Comprehension Three

Please have a read on Dr Nel Syed and his team's research on how radiotherapy helps patients with Glioblastoma

https://www.imperial.ac.uk/news/234035/new-treatment-could-boost-radiotherapy-effectiveness/

1. Where did the study take place?

   Imperial College London.

2. What is the name of the amino acid that Dr Nel Syed and his team discovered that would help increase sensitivity to radiotherapy if removed?

   Arginine
   Glioblastoma cells produce this amino acid and remove it via the drug ADI-PEG20, which increases its sensitivity to radiotherapy.

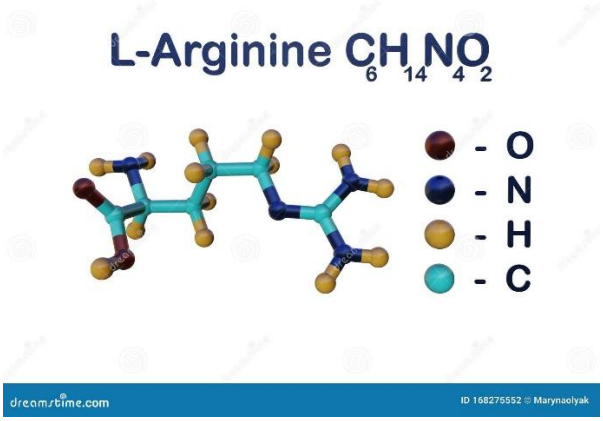

Figure 1: Structure of Arginine.
It contains carbon (C), Hydrogen (H), Nitrogen (N) and Oxygen (O)

3. What is the percentage of glioblastoma cases that can make arginine?

   70%

4. Which cancers were more effective in response to ADI-PEG20?

   Arginine-producing tumours

5. What type of cell can also remove the amino acid?

Immune cells are predominantly T lymphocytes.

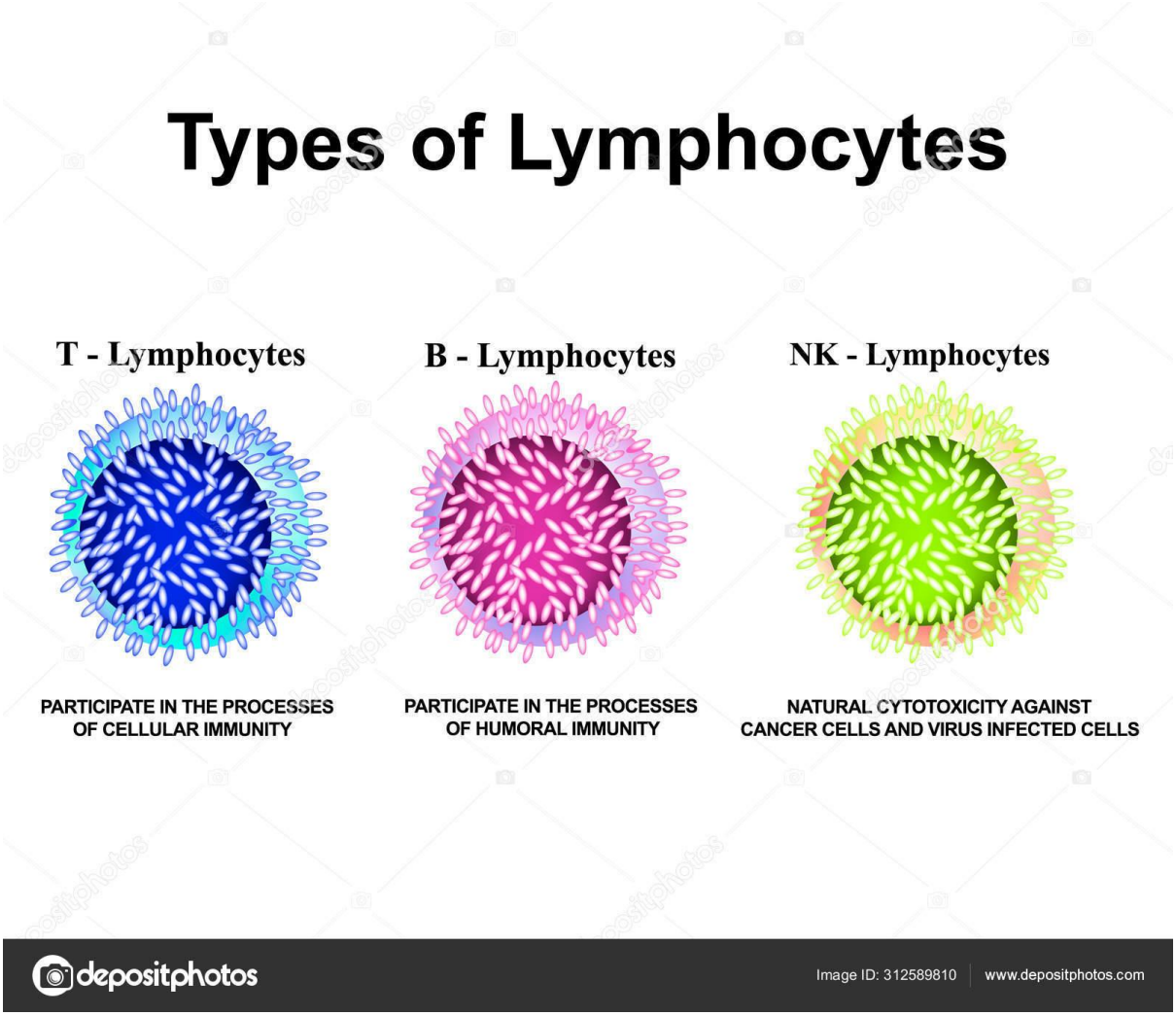

Figure 2: Types of lymphocytes

6. What is the function of amino acids?

They combine to form a polypeptide chain, which then forms a protein. Proteins are found in hormones, structures, antibodies, enzymes, and other examples.

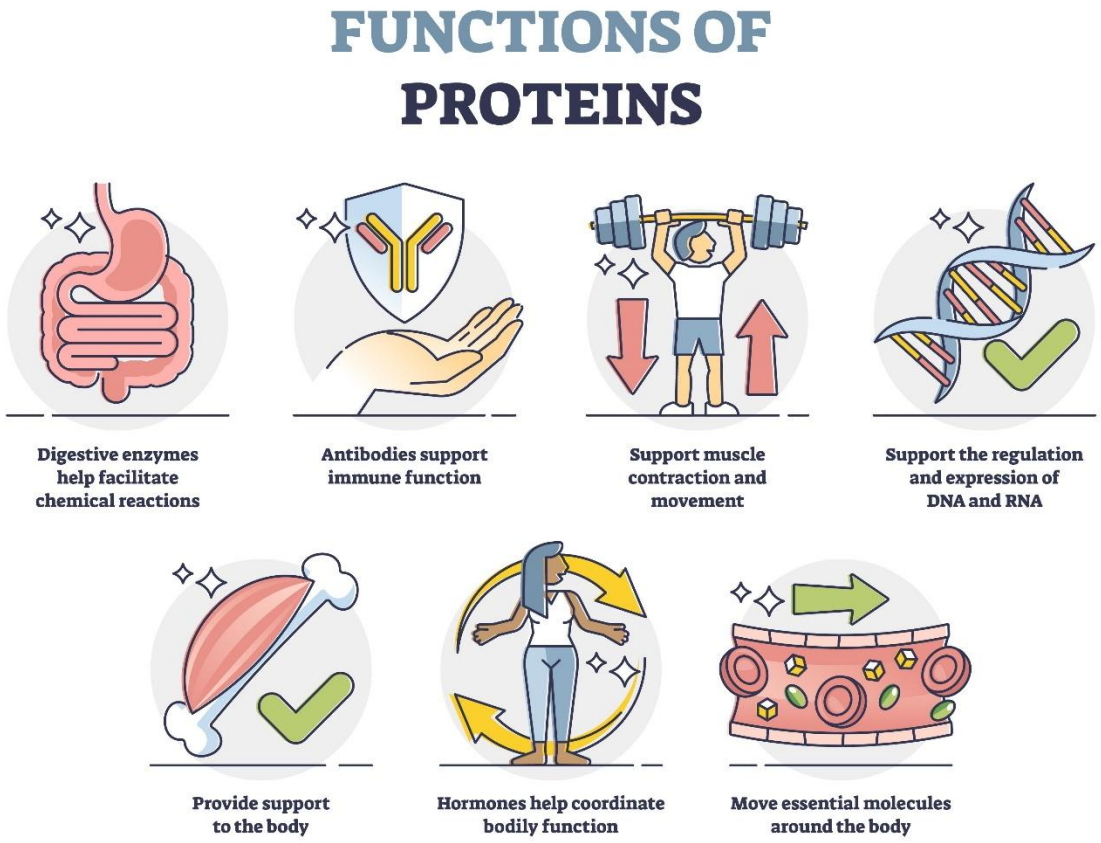

Figure 3: Types of roles conducted by proteins

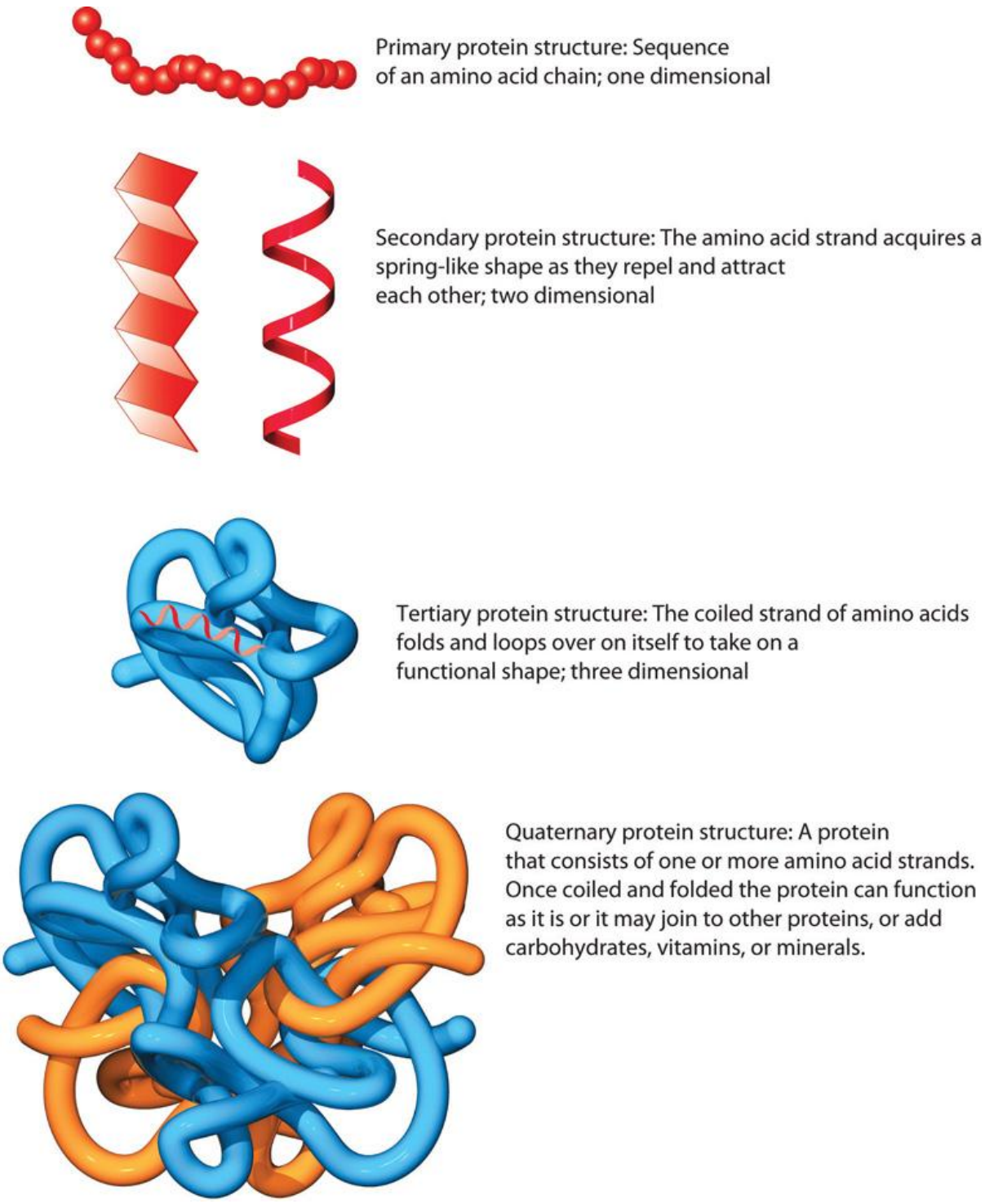

Figure 4: Protein structure (Creative Commons, 2025)

7. What is the percent rate of overall survival of people with glioblastoma for more than ten years?

   Less than one percent.

8. How is glioblastoma commonly treated?

   Surgery followed by radiotherapy and chemotherapy

9. How do you think the removal of arginine can increase sensitivity?

   By pausing the production of arginine via its enzyme argininosuccinate synthase 1 (ASS1), it can downregulate genes involved in DNA repair such as the PARP pathway

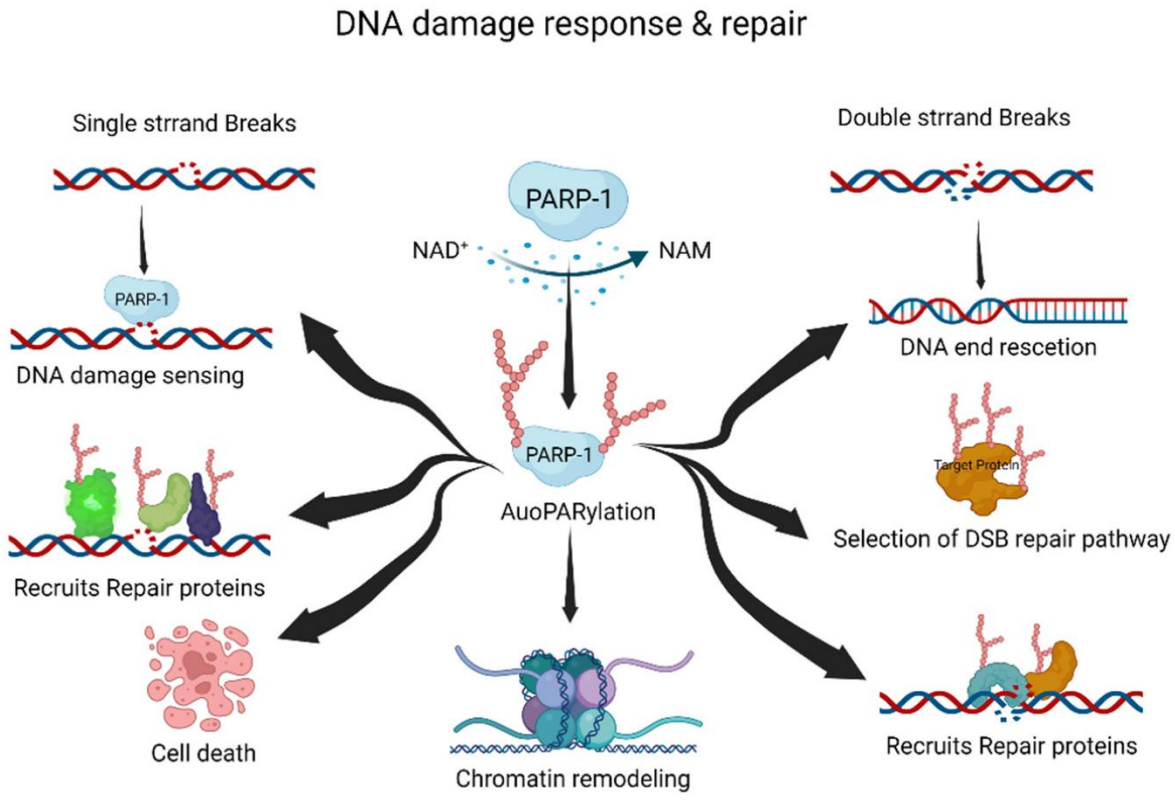

Figure 5: The function of PARP (Kang *et al*., 2022)

Poly ADP-ribosylation (PARylation) is a type of post-translational modification (PTM) that regulates cells. However, when there is a lack of control it can result in changes to the cell and can cause disease. It contains units called ADP-ribose (PAR).

The most common enzyme is PARP-1 found in the nucleus of the cell. Arginine is a basic amino acid and the structure of PARP is enriched with arginine and proline. It increases the rate of PARylation to form PAR using nicotinamide adenine dinucleotide (NAD+) as a substrate. This forms nicotinamide (NAM). PARP-1 is stimulated by DNA Damage Response (DDR) which is commonly stimulated by Double-Strand Breaks (DSB) or Single Strand Breaks (SSB). SSB is directly caused by metabolite chemicals

found inside the cell or via DNA decay. DSB is induced by DNA replication, radiation, DNA repair, and toxic chemicals.

PARP joins the PAR unit onto the carboxylic acid (COOH) of the amino acid structure of acidic amino acids like glutamic acid, aspartate, or basic amino acids like lysine. This may alter the structure of chromatin, affect protein-protein interactions, and DNA interactions due to the negative charge, and increase recruitment of DNA repair proteins to damaged sites. These are important processes for DDR repair pathways. PAR is subsequently released from chromatin and is degraded to maintain the stability of the genome and maintain the cellular internal environment (homeostasis). PARP1 can do PARylation automatically.

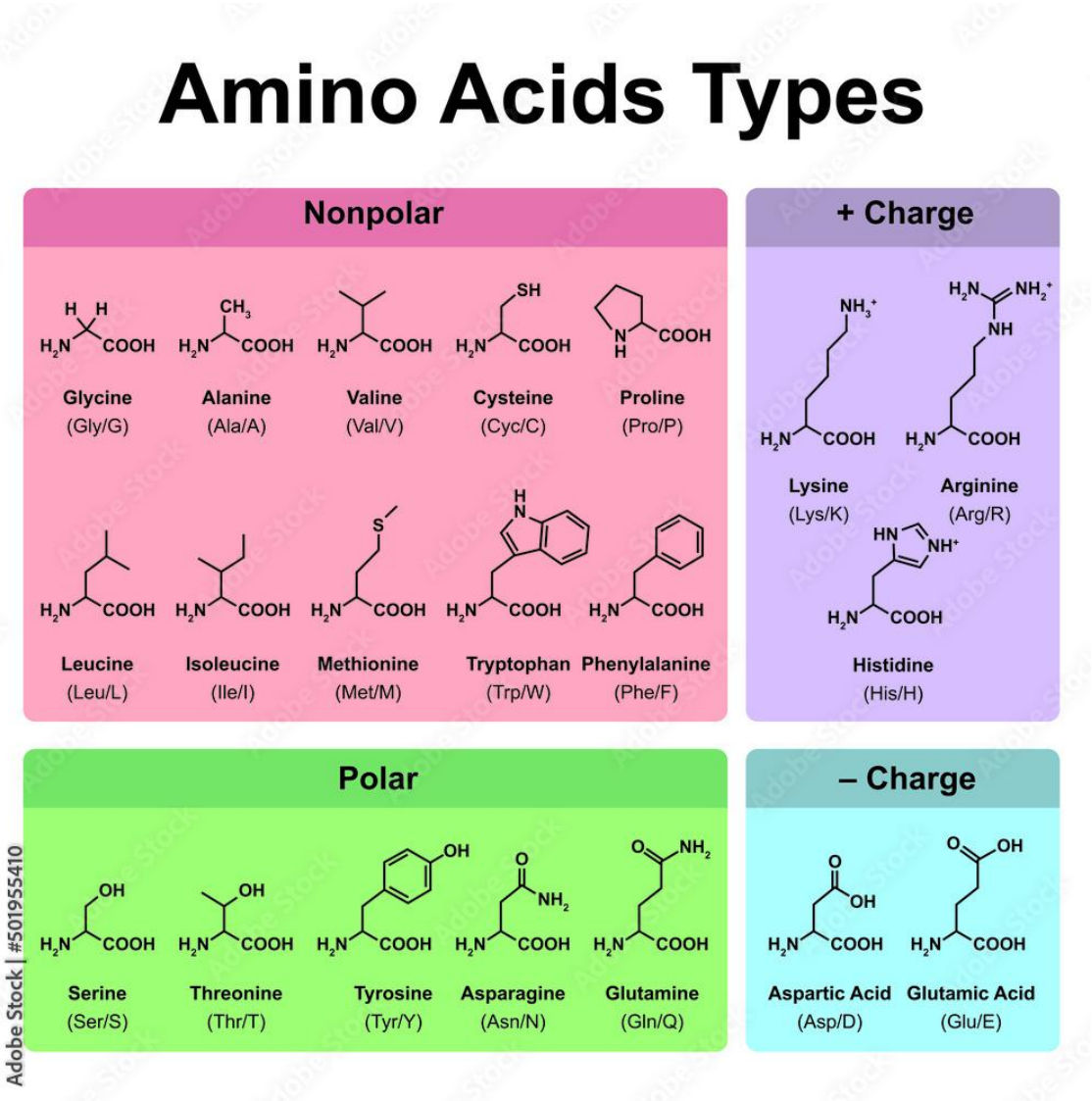

Figure 6: Types of amino acids

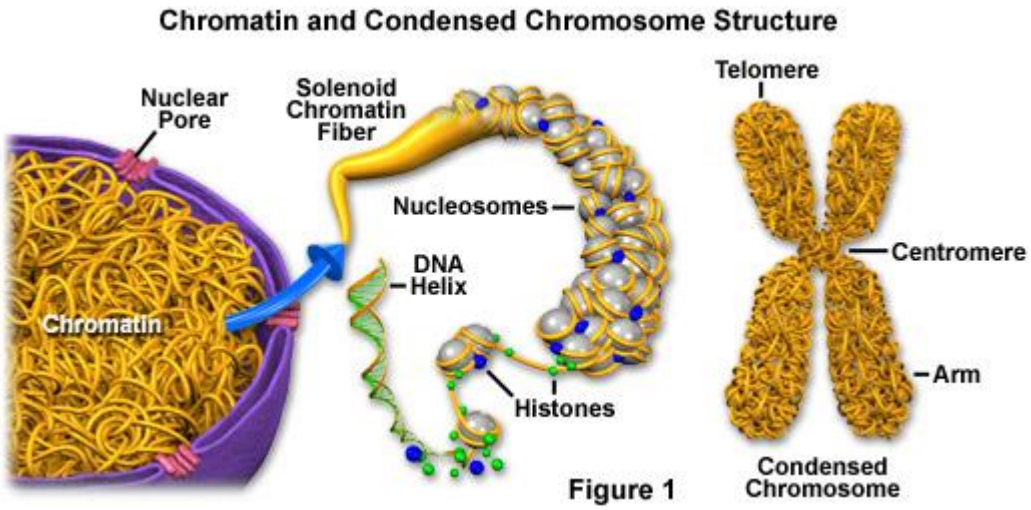

Figure 7: The structure of the chromatin containing DNA and histone proteins to tightly pack the DNA in mammalian cells (Creative Commons, 2025).

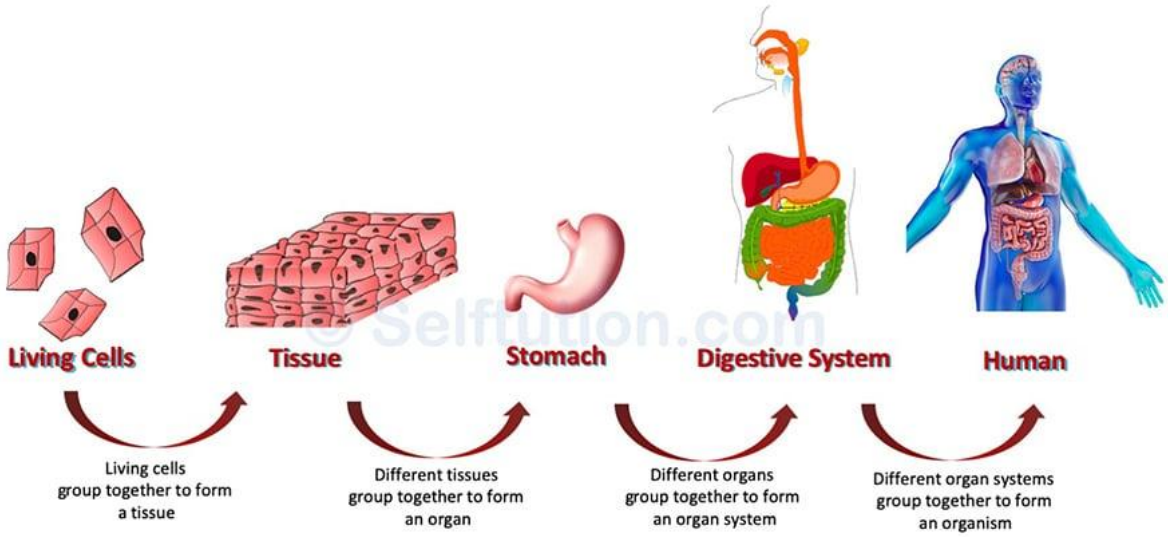

Figure 8: The organizational structure of the cell to form system.

10. What does the team hope to do in the remaining 30% that are unable to make arginine?

They hope to examine whether ADI-PEG20 can work. All GBM can be treated if arginine is removed.

Further reading and reference list

Brain Tumour Research (2025) *ADI-PEG20 in combination with radiotherapy*. Available at: https://braintumourresearch.org/blogs/research-campaigning-news/adi-peg20-in-combination-with-radiotherapy (Accessed: 13th June 2025)

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