Primary response: First time you come into contact with the virus/pathogen

- Some B cells morph into plasma cells which start producing AB’s (7th-14th day)
- Other B cells produce germ cells that are immortal – they hide in your spleen and become memory cells

Secondary response: Second time you come into contact with it

- Significant increase of AB’s produced very quickly
- Virus immediately gotten rid of

5-10% of the cells that are activated become memory cells after an immune response, whilst the rest die off. Every time you encounter the same virus, you end up with a larger number of memory cells. Also, the sicker you get, the bigger your T cell response, the larger your number of memory cells too. However, if you have an overstimulation of your immune system, you use your entire cohort of T cells and create no memory cells.
Cancer
Cancers are all different... We fight cancers on a regular basis but don’t feel it as most of the cancers are weakly immunogenic.

30% of people that die with cancer had an I.S that wasn’t good enough to combat that specific type of cancer, whilst the 70% alive with cancer have T cells reacting to them.

Carcinogens
They induce cancer by influencing your body to make a cell that keeps growing and ends up taking energy from you = kills you.

1. Chemicals (benzene)
2. Ionising radiation
3. Biological viruses (HBV, EBV, papilloma)
4. Hormonal (too much/little oestrogen promotes certain cancers)

Additionally, sources of inflammation (from obesity, allergens, toxic chemicals & microbial/viral infections) can also contribute to cancer. There’s a link between obesity and the predisposition of cancer.

Viral and UV related tumours (e.g. skin cancer) result in a STRONG immune response/attack.

RAG knockout mice
Animal models show I.S works to fight cancer. Mice share the same I.S are us so we can conclude results.

RAG knockout (don’t possess Recombinant Activating Gene. RAG-/- mice were bred, they do not have NK cells, T cells and B cells = adaptive immune system is affected.

Consequently, the number of sarcoma’s (skin cancer) is spontaneously introduced and massively greater in those RAG ko’d compared to the controls. This also applies to many other cancers.

Post-transplant
Those having organ transplants have to be immunosuppressed = post treatment there’s an increased risk of developing certain cancers (bladder, melanoma, colon, lung, pancreatic & kidney).

The biology
• Histopathological studies (areas of body taken out and studied) show that tumours are surrounded by mononuclear cells (monocytes, macrophages, NK cells, T-cells).
• When you have cancer, your lymph nodes are checked out as they’re draining sites of tumour growth, and so you can spot cancer cells in your lymph nodes (as well as lymphocytes and macrophages). These are called metastases – meaning a part has broken off the tumour and is travelling around in your body to brain/liver/wherever.
  With breast cancer, it tends to travel to liver, bones and lungs.
• If you have localised cancer, it can be surgically removed.
3 steps to getting a working T-cell

(1) Linear Commitment: TCR is needed (toothbrush)
Without TCR, an AB can’t recognise an antigen
- CTL: TCR + CD8
- Th: TCR + CD4

When T cells develop in the thymus, they go through a sequence of loss and gain of surface molecules
1. Pro T cells are double negative (CD4- CD8-) but express CD25 which is what they all start with
2. They then rearrange their TCR, becoming immature T cells (CD4+ CD8+) that express double positive
3. They drop one and differentiate into CD4+ CD8- OR CD4- CD8+ = mature

(2) Repertoire selection/functional maturation: Recognise non-self and ignore self-antigens

This knowledge is given in the thymus – corticomedullary junction, how?

The cells of the outer layer of the thymus are covered in MHC-1 & 2 and are self-antigen expressed. The T cells have to bind to the MHC’s
- If they have a LOW strength of attraction = dies [PROGRAMMED CELL DEATH]
- If they have a HIGH strength of attraction = dies (apoptosed) [NEGATIVE SELECTION]
- If they have an APPROPRIATE strength of attraction = mature, develop, grow [POSITIVE SELECTION]
T regulatory cells

T regs switch things off. This can be helpful for organ transplants if you can create and inject them.

It’s important you have a balance between: Cells that kill ↔ Switching off cell
Otherwise you get a lymphoproliferative response (proliferation of cells from lymph) = produce too many B cells than T.

MOA of T regs

1) Convert T cells to T regs (block activation)
2) Interfere with T cell function: Deactivate Th and CTL (functionally unresponsive)
3) Interfere with APC’s: Induce DC to apoptosed AND downregulate B7 or MHC = no stimulation = create T reg or apoptosed

T cell antigen recognition

- Activation of T cell and the cell gets killed
- Cytokine release
- Induce tolerance/anergy (lack of co-stimulation – opposite of energy)
- Apoptosis

Activation of CD4 & CD8

CD4: (Th cells) help CTL and B cells by releasing cytokines
CD8: (CTL) kills cells that express antigens that caused their activation

(SWITCH ON) Activation requires 2 signals for immune cells to become effector cells and memory cells

1) Antigen-MHC (with CD4/CD8 complex) with TCR
2) B7-CD28 ligand interaction = proliferate
   A lack of this co-stimulation = anergy = die