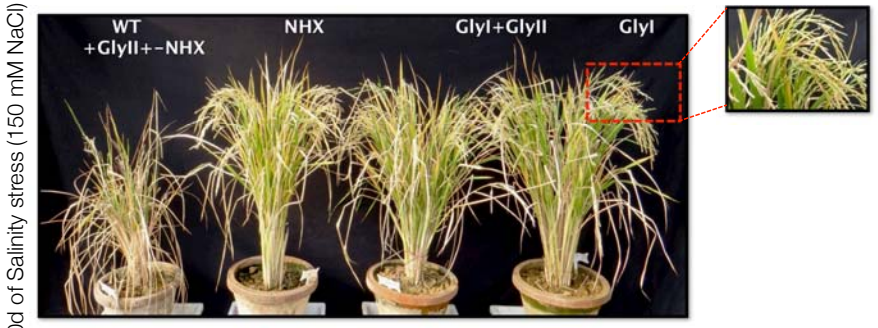
NASA satellites unlock secret to Northern India’s vanishing water



Haryana, Punjab, Rajasthan and Delhi (the grain baskets of India) lost 109 cubic km of ground water in last 6 yrs (2002-08)



Triple transgenic rice plants for durable stress tolerance



Triple (Gly+GlyII+NHX) transgenic rice plants show better reproductive growth as compared to double (GlyI+GlyII) or single (NHX1) transgenic lines and WT plants under salinity stress conditions

ICGEB An intergovernmental organization in the United Nations Common System

80+ Signatory States, 60+ Member States, 3 Components:
Trieste (Italy) - New Delhi (India) - CapeTown (South Africa)
and a network of 40+ Affiliated Centres

Developing knowledge

From: [redacted] <[redacted]@aasciences.org>
Date: 19 ottobre 2013 11:24:00 CEST
To: "[redacted]@icgeb.org" <[redacted]@icgeb.org>
Subject: FW: Workshop on Cell Biology/Regenerative Medicine

Dear Dr. Ripandelli,

The African Academy of Sciences is organising a workshop on **Capacity Building in Cell Biology and Regenerative Medicine** which will take place from 11th to 13th November 2013 in Nairobi, Kenya. The meeting will be held at the African Academy of Sciences (AAS). It gives us great pleasure to invite you to the workshop.

A group of scientists from Africa, India, Brazil and China held a meeting during the 23rd TWAS meeting that was held in Tianjin, China in September 2012. A proposal was made to initiate activities that would enhance the capacity of young African scientists in the areas of cell therapy and regenerative medicine so as to build capacity in this field. Cell biology/ regenerative medicine will play a big role in the future to improve health in areas like skin cover for burns, muscle and bone loss, corneal regeneration, haemoglobinopathies, spinal cord injuries, myocardial regeneration etc. AAS was requested to spearhead this initiative and a workshop has been organized to link young African scientists and key experts from India, China and Brazil.

All participants should arrange to arrive in Nairobi on 10th November and leave on 14th November 2013. I hope that you will be able to participate and contribute to the deliberations of this workshop.

Looking forward to your confirmation,

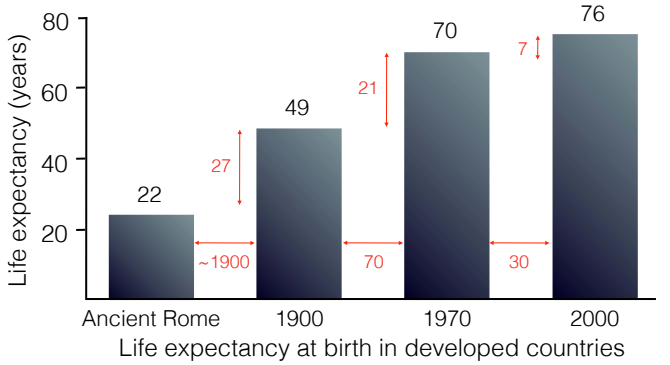
Kind regards,

[redacted]

For:
[redacted]
Executive Director, AAS

What's next?

How long shall we live?



Life expectancy at birth among men and women in 2012 in the 10 top-ranked countries

	Men			Women	
Rank	Country	Life expectancy	Rank	Country	Life expectancy
1	Iceland	81.2	1	Japan	87
2	Switzerland	80.7	2	Spain	85.1
3	Australia	80.5	3	Switzerland	85.1
4	Israel	80.2	4	Singapore	85.1
5	Singapore	80.2	5	Italy	85
6	New Zealand	80.2	6	France	84.9
7	Italy	80.2	7	Australia	84.6
8	Japan	80	8	Republic of Korea	84.6
9	Sweden	80	9	Luxembourg	84.1
10	Luxembourg	79.7	10	Portugal	84

World Health Organization
World Health Statistics 2014

World Health Statistics 2014

Large gains in life expectancy

News release

15 May 2014 | GENEVA - People everywhere are living longer, according to the "World Health Statistics 2014" published today by WHO. Based on global averages, a girl who was born in 2012 can expect to live to around 73 years, and a boy to the age of 68. This is six years longer than the average global life expectancy for a child born in 1990.

WHO's annual statistics report shows that low-income countries have made the greatest progress, with an average increase in life expectancy by 9 years from 1990 to 2012. The top six countries where life expectancy increased the most were Liberia which saw a 20-year increase (from 42 years in 1990 to 62 years in 2012) followed by Ethiopia (from 45 to 64 years), Maldives (58 to 77 years), Cambodia (54 to 72 years), Timor-Leste (50 to 66 years) and Rwanda (48 to 65 years).

"An important reason why global life expectancy has improved so much is that fewer children are dying before their fifth birthday," says Dr Margaret Chan, WHO Director-General. "But there is still a major rich-poor divide: people in high-income countries continue to have a much better chance of living longer than people in low-income countries."

Aging correlates with the sudden or progressive exhaustion of regenerative capacity in most organs and tissues after birth

Nicolas-Sebastien Adam, Paris, Louvre

Rubens, Philadelphia

"The hound of Zeus, the tawny eagle, ... feasting on thy liver til he hath gnawn it black"

Aeschylys, Prometeus Bound

How long shall we live?

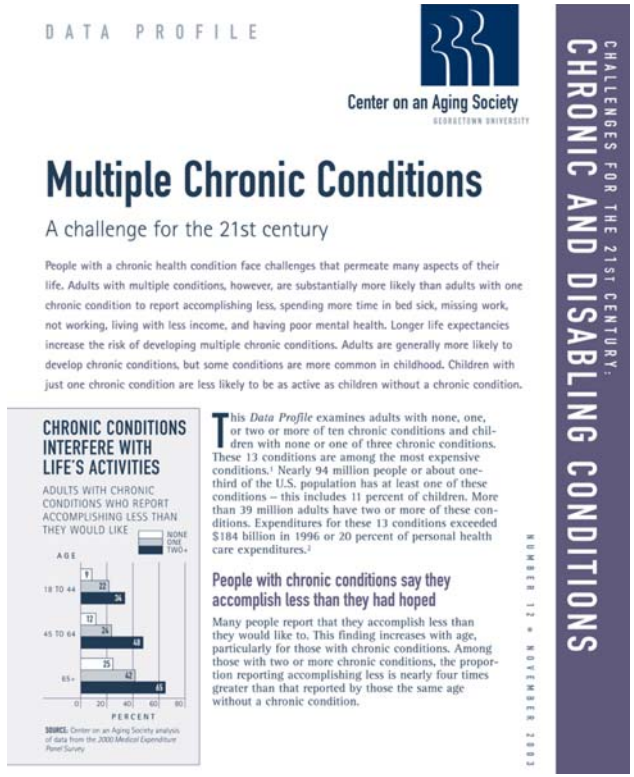
Maximum life span for the human species (unchanged in the last 100,000 years): ~125 years

The longest-lived human being is Jeanne Calment (122.5 years), died in France, in August 1997

Maximum life span in other species:

Rat: 3 years
Squirrel: 25 years
Sheep: 12 years
Turtle: 150 years
Dog: 15-30 years
Fly: 3 months
Canary 15 years
Bat 50 years

In animal studies, maximum life span is often taken to be the mean life span of the most long-lived 10% of a given cohort. By another definition, however, maximum life span corresponds to the age at which the oldest known member of a species or experimental group has died. Calculation of the maximum life span in the latter sense depends upon initial sample size.


DATA PROFILE

Center on an Aging Society
GEORGETOWN UNIVERSITY

Multiple Chronic Conditions

A challenge for the 21st century

People with a chronic health condition face challenges that permeate many aspects of their life. Adults with multiple conditions, however, are substantially more likely than adults with one chronic condition to report accomplishing less, spending more time in bed sick, missing work, not working, living with less income, and having poor mental health. Longer life expectancies increase the risk of developing multiple chronic conditions. Adults are generally more likely to develop chronic conditions, but some conditions are more common in childhood. Children with just one chronic condition are less likely to be as active as children without a chronic condition.

CHRONIC CONDITIONS INTERFERE WITH LIFE'S ACTIVITIES

ADULTS WITH CHRONIC CONDITIONS WHO REPORT ACCOMPLISHING LESS THAN THEY WOULD LIKE

AGE
NONE
ONE
TWO+
18 TO 44
45 TO 64
65+
PERCENT

This *Data Profile* examines adults with none, one, or two or more of ten chronic conditions and children with none or one of three chronic conditions. These 13 conditions are among the most expensive conditions.[1] Nearly 94 million people or about one-third of the U.S. population has at least one of these conditions – this includes 11 percent of children. More than 39 million adults have two or more of these conditions. Expenditures for these 13 conditions exceeded $184 billion in 1996 or 20 percent of personal health care expenditures.[2]

People with chronic conditions say they accomplish less than they had hoped

Many people report that they accomplish less than they would like to. This finding increases with age, particularly for those with chronic conditions. Among those with two or more chronic conditions, the proportion reporting accomplishing less is nearly four times greater than that reported by those the same age without a chronic condition.

NUMBER 12 • NOVEMBER 2003

CHALLENGES FOR THE 21ST CENTURY:
CHRONIC AND DISABLING CONDITIONS

- Heart failure
- Arthrosis
- Diabetes
- Alzheimer's disease
- Parkinson's disease
- Hearing impairment
- Age-related macular degeneration
- Cataract

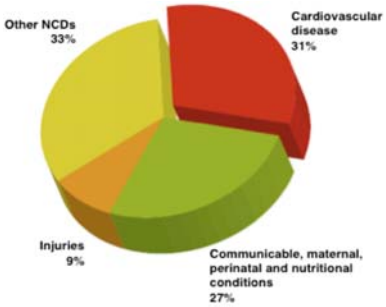
The tremendous burden of cardiovascular disorders

Cardiovascular disorders are the most common, serious, chronic, life-threatening disease causing more deaths, disability and economic costs than all other diseases, including cancer.

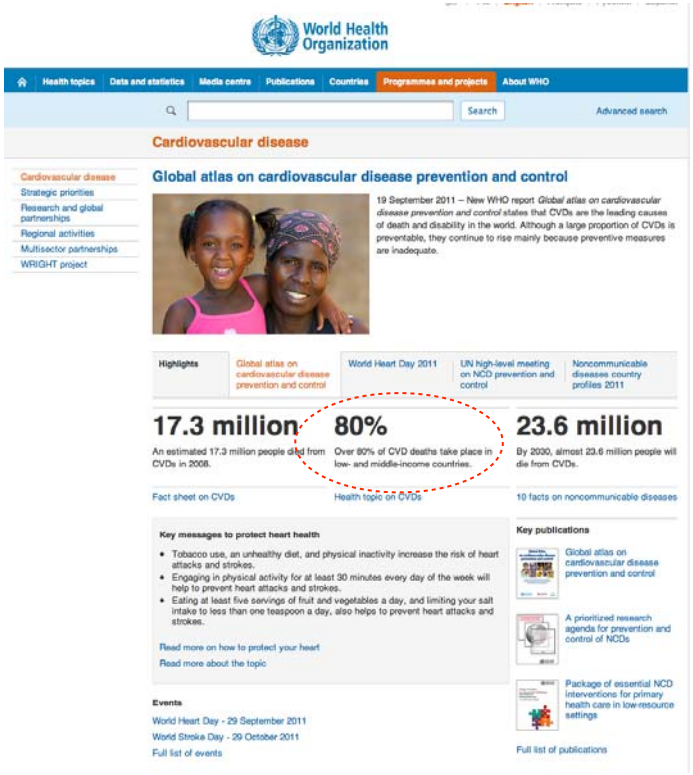
More than **1 person out of 3** dies because of cardiovascular disorders, including myocardial infarction (42%) or stroke (36%). The total deaths due to these diseases per year is **>17 million people** worldwide.

More than 50% of patients with ischemic cardiomyopathy develop towards heart failure; there are **15 million new cases of heart failure** each year worldwide, a number that is rapidly increasing because of the aging population.

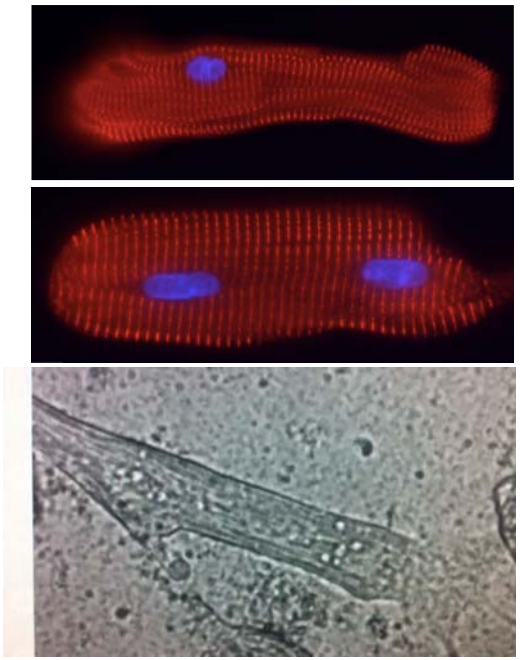
Causes of death
World Health Organization, 2011



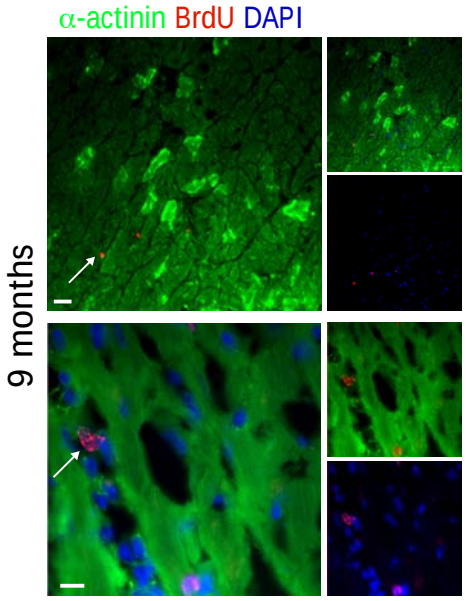
Global Atlas on cardiovascular disease prevention and control, WHO 2011



Adult cardiomyocytes do not proliferate



Cultured primary rat cardiomyocytes



In vivo BrdU incorporation in adult rats

There is a pressing need to develop novel therapeutics for highly prevalent degenerative disorders

Ischemic cardiomyopathy and heart failure (HF)
15 million HF patients worldwide; 50% of patients with HF die within 4 years

Neurodegeneration
30% of people over 80 years develop Alzheimer disease, and 1-3% of those over 65 years of age develop Parkinson's disease

Diabetes mellitus
>170 million people affected worldwide. Both Type 1 (autoimmune) and Type 2 (due to insulin resistance) diabetes are eventually determined by β-cell loss

Retinal degeneration
Age-related macular degeneration (AMD) is the leading cause of irreversible blindness, mostly affecting people over the age of 50. Prevalence of 30% in people over age 75

Presbycusis (Age-related hearing loss)
Due to degeneration of hair cells of the cochlea and giant stereociliary cells. Affects >50% people over age 75

Time line showing the development of drugs against heart failure

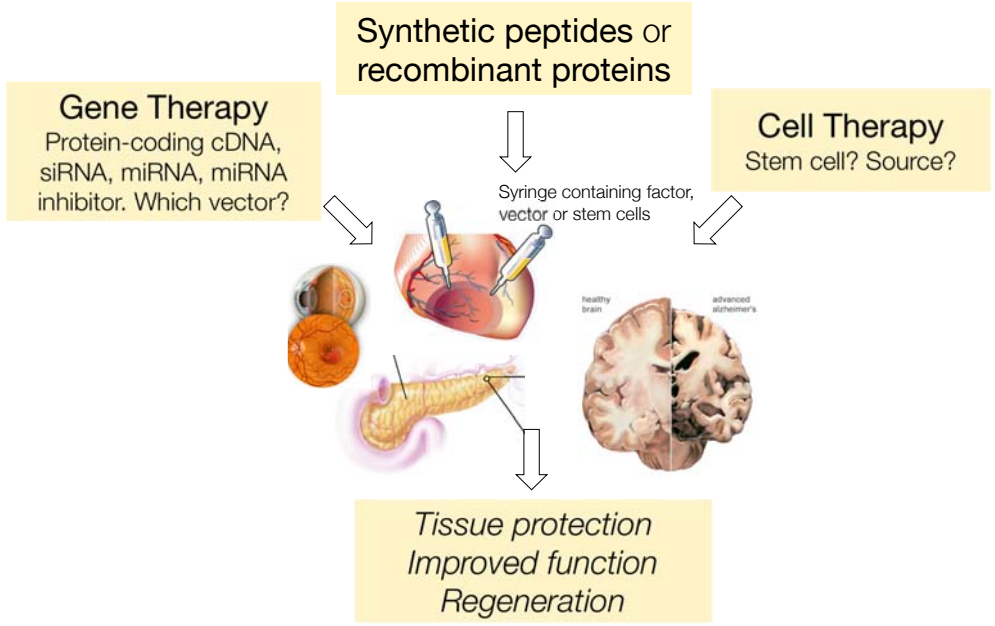
1910
1920
1930
1940
1950
1960
1970
1980
1990
2000
2010
2020

Digitalis
Diuretics

Aldosterone antagonists
ACE inhibitors, Beta-blockers

Angiotensin II receptor blockers (ARBs)

Biotherapeutics for degenerative conditions



miRNAs increasing cardiac regeneration