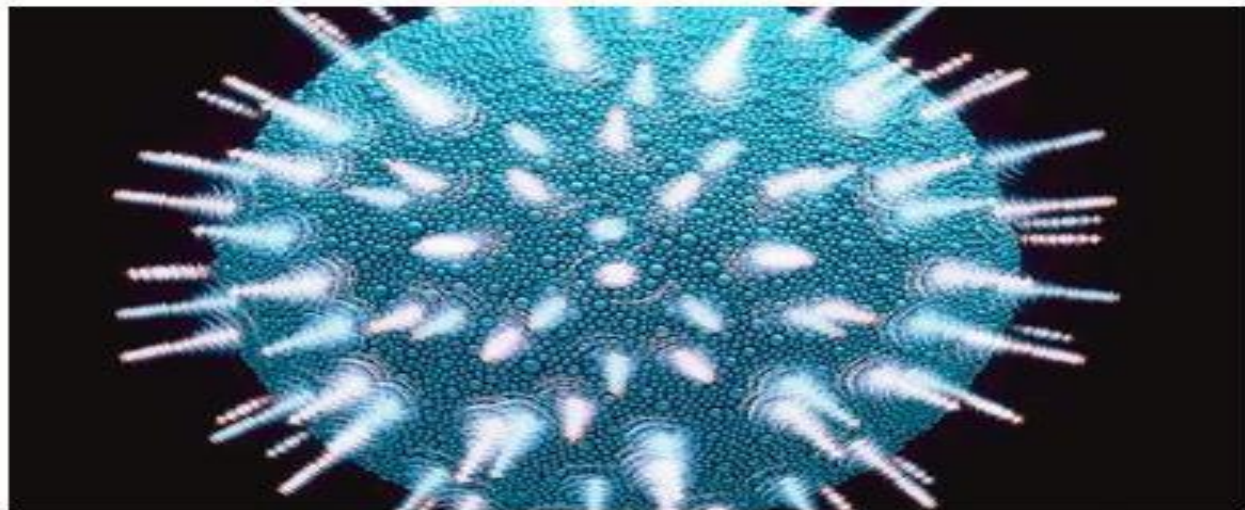


The Guardian

International edition ▼

HIV baby infected in womb is in long-term remission, doctors confirm

American girl, now three, was treated with aggressive cocktail of Aids drugs after birth and has remained infection-free



▲ The human immunodeficiency virus. Doctors are cautious about saying the child is cured as there is as yet no definition for a cure for HIV as there is for certain cancers. Photograph: Michael Freeman/Corbis

Associated Press

Thu 24 Oct 2013 12.22 BST





From “One Size Fits All!!” to
Personalised/Precisioned Medicine – Thought
Journey

Divya

Disclaimer

THE VIEWS AND OPINIONS EXPRESSED IN THIS PRESENTATION ARE THOSE OF THE AUTHOR AND DO NOT NECESSARILY REPRESENT OFFICIAL POLICY OR VIEWS OF NOVO NORDISK.

History

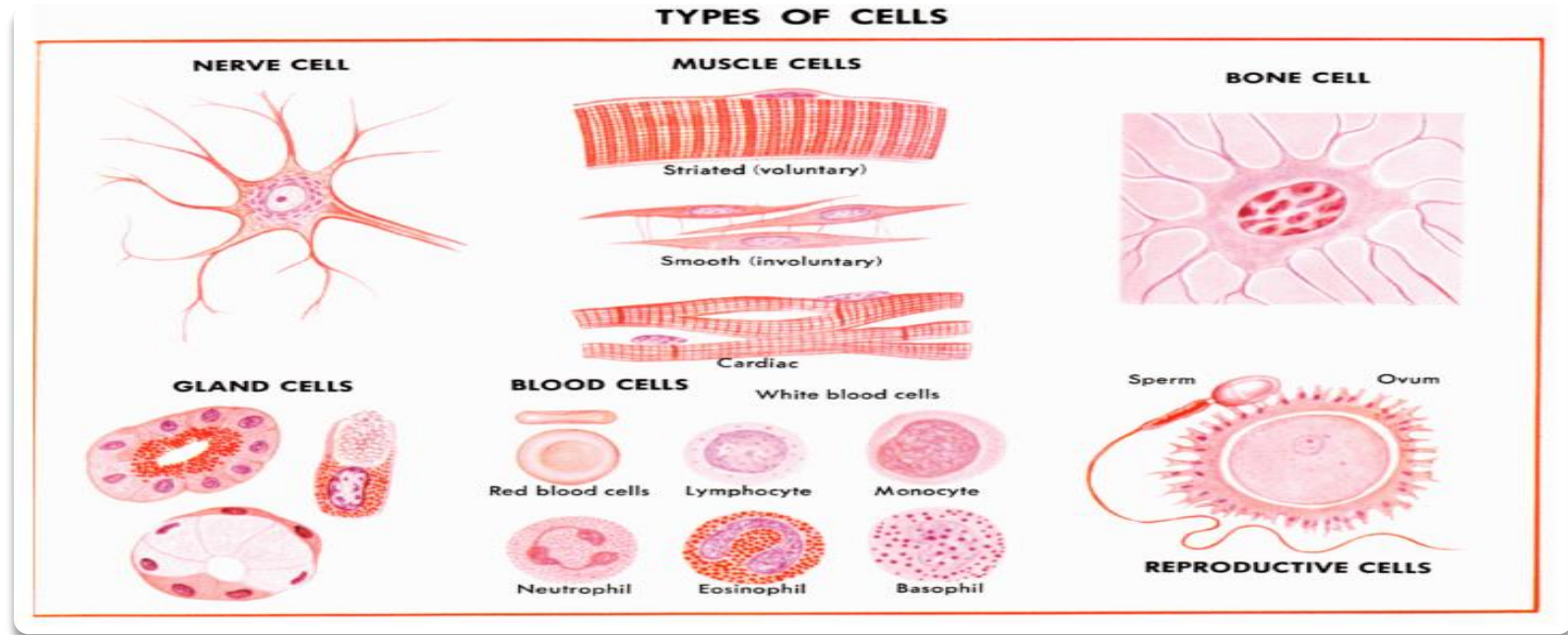
- ❑ **400 B.C.** Hippocrates noted “It is more important to know what sort of person has a disease than to know what sort of disease a person has.”
- ❑ **1953:** Francis Crick & James Watson discovered – DNA
- ❑ **1970's:** Frederick Sanger – developed Sequencing technique
- ❑ **1990:** HGP begins, termed as one of the biggest research projects of modern science has.”

Behind the scenes – Touch up on cells, DNA & Genome

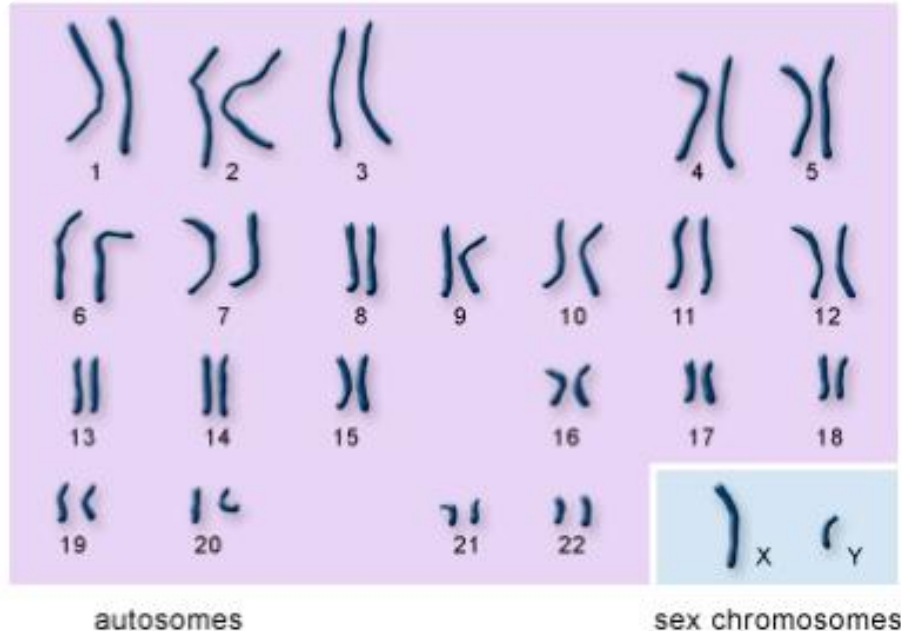


50-100 Trillion cells

Many different types of cells from Human body

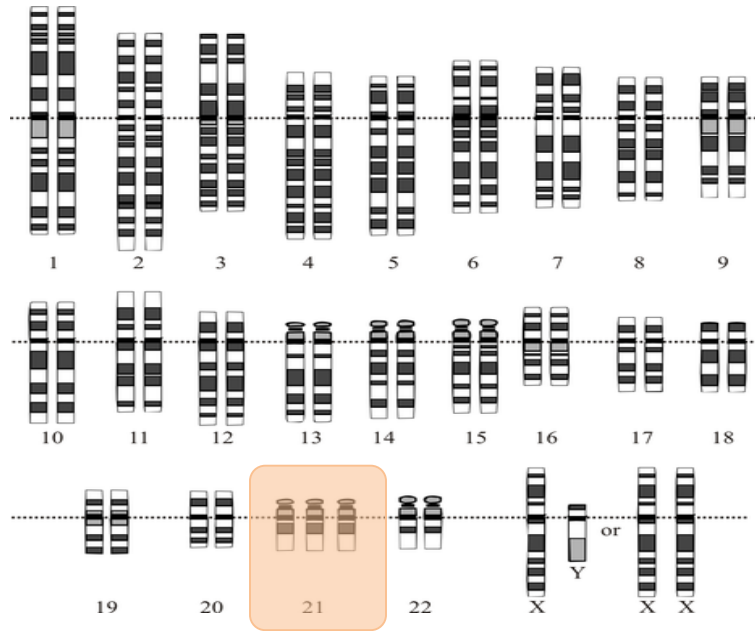


Chromosomes



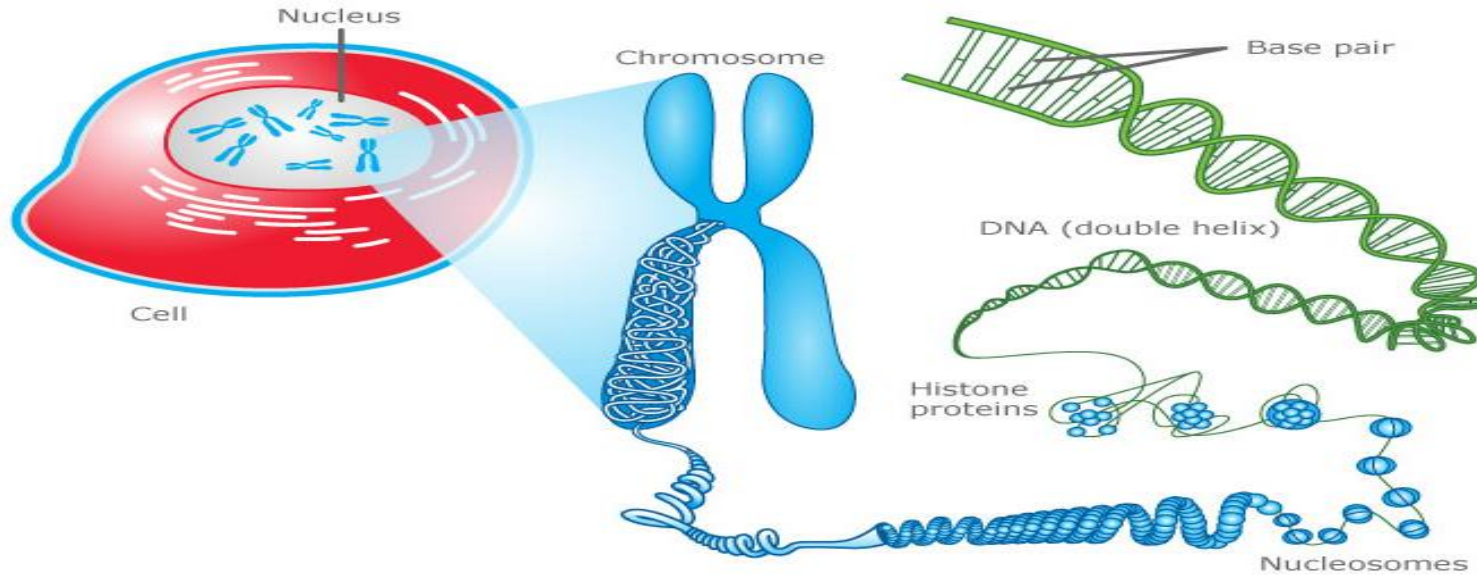
- DNA – Packaged into chromosomes
- People have **2 copies of 23 chromosomes**(one from each parent)
- Roughly – **3 billion base pairs * 2**(Human)

Chromosomal Abnormality

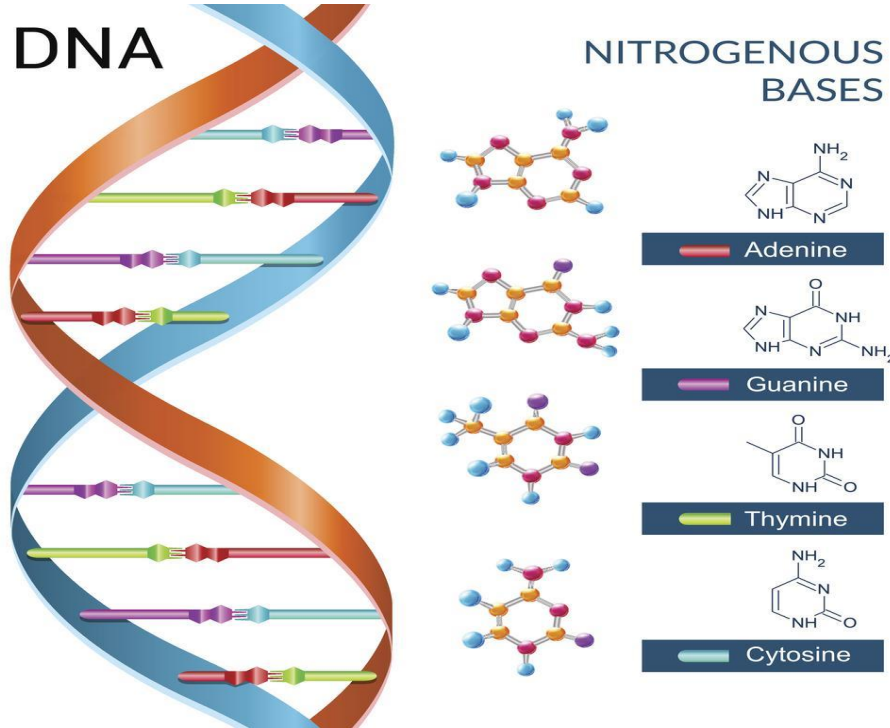


- Down's Syndrome/Trisomy 21
- **Caused by – failure of 21st chromosome** to separate during egg/sperm development.
- Mosaic Down Syndrome.
- Associated – Physical growth delays, characteristic facial features and mild to moderate intellectual disability

DNA packaging

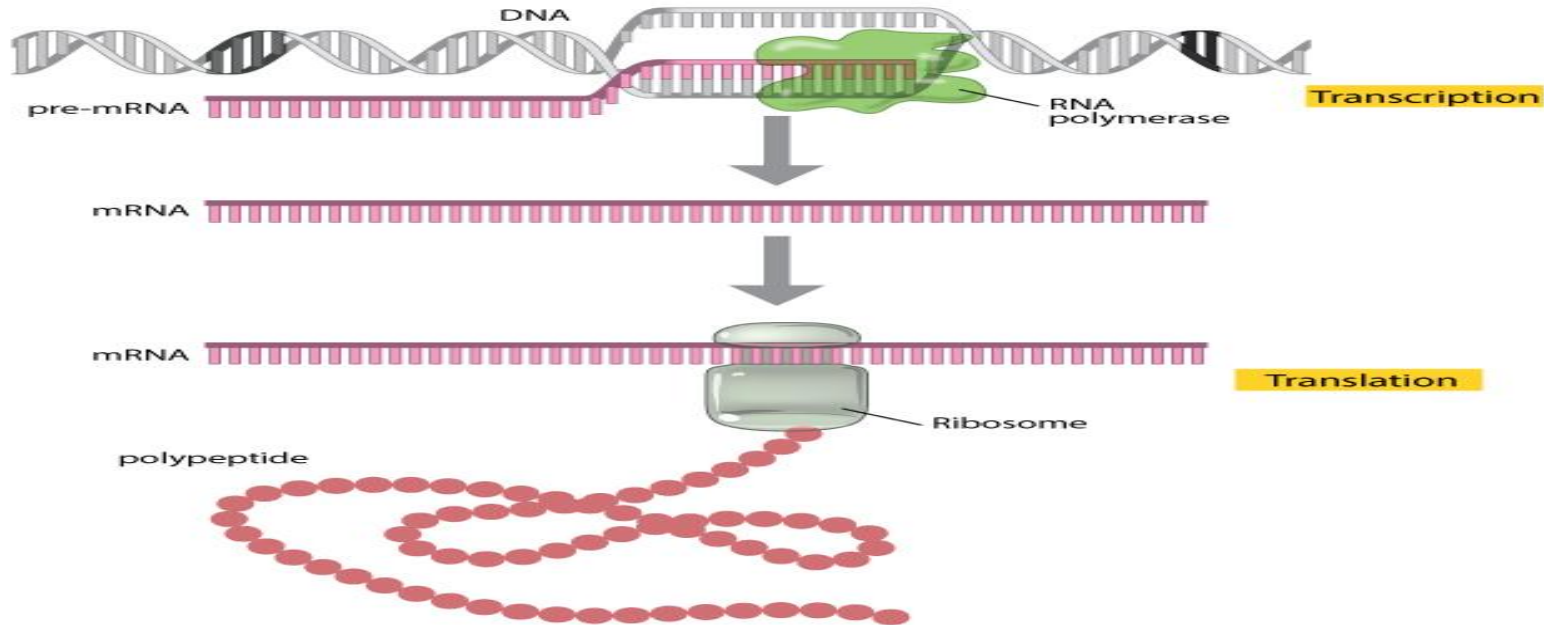


DNA(Deoxy Ribo Nucleic Acid)



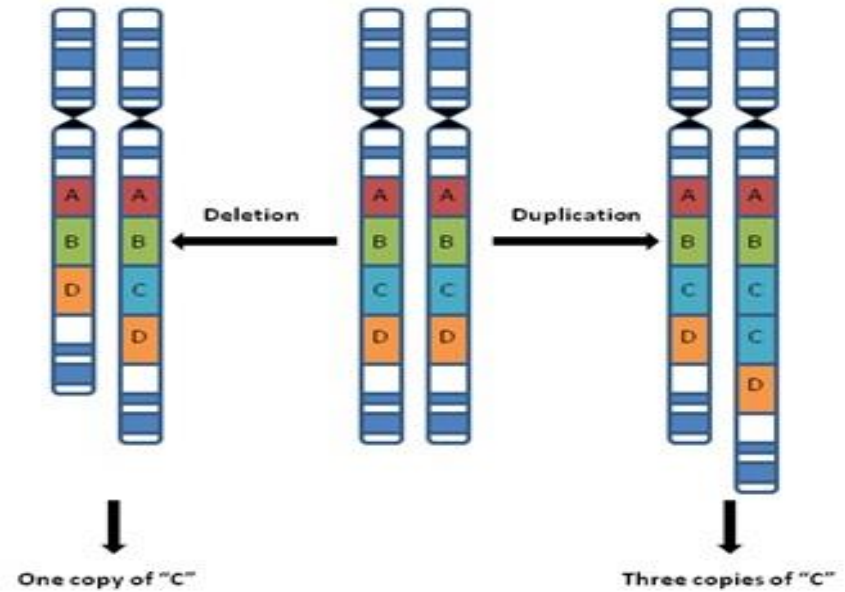
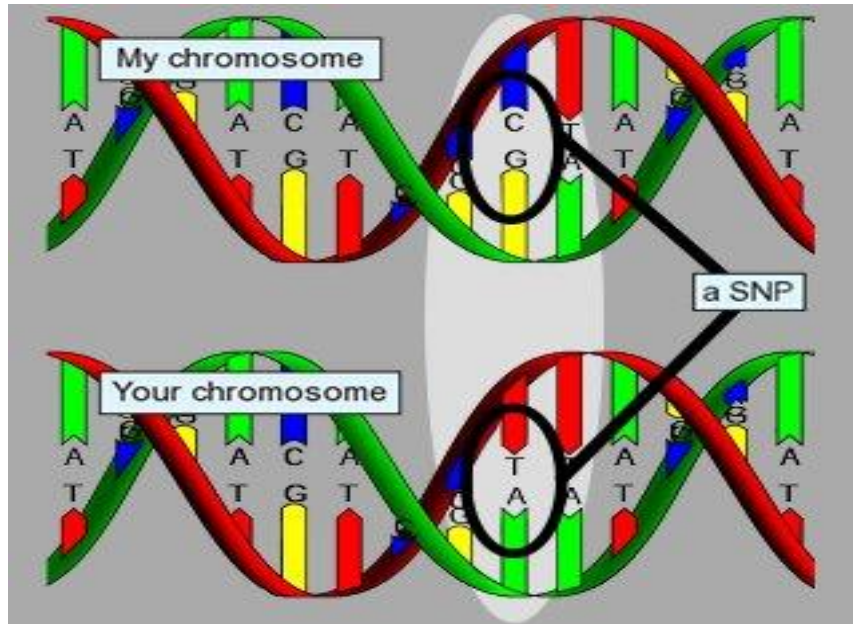
- **Double Helical structure**
- Genome Unravalled – 200 phonebooks, 1000 page phone books
- **Unique recipe** - you

DNA Transcription – Gene Expression



SNP's & CNV's

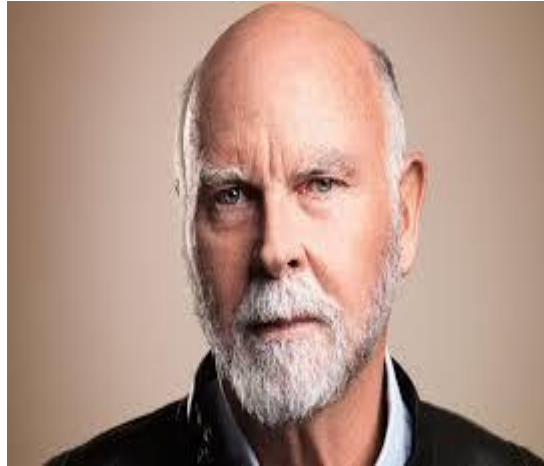
Refer to slide#8 & #10



Story of Human Genome project



Steve Quake



Craig Venter



Ozzy Osbourne – Rock star – “Black Rain”[2007], “Scream”[2010]



Next Steps – field of genetics in relation to sequencing

- Next Generation Sequencing machines:
- 454 DNA sequencer – Roche (1st developed by 454 Life sciences & purchased by Roche – 2007, Read length – 700 bp, Data output per run – 0.7gb)
- Illumina Genome Analyser II sequencing machine (Read length – 100*100 bp paired end, Data output per run – 600gb)
- 1000 Genome sequencing project.



Why Sequence Genomes?



Jim Wright – Charcot – Marie – Tooth disease

Why _ _* consider sequencing?

You Might*

- Information is wealth
- To know sensitivity to medicines/Drugs (Pharmacogenomics)
- Want to know if you may get certain disease
- Curiosity

You might not*

- Is Information a wealth?
- Most disease are really complex, we don't know how to make use of the info.
- Unnecessary worry – Genetic discrimination by employers, insurance companies

Impact – Genomics in Medicine

- Pre-disposition Testing – Determines who is at a risk for disease
- Pharmacogenomics – Determines which and how much of the drug is best for an individual.

Examples – Predisposition Testing

- **BRCA1/BRCA2**
 - Screening in women with a significant family history of Breast cancer/Ovarian cancer may help in early diagnosis if present.
- **Long QT syndrome(Cardiac Condition):**
 - Screening of individuals with LQTS may help establish what type of LQTS is present and guide disease management. (As different mutations can cause arrhythmia)

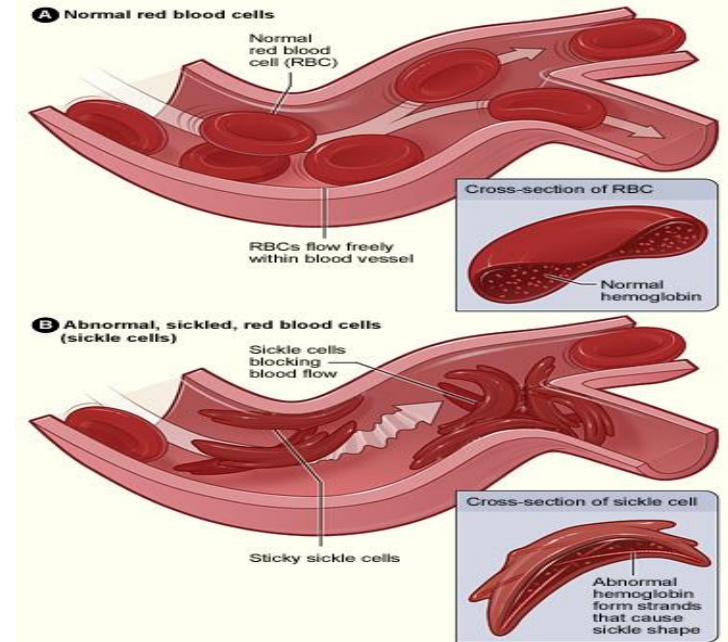
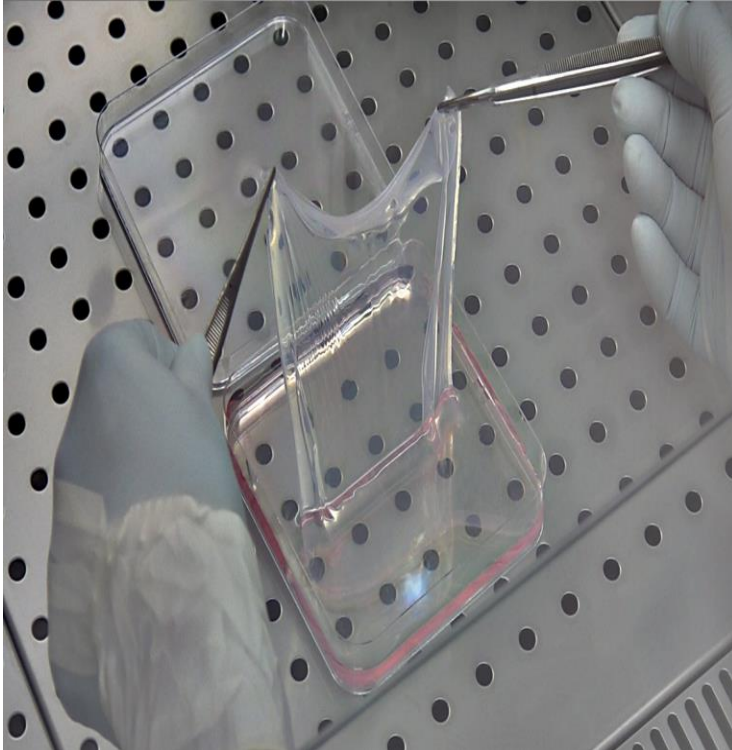
Pharmacogenomics

- For a certain percentage of individuals with hypertension, depression & diabetes do not respond to drug treatment.
- People differ in how they respond to drugs in part due to genetics
- Genetic factors influence:
 - Drug Concentration in the body
 - How active a drug is against its target

Based on Pharmacogenomics – Matching Drug to disease

- Her2(Human epidermal growth factor receptor 2) Breast Cancer
- Treatment - Herceptin (chemical name: trastuzumab), Nerlynx (chemical name: neratinib) *et cetera*.
- IRESSA® is a targeted therapy – a tablet taken once daily , NSCLC with certain types of abnormal epidermal growth factor receptor(EGFR) genes.

Recent Innovations

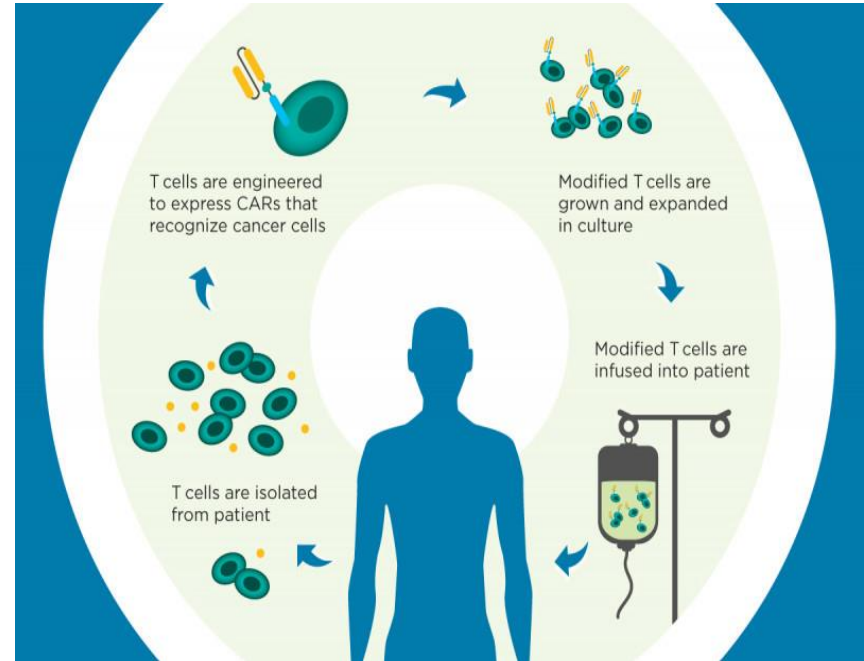


Cure for sickle cell anaemia

(Cont'd)



Allison Corona, 25, Leber congenital Amaurosis - Luxturna.



“Giving patients a living drug”

Statistical & Programming Challenge's

- Processing Large scale data
- Functional effect and impact of genetic variation
- Translation of study data into medical practice
- Disease classification system

Processing Large scale data

- The computing resources needed to handle genome data will soon exceed those of Twitter and YouTube, says a team of biologists and computer scientists who are worried that their discipline is not geared up to cope with the coming genomics flood.
- Human genomes – 20-25k genes, 3 million bp, which in turn leads to 100 gb of data, equivalent to 102,400 photos.
- Sequencing multiple genomes will add upto hundreds of petabytes, and the data created by gene interactions will multiply it further.

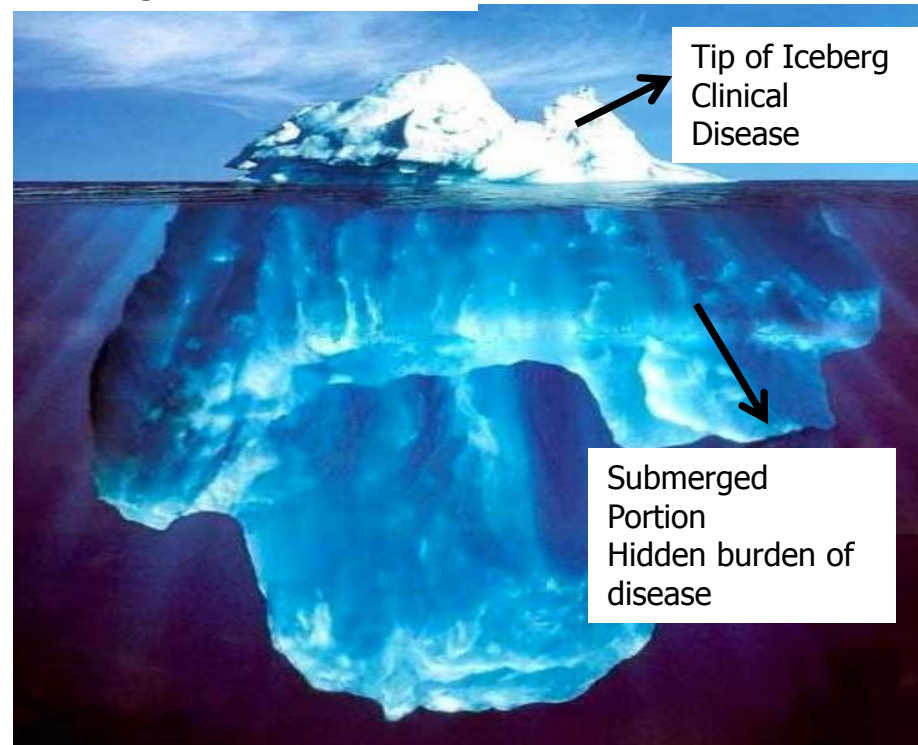
Functional effect and impact of genetic variation

- In real-world sequencing approaches, read lengths are short (that is, ≤ 250 nucleotides) and can contain sequence errors.
- When considered alone, an error is indistinguishable from a sequence variant.
- This problem can be overcome by increasing the number of sequencing reads: even if reads contain a 1% variant-error rate, the combination of eight identical reads that cover the location of the variant will produce a strongly supported variant call with an associated error rate of 10^{-6}
- With this kind of data – evolve many models, simulations but statistical analysis has not been that broadened.

Translation of Study Data into Medical Practice*

- These new sequencing technologies, help us identify gene mutations, which in turn helps in developing novel therapies.
- Genomic & Phenotypic data can then be combined with epidemiological data to design disease prevention campaigns

Iceberg Phenomenon



*Discussed in personalised medicine conference organised by European commission in July 2016

Disease Classification System

- WHO, ICD-10 (7 digits), October 1 2015 change from ICD-9 to ICD-10
- Achilles Tendon Strain S86.011 D (1st character – body system, next 2 digits indicates disease, Subsequent digits adds more specificity, last alphabet – initial/subsequent encounter).
- But while utilizing genomics, we have to use the information such as: common genes underlying a disease, environmental factors.
- Example: Cardiovascular, Diabetes – lifestyle changes

Conclusion

- HGP
- Why/Why not sequencing
- Recent advances
- Challenges: Large scale data, Error rate, Translating data to medical practice & Disease classification system

Acknowledgements

1. <https://www.technologyreview.com/s/609380/gene-therapy-grafts-have-repaired-a-childs-devastating-skin-disorder/>
2. <http://www.nejm.org/doi/full/10.1056/NEJMoa1609677>
3. <https://edition.cnn.com/2017/03/03/health/sickle-cell-anemia/index.html>
4. <https://www.theguardian.com/news/datablog/2013/mar/15/john-snow-cholera-map>

“Innovations &
care”

It's just the beginning
Thank You!!