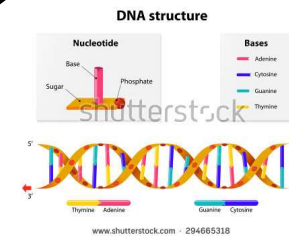
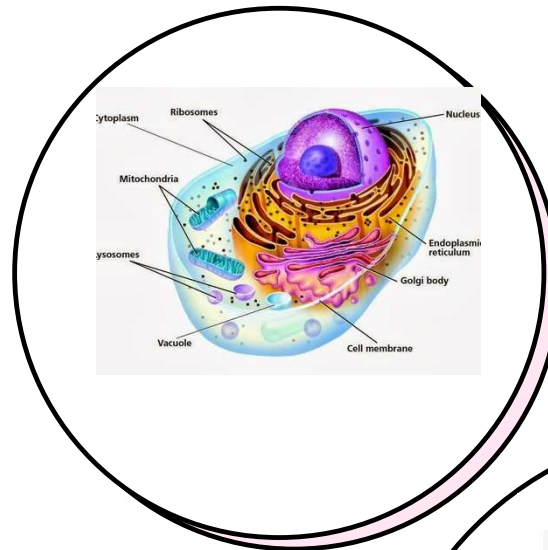


MEDICAL MATTERS UPDATE 22ND JUNE 2023

JAN ATHIS
U3A SCIENCE
GROUP





Jan's mantra for Good Health –

“Know your genome” and “Look after your immune system”

*Assumes know implications of
genotype*

Easier said than done!!

The total length of the human reference genome.... is over 3 billion base pairs.

genome = 22 paired chromosomes, (autosomes), plus pair of sex chromosomes (XX) in the female, and (XY) in the male. (20,000-25,000 genes)

[Human genome - Wikipedia](#)

70% of original human genome (published 20 years ago) from **one person**

Latest version (pangenome)- data from 47 people from Africa, Asia, the Americas and Europe

<https://www.bbc.co.uk/news/science-environment-65539594>

99.9% of human genes are similar to each other *Biologist* 63 (4) 2016

98% of our DNA sequence is the same as that of a chimpanzee

1-2% difference is the equivalent of 10s of millions of different base pairs

Discovering which genes (if any) affect disease susceptibility could help with **diagnosis** –
and **POTENTIALLY treatment**

Basic question do you want to know what disease you're likely or might develop

- 1) if there's no treatment, or treatment benefits parent, not children
- 2) if the disease is devastating



Genetics and Health / Disease

UK gov are supporting prospective study for whole genome sequencing of 100,000 babies to be screened for 200 rare (potentially) treatable, but not necessarily curable conditions
(eg bone marrow transplant for babies with immune system failure).

heel prick test currently test for 9 conditions

Will parents support this approach or would they prefer ignorance?

MLD metachromatic leukodystrophy is a genetic disease, causing toxic build-up of lipids etc in myelin of CNS, resulting in progressive CNS and NS failure. Babies diagnosed unlikely to live to 5years.

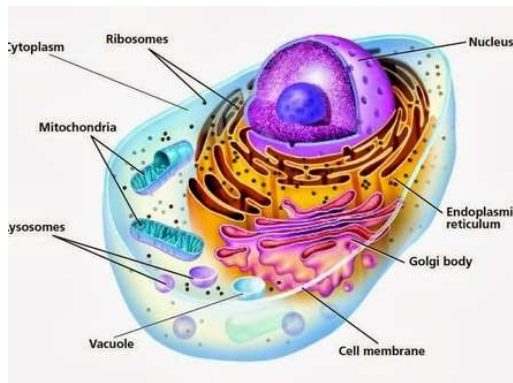
Recent treatment : - patient's cells harvested, genetically manipulated and reintroduced. This is NOT a cure

Cost = more than £2.8 million per patient



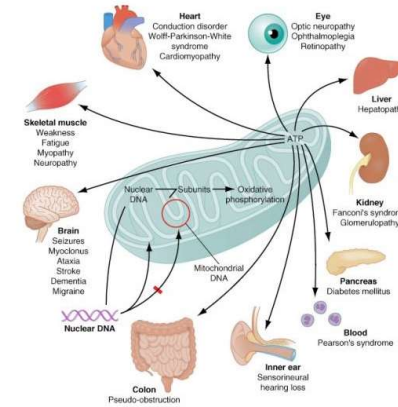
Genetics and Health / Disease

Mitochondrial Disease – and “3-Parent” Babies <https://www.nature.com/articles/d41586-023-01585-x>



Mitochondria = “Power House of cells”
Occur in almost ALL cells (not sperm) .
Uniquely have own DNA that is inherited from mother (via ovum)
Believed to have been derived from Archaea

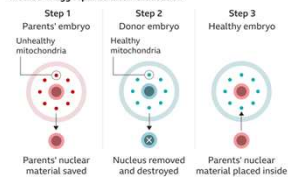
Faulty genes in mitochondria lead to
“Mitochondrial Disease” which can
compromise every body system but varies
in severity



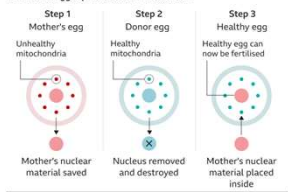
Fauci AS, Kasper DL, et al.: Harrison's Principles of Internal Medicine, 17th Edition

Two ways mitochondrial donation can work

Method 1: Egg repaired after fertilisation



Method 2: Egg repaired before fertilisation



The [first baby born via this technique](#) was in US in 2016

This donor DNA is only relevant for making effective mitochondria, does not affect other traits such as appearance and [does not constitute a "third parent"](#).

At least one such baby born in UK but no papers yet to protect parents & children from unwanted publicity
(*Louise Brown IVF resulted in = death threats*)



Source: MFEA
02/07/2023



Cancer

New study to test for 50 different cancers

<https://www.ox.ac.uk/news/2023-06-02-multi-cancer-blood-test-shows-real-promise-nhs-trial>

“SYMPLIFY” MCED trial started July 2021

Participants selected on basis of symptoms indicative of cancer

1st Blood sample



12 Months

2nd Blood sample



12 Months

3rd Blood sample

50% of samples → Galleri MCED test

50% of samples, stored for future MCED test
ONLY IF person gets cancer diagnosis

MultiCancer Early Detection test (MCED Galleri test) detects chemical changes in cell-free DNA [cfDNA] part of which is **ctDNA [tumour cell DNA]**) that has leaked into blood plasma from lysed tumour cells.

Galleri test has low false +ve rate (<1%) But positive **does not mean that a person definitely has cancer**.
They might have cancer - follow-up tests needed



Cancer

SYMPLIFY MCED trial

Results: correctly revealed two out of every three cancers in more than 5,000 people

[6238; 5,461 evaluable patients]

correctly identified the original site of cancer in 85% of those cases.

‘The high overall specificity, positive predictive value, and accuracy of the cancer signal detected and cancer signal origin prediction that was reported across cancer types in the SYMPLIFY study indicate that a positive MCED test could be used to confirm that symptomatic patients should be evaluated for cancer before pursuing other diagnoses.’ Oxford Cancer, Oxford university

"This quick and simple blood test could mark the beginning of a revolution in cancer detection and treatment here and around the world,"

England's Chief Executive Amanda Pritchard.



Antibiotics

February 2023: Genetic link identified to neonatal susceptibility to antibiotic induced cochlear hair cell damage (deafness), allowing selection appropriate antibiotic

<https://www.nice.org.uk/news/article/nice-recommends-genetic-test-to-prevent-newborn-babies-going-deaf>

Reminder about antibiotics (as if you need it!)

factory farming is the greatest use of antibiotics worldwide

in some countries antibiotics are over the counter drugs IE no prescription needed

annually antimicrobial resistance results in **1.3 million direct deaths & 5 million deaths indirect deaths**

new antibiotics not developed because of profitability (pharmaceutical companies develop drugs to SELL – antibiotics wanted for JIC – not for routine use so pharma not getting money for development work)

Proposed that **NHS uses Netflix model** IE **pay a flat fee to decouple payment from usage** (being trialled in Canada and USA)

The Lancet criticises the model as not supporting small pharma that may be as able as Giant pharma to identify very useful antibiotics as Giant Pharma

May 2023 – New Gov Money <https://www.gov.uk/government/news/39-million-for-amr-research-as-uk-launches-global-health-framework>

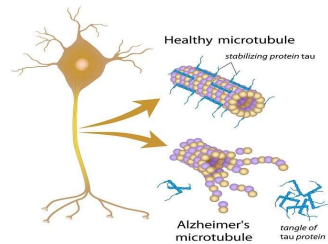
02/07/2023

Alzheimer's Dementia (AD)

1970-80s Plaques and Tangles found in brains of AD patients (**post mortem!!**)



Amyloid protein
(**Cytotoxic**)
no 'normal' function in
body



TAU proteins
[Tubulin Associated Unit]
help maintain microtubules
open allowing exchange of
information and nutrients

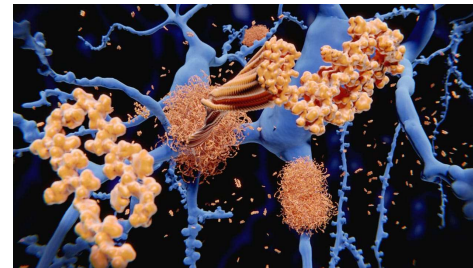


Diagram of AD brain
Blue = Nervous system
Brown = plaques &
tangles

BY DEFINITION – Alzheimer's involves PRESENCE of amyloid, but often diagnosis made **without** this being assessed [*doesn't affect current treatment*]

Presence of TAU seems best correlate of clinical picture



Early-stage Alzheimer's disease

<https://www.alzheimers.org.uk/blog/lecanemab-new-drug-early-stage-alzheimers-disease>
<https://www.nejm.org/doi/full/10.1056/NEJMoa2212948>

January 2023 US Food and Drug Administration (FDA) approved immunotherapy drug LECANEMAB (aka BAN2401, marketed as Leqembi) as a treatment for early Alzheimer's disease

Study Design ("Clarity – AD" Phase 3 Clinical Trial Cohort 1800 matched for presence of amyloid protein (1795 people reported Nov 2022))

Establish baseline Cognitive Function (as assessed by interviewing patient & Carer), then repeat 3-monthly for 18 months.

Caregiver included to assess their burden since Alzheimer's has adverse effects beyond those actually experienced by the patient

Results (taken from Alzheimer's Soc report)

Cognitive decline in both treatment and placebo group

27% slower in the treatment group Meaningful to the patients

Quality of Life also improved in treatment group

Amyloid 400 brains from the treatment group scanned; 70% had lower amyloid than prior to treatment cf 5% increase in the placebo group

LECANEMAB works with immune system to clear amyloid protein from brains of people living with early-stage Alzheimer's disease

Treatment not Prevention

Adverse Effects include

Brain Bleeds (17% treated group, to 9% in the placebo group)

brain swelling with inflammation 13% treatment group , < 2% in the placebo growth

Deaths two deaths in the treatment group (=0.7% ; 0.8% in placebo group) Participants 50 – 90 yrs

Second major trial of this drug is starting in 2023

02/07/2023



Thank You

Discussion Time