
Swiss Re
Institute
Genomic Medicine
Launching our latest R&D publication
Dr. Christoph Nabholz, Head R&D Life & Health, 7 Nov 2017

Key facts about genomic medicine in clinical practice

Genomic medicine in medical practice

Vincent Mooser, Jacques Fellay (CHUV University Hospital, Lausanne)

Number of letters (nucleotides) in the human genome	4 (A, C, T, G)
Size of the human genome	3.2 billion letters, corresponding to the size of 1000 bibles
Size of the coding portion of the human genome (exome)	40 million base pairs / 1.5% of the size of the genome
Portion of individual genome shared with reference genome	99.9%
Number of variants in individual genomes (compared to a reference genome)	4 million
Cumulative number of variants identified in 10000 genomes sequenced[3]	150 million
Costs of sequencing 1 human genome between 1990 and 2001	USD 2.5 B
Costs of sequencing 1 human genome in 2016	USD 1000
Number of PubMed hits while querying for – "Precision medicine" – "Personalized medicine" – "Genomic medicine" – "Pharmacogenomic"	Query on Jan 5th, 2017 (number of hits for years 2014–2016) – 11 230 (5 835) – 8 343 (4 604) – 5 941 (3 688) – 15 773 (3 469)

Number of genes in the human genome	20 000
Number of rare diseases due to a single gene defect	5000
Cumulative prevalence of patients affected by rare diseases in the population	10%
Number of highly penetrant clinically actionable genes[4]	59
Cumulative prevalence of carriers of highly penetrant clinically actionable mutations[5]	3.5%
Risk increase for coronary artery disease among quintile of the population with highest genetic score based on common variants, compared to lowest quintile[6]	1.9 (90% increase)
Number of drugs with pharmacogenetic/genomic in FDA label*	170
Number of pharmacogenomic applications with proven clinical utility (outside oncology)[7]	2

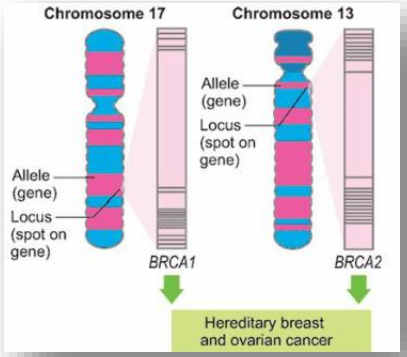
Rapid evolution of genetic testing technologies observed since the human genome sequence in 2003

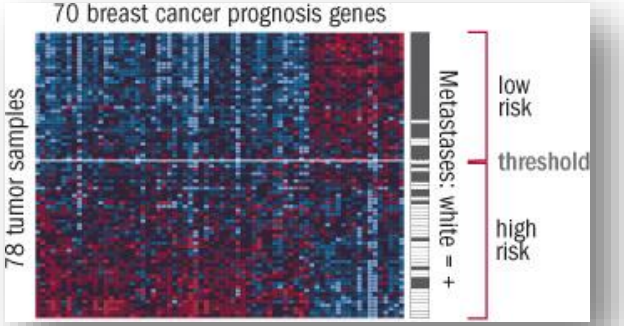
Single Gene Testing

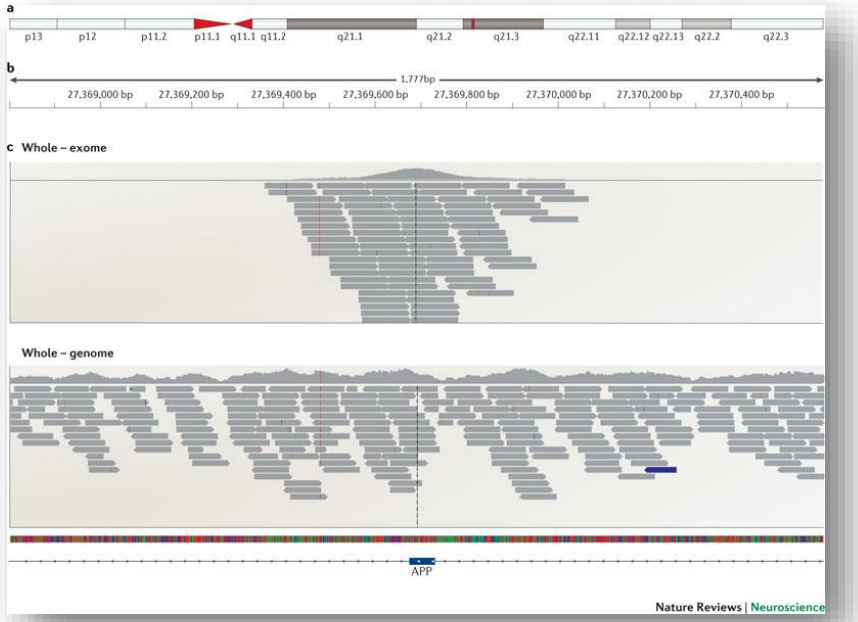
Gene Panels

Whole Exome Sequencing

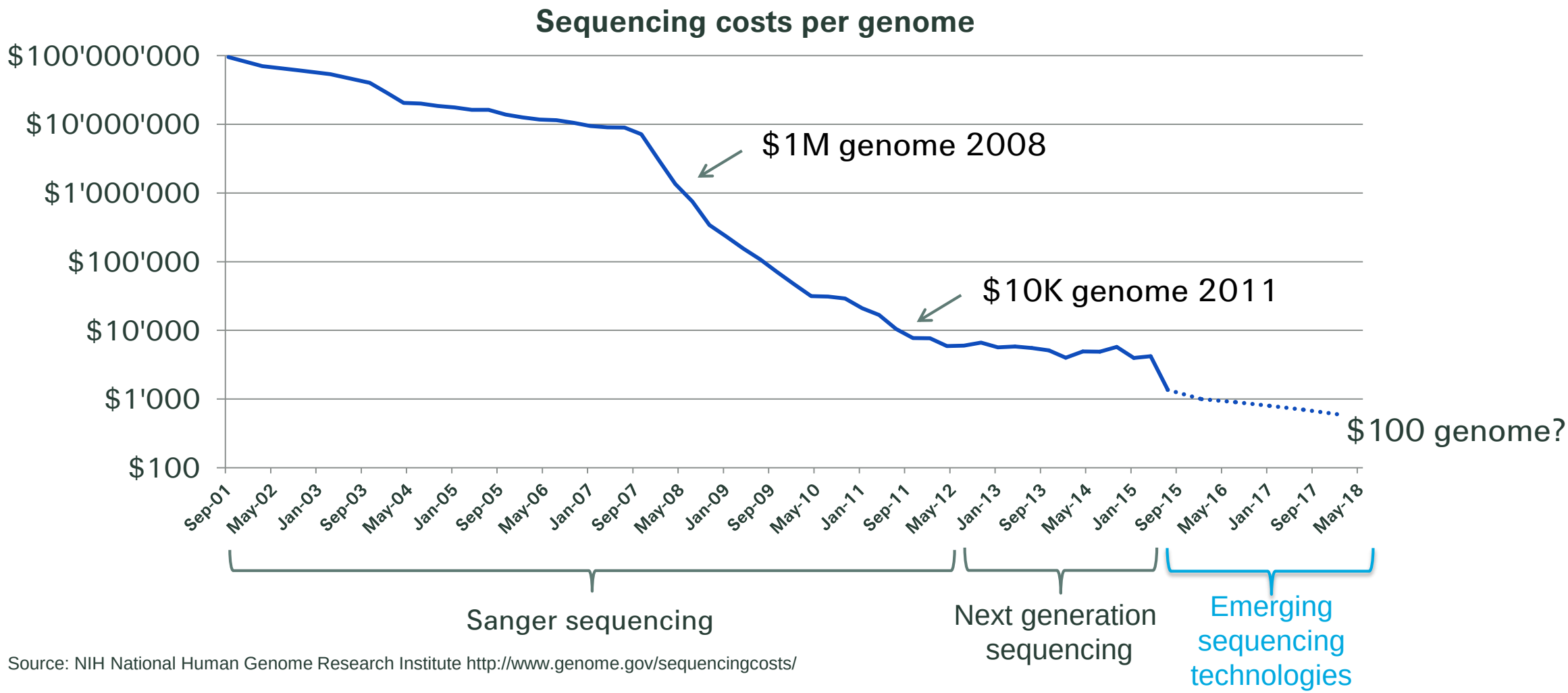
Whole Genome Sequencing







Full genome sequencing has become affordable

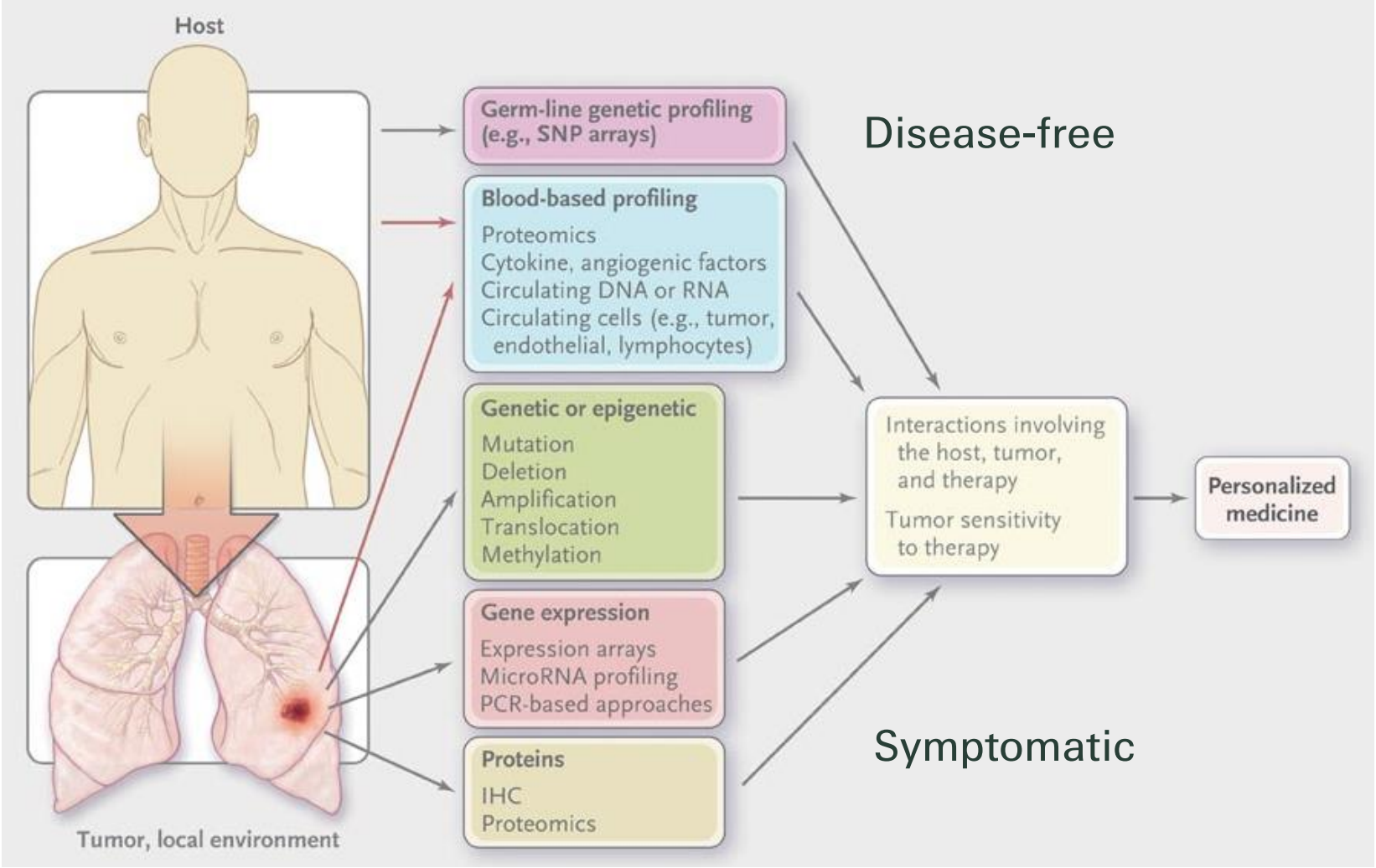


Source: NIH National Human Genome Research Institute http://www.genome.gov/sequencingcosts/

Molecular-profiling has become key to the development of personalised therapy

Personalised medicine

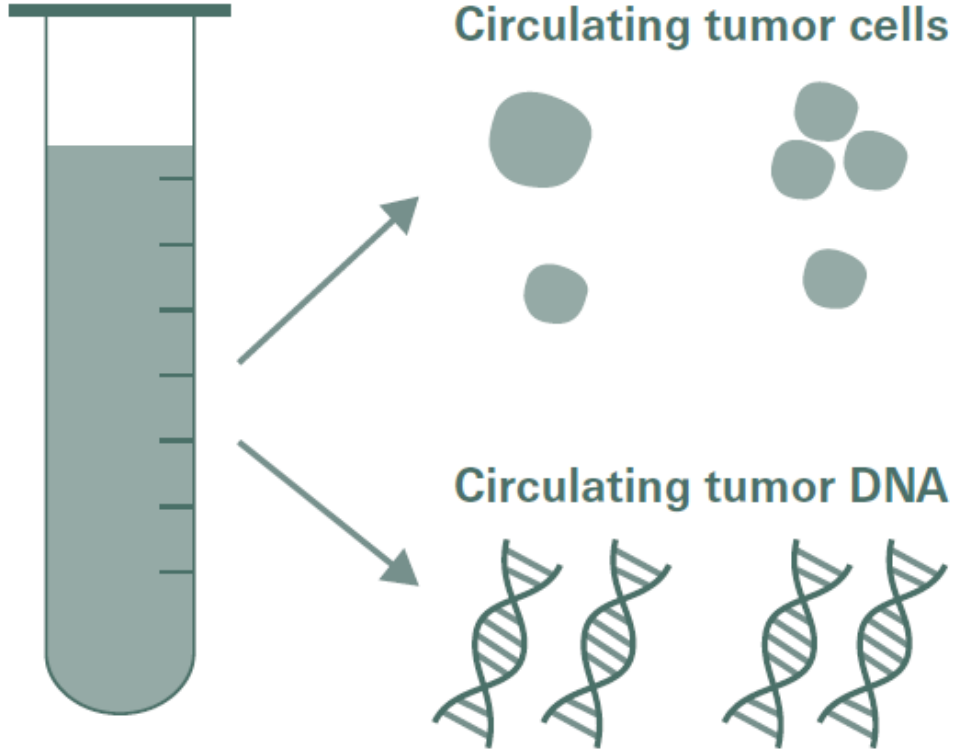
Understanding of genetic variability between individuals and using such personalised information for targeted healthcare



Source: Herbst R et al. N Engl J Med 2008; 359: 1367

Liquid biopsy is a novel cancer blood test that has the potential to revolutionize cancer care and provide personalized therapy guidance

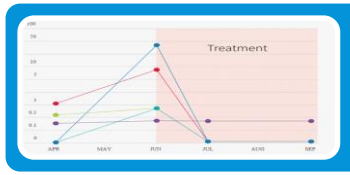
Liquid biopsy in Oncology
Nicola Aceto (University of Basel)



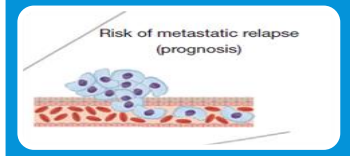
Key applications
- CTC counts for good vs bad prognosis assessment
- Ex vivo culture and testing of drug susceptibility
- Molecular analysis for patient stratification
- Understanding the biology of the metastatic process

Key applications
- Quantification of minimal residual disease
- Patient stratification
- Companion diagnostic / treatment eligibility
- Early cancer detection

Liquid biopsy provides the molecular understanding of the cancer and provides the hope to better manage cancer treatment through:

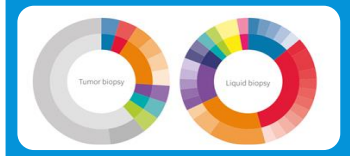


Real-time monitoring of treatment responses and resistance to therapy

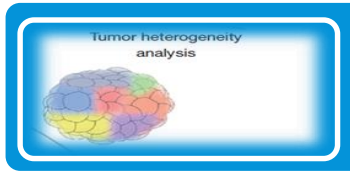


Detecting cancer relapse

Development of targeted therapies



Stratification and therapeutic decision making

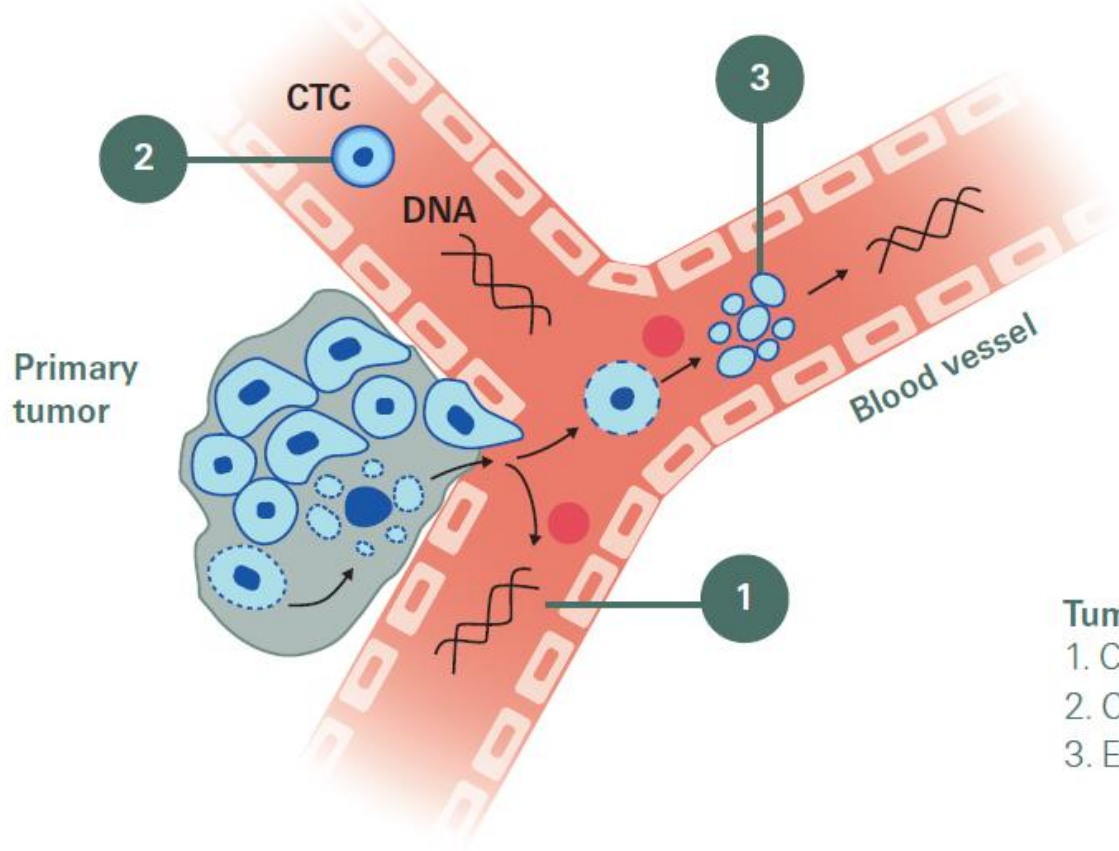


Better understanding of tumour evolution

Used as a cancer screening tool liquid biopsy has the potential to lead to overdiagnosis and impact cancer products

Liquid biopsy – a new blood test for cancer challenges the insurance industry

Giselle Abangma, Christoph Nabholz, Florian Rechfeld, John Schoonbee (Swiss Re)



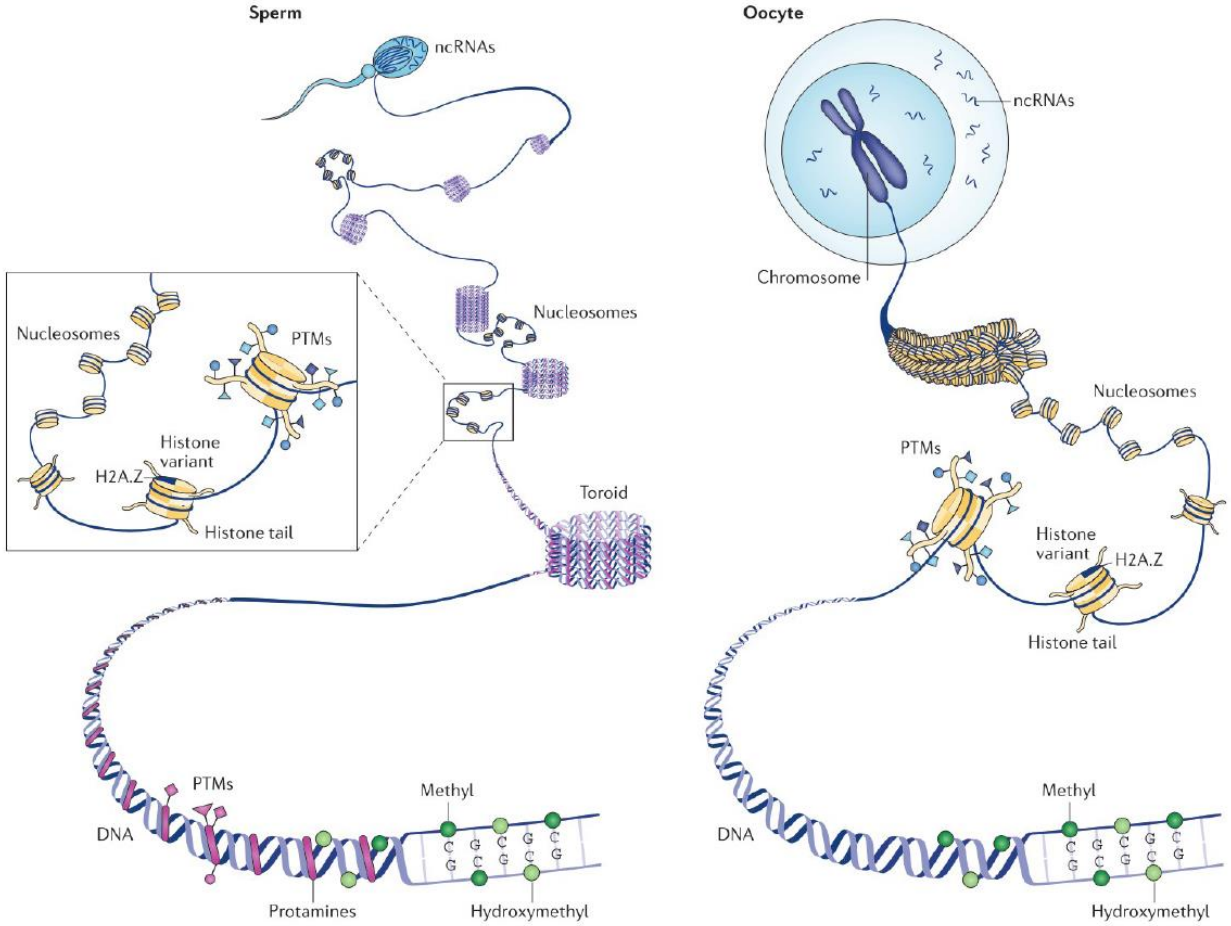
Tumor biomarkers in blood

1. Cell-free DNA (cfDNA)
2. Circulating tumor cells (CTCs)
3. Exosomes and micro vesicles

Heritable modification of the genome that does not change the DNA sequence

Transgenerational epigenetic inheritance: a paradigm shift in biology and medicine

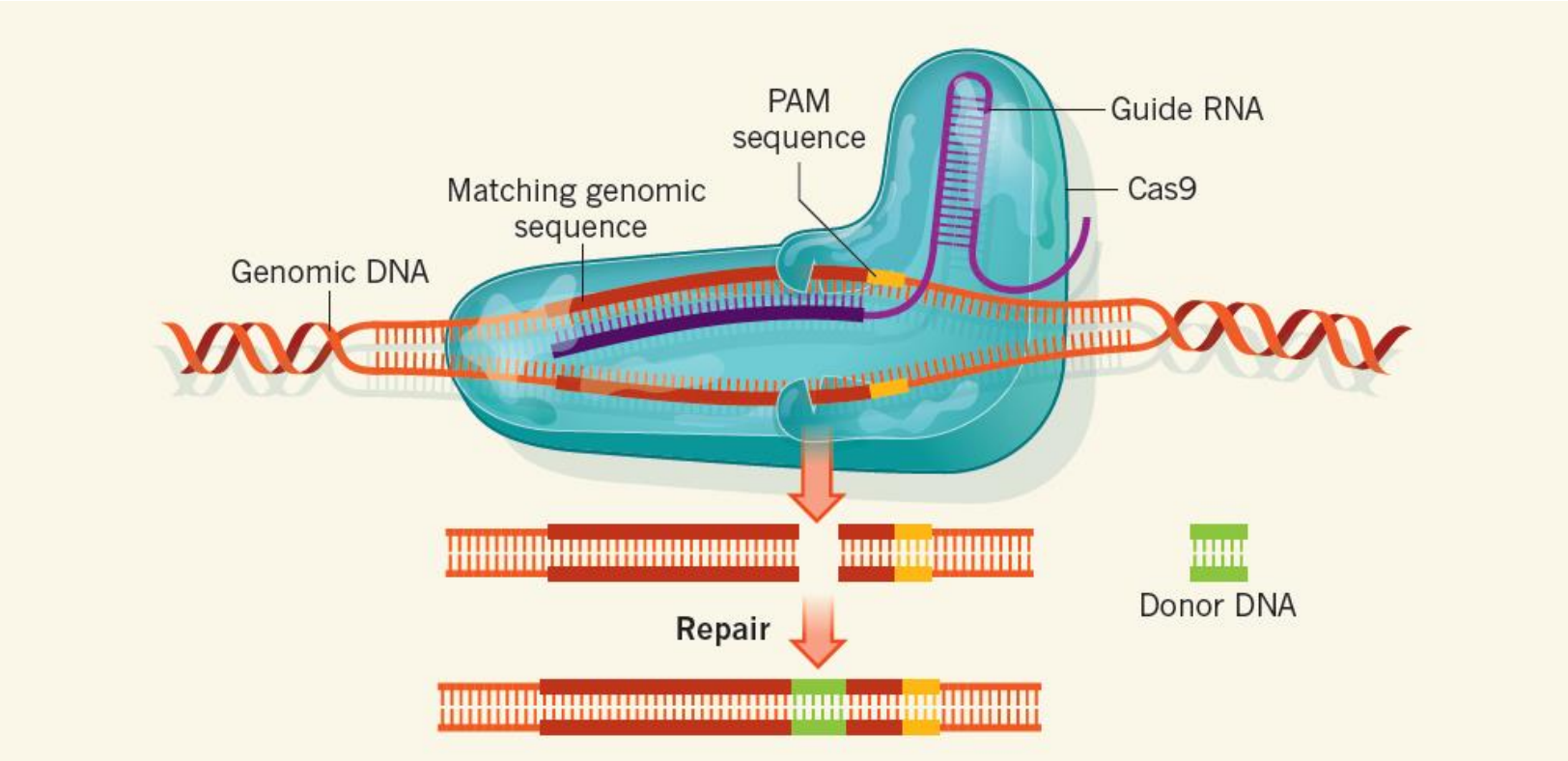
Johannes Bohacek, Isabelle Mansuy (ETH and University of Zurich)



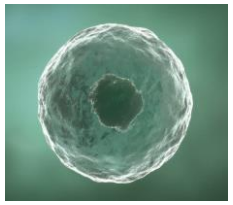
Gene editing could be used to cure genetic disease but is it ethical?

CRISPR – hacking the biological hard drive

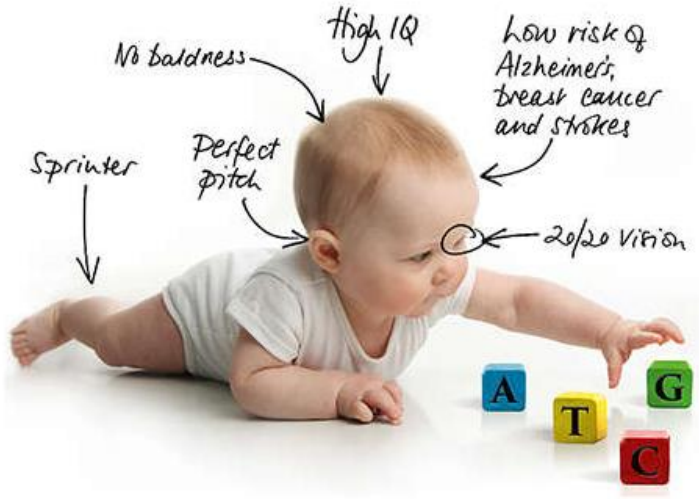
Thomas Wildhaber, Séverine Rion, Christoph Nabholz (Swiss Re)

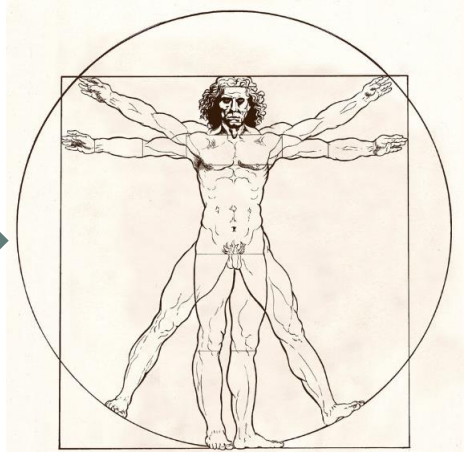


Human gene manipulation – Hopes and Fears



Embryonic
Stem Cell





Big Hope:

- Cure of genetic diseases

Big Fear:

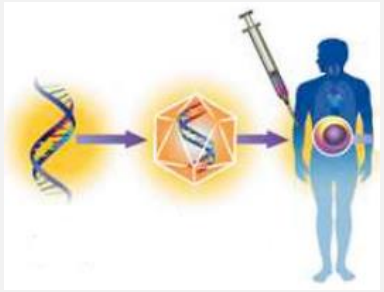
- Designer baby

Therapeutic approaches

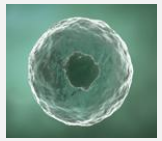
Gene therapy

Change gene defect

Treatment of affected tissue



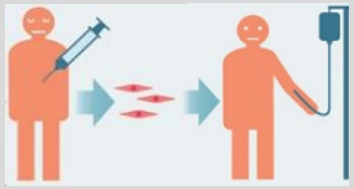
Embryonic therapy



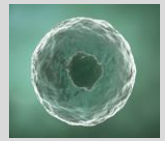
Cell therapy

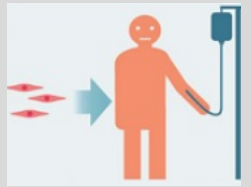
Reprogramming of stem cells to replace defective tissue

Adult stem cells



Embryonic stem cells





International law – Embryonic stem cell research

Country	Research permitted / prohibited	Country	Research permitted / prohibited
Australia	✓	Japan	✓
Canada	✓	Netherland	✗
Denmark	✓	Norway	✗
China	✓	Poland	✗
France	✗ highly restricted	Singapore	✓ no specific law
Germany	✗	South Korea	✓
Iceland	✓	Spain	✓
India	✓	USA	(✓) no gov. funding
Italy	✗	UK	✓

Insurance impact

Casualty

- Biohacking
  - Modified organisms may escape and lead to ecosystem impact
- Genetic Modified Organism
  - Regulatory restriction may lead to food recall
- Medical malpractice
  - Fatalities and health consequences may lead to liabilities

Life & Health

- New promising high tech therapies
  - Small patient groups with very high cost to health care system
- Risk of developing diseases
  - Good genes turn into bad ones and cause devastating diseases e.g. cancer
- Enhanced life span
  - Higher life expectancy will have pricing implications to pension, life insurance and disability insurance

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