

# Science Group 24 March 2022

Biomedical Report  
Selected by Jan Athis

**Things that have caught my eye (more often EARS – Radio 4!) and that aren't all about Covid!**

## Biomedical Report March 2022

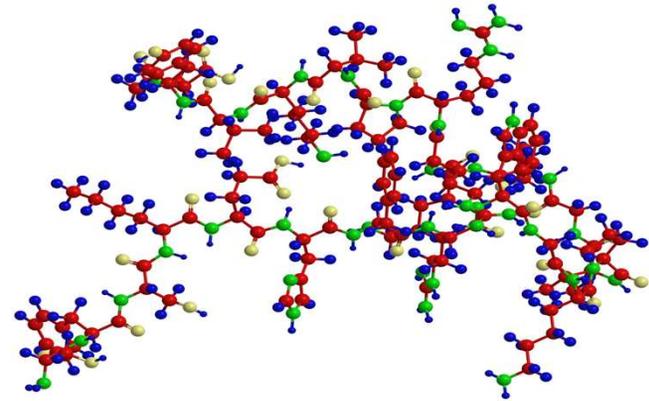
**PROTEINS** (strings of amino acids) are **LIFE**

**No PROTEINS – No LIFE** (*as we know it*)

The **FUNCTIONALITY** of a protein depends on its **STRUCTURE** (folding)

Determining the structure of proteins underpins understanding of diseases and thereby treatments. Some diseases (eg cystic fibrosis) are due to mal-folding of key proteins

It took Dorothy Hodgkin **30 years** (and a brilliant mind) to determine the structure of insulin (peptide hormone) using the standard technique of X-ray crystallography



**Nov 2020** Algorithm (neural network) “alphafold” can create a 3D shape from an amino acid sequence with greater accuracy than 100 other competitors in annual “prediction” challenge.

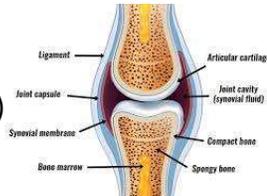
“Nature”: Nov 2020 **‘It will change everything’**

**I’ll concentrate on proteins in the rest of this summary**

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### OSTEOARTHRITIS

Cartilage wears down ;  
synovial fluid (lubricant)  
decreases; bone ends  
grind on each other



lubrication complex of synovial fluid = hyaluronic acid ie backbone with feathery **glycoprotein** (lubricin) subunits that bind water plus a lipid subunit.

An **artificial** version of this has been produced (*New Sci Oct 2021*). The **protein** holds water (lubricant) and the complex aids cartilage regeneration

### CANCER

"cancer pathways" 100,000s genes and their **proteins** involved in cancer pathways. But each cancer **unique to the person** (different combinations of mutations causing the uncontrolled proliferation). Chemotherapy indiscriminate killing of rapidly dividing cells (*i.e. cancer cells but also e.g. those in gut and hair follicles – fatigue, nausea, hair loss etc*)

#### Alternative approach

Personalised Medicine determine & interfere with specific **proteins** so slowing proliferation or killing rogue cells.

Monoclonal antibodies are lab produced **proteins** – (i) aid destruction of cancer cells by immune system (ii) directly stop cancer cells from growing / surviving (iii) carry toxins to cancer cells.

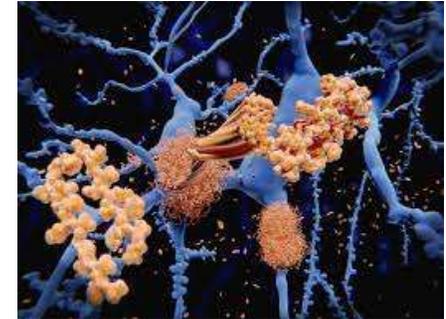
Diagnosis engineered bacterium (*Acinetobacter baylyi*) to ID single letter mutation in KRAS gene (indicative of cancer in gut; better than using faecal sampling where endogenous enzymes can “chew up” DNA)

Can also be used to identify eg cholera in drinking water; malaria in mosquito breeding waters; toxic fungi on crops (ergot)

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**DEMENTIA (Alzheimer's)** is associated with presence of “amyloid **protein**” in the brain, that may interfere with neurological function; cause or effect?

Immunization against  $\beta$ -amyloid has been explored for 20 years, as yet unsuccessfully, as treatment for Alzheimer's and immunotherapy has come under considerable criticism following the negative results of several phase III clinical trials (<https://pubmed.ncbi.nlm.nih.gov/33260956/>)



**Last year (2021)** A promising new approach to potentially treating, and vaccinating against Alzheimer's disease has been developed by researchers at the University of Leicester, the University Medical Center, Göttingen, and the medical research charity LifeArc.

Rather than focus on the amyloid beta ( $A\beta$ ) protein plaques in the brain, the antibody and vaccine both target a different, soluble form of the **protein**, which is thought to be highly toxic. The team's studies, reported in *Molecular Psychiatry*, showed that both the antibody-based treatment and the protein-based vaccine reduced Alzheimer's symptoms in mouse models of the disease..

(remember – antibodies are also proteins!!!!)

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**VACCINATION** - NOT anti-coronavirus vaccinations!! (did you know there are over 20 CoVid 19 vaccines currently in use?)

**CERVICAL CANCER** – caused by human papilloma **viruses (>100 types)** New vaccine (2022) active against wide range of HPV  
Could mean one screen only needed in lifetime (currently “regularly” between 25y & 64y)

**MALARIA** – caused by plasmodium (protozoan parasite a eukaryote NOT bacteria NOT virus), transmitted by mosquitos  
Kills 250,000 children every year in African countries

**Oct 2021** the first vaccine ever for malaria was approved for use even though only has a 30% protection against severe disease

**SICKLE CELL DISEASE (SCD)** the commonest genetic blood disease 300,000 births annually worldwide

SCD is aberration in red blood cell [rbc] formation persists in population as offers some protection from malaria (the distorted rbc do not easily harbour plasmodium, but have impaired O<sub>2</sub> carrying capacity. Also, too many distorted rbc will jam in blood vessels in joints causing excruciating pain).

Current treatments hydroxycarbamide tablets and regular blood transfusions (not always effective for severe disease).

**Oct 2021** . Crizanlizumab is a new intravenous treatment option [30min infusion every month] that can be taken on its own or alongside hydroxycarbamide. It is a monoclonal **antibody** that locks up p-selectin – a **glycoprotein** involved in coagulation.

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**Jan's mantra for Good Health – “Know your genome & look after your immune system”**

Human genome project **>10yrs** (Oct 1990 - Apr 2003), two years ahead of schedule  
and cost around **\$3billion** – which was less than the original estimated budget.

So, 20 years ago, not a lot of people could know their Whole Genome  
Sequence (WGS) !!

**But we could look after our immune systems**

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### **THREE years ago .....**

Nov 2018 “Cambridge-based **Veritas Genetics** lowered its **\$999** whole genome sequencing and interpretation service to **\$199 for two days**, or to the first 1,000 people who bought spit kits.”

**And the WGS could be measured in a matter of couple of hours**

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This is **HUGE** step forward but genetic component of many diseases still unknown - Some involve 100s genes PLUS epigenetic factors. Also – some genes have multiple actions (*a random example - the **protein** coded by *Pdxi* gene influences embryonic pancreatic development AND switches insulin gene on / off*)

**Example:** “repeat expansion disorders” caused by insertion of short repetitive chunks of DNA into genetic code are associated with some neurodegenerative & movement diseases (eg Fragile X syndrome, Huntingdon's Chorea, Friederich's ataxia & some forms of amyotrophic lateral sclerosis (*ALS – a form of MND*) & frontal lobe dementia.

Comparing WGS of people with rare disorders with WGS of healthy people by a new algorithm can spot repeated elements in genome– with correct (rapid) diagnosis comes **opportunity** for proper treatment – particularly in relation to children where early diagnosis could make most difference

Identifying genetic disturbance can aid diagnosis – but then what???



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**THANK YOU**

**Any Questions?**