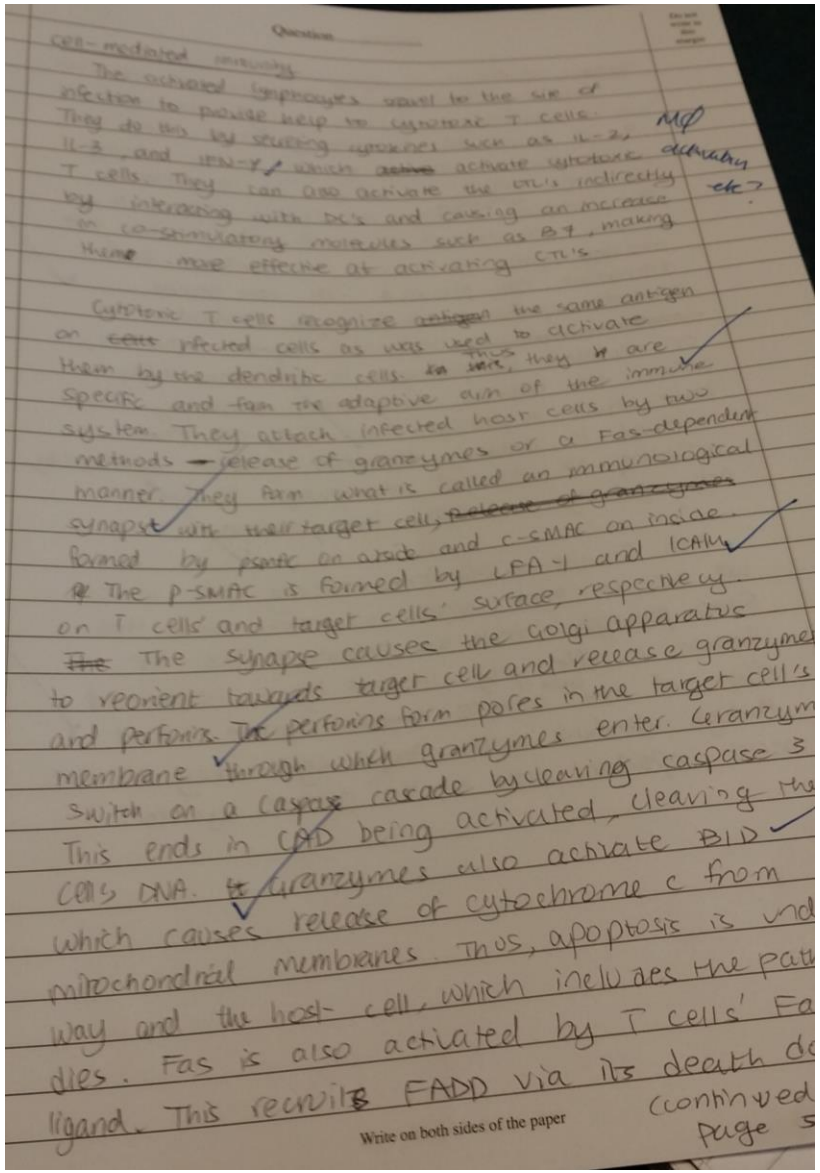

Question

cell-mediated immunity

The activated lymphocytes travel to the site of infection to provide help to cytotoxic T cells. They do this by secreting cytokines such as IL-2, IL-6 and IFN-γ which activate cytotoxic T cells. They can also activate the CTL's indirectly by interacting with DC's and causing an increase in co-stimulatory molecules such as B7, making them more effective at activating CTL's.

Cytotoxic T cells recognise the same antigen on infected cells as was used to activate them by the dendritic cells. In this way, they are specific and form the adaptive aim of the immune system. They attach infected host cells by two methods - release of granzymes or a Fas-dependent manner. They form what is called an immunological synapse with their target cell, formed by pSMAC on inside. The p-SMAC is formed by LFA-1 and ICAM on T cells' and target cells' surface, respectively.

The synapse causes the Golgi apparatus to reorient towards target cell and release granzyme and perforin. The perforins form pores in the target cell's membrane through which granzymes enter. Granzym switch on a caspase cascade by cleaving caspase 3 This ends in CAD being activated, cleaving the cells DNA. Granzymes also activate BID which causes release of cytochrome c from mitochondrial membranes. Thus, apoptosis is und way and the host cell, which includes the path dies. Fas is also activated by T cells' Fa ligand. This recruits FADD via its death do

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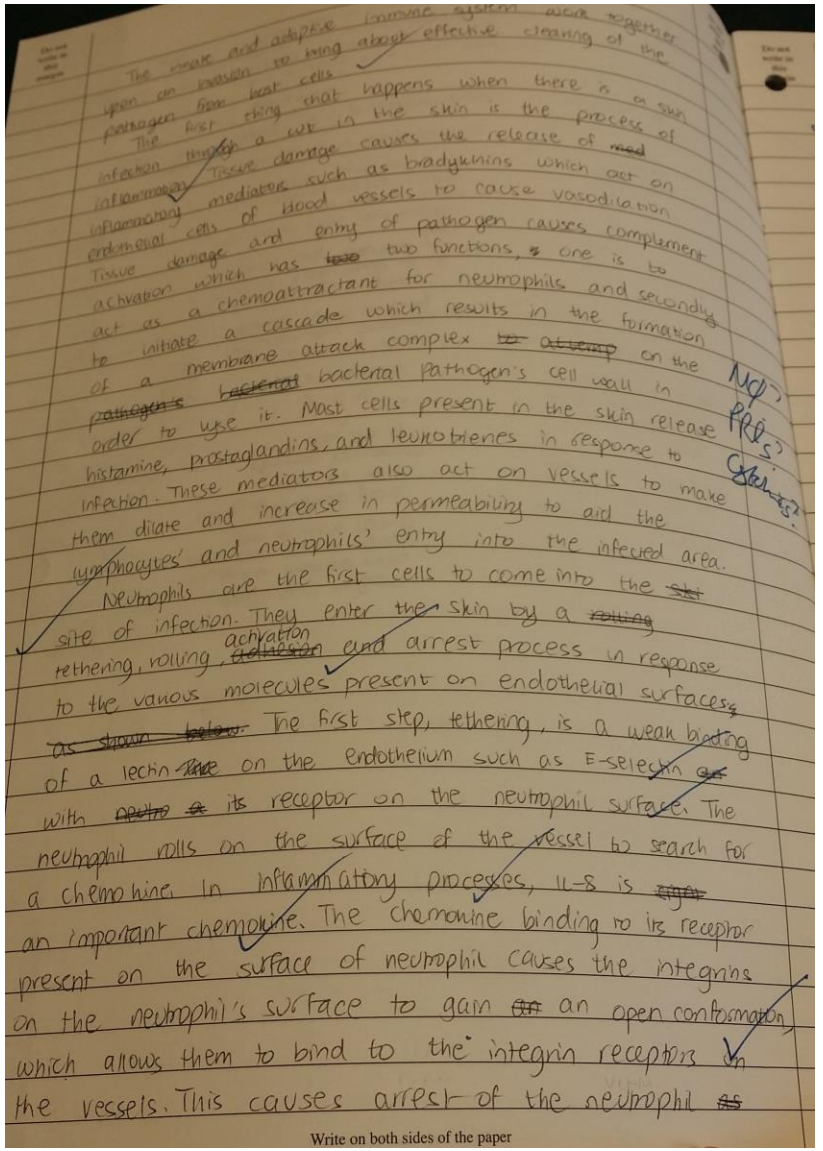
continued page 5



The innate and adaptive immune system work together upon an invasion to bring about effective clearing of the pathogen from host cells.

The first thing that happens when there is an infection through a cut in the skin is the process of inflammation. Tissue damage causes the release of inflammatory mediators such as bradykinins which act on endothelial cells of blood vessels to cause vasodilation Tissue damage and entry of pathogen causes complement activation which has two functions, one is to act as a chemoattractant for neutrophils and secondly to initiate a cascade which results in the formation of a membrane attack complex on the bacterial pathogen's cell wall in order to lyse it. Mast cells present in the skin release histamine, prostaglandins, and leukotrienes in response to infection. These mediators also act on vessels to make them dilate and increase in permeability to aid the lymphocytes' and neutrophils' entry into the infected area.

Neutrophils are the first cells to come into the site of infection. They enter the skin by a tethering, rolling, activation and arrest process in response to the various molecules present on endothelial surfaces, as shown below. The first step, tethering, is a weak binding of a lectin on the endothelium such as E-selectin with its receptor on the neutrophil surface. The neutrophil rolls on the surface of the vessel to search for a chemokine. In inflammatory processes, IL-8 is an important chemokine. The chemokine binding to its receptor present on the surface of neutrophil causes the integrins on the neutrophil's surface to gain an open conformation which allows them to bind to the integrin receptors on the vessels. This causes arrest of the neutrophil

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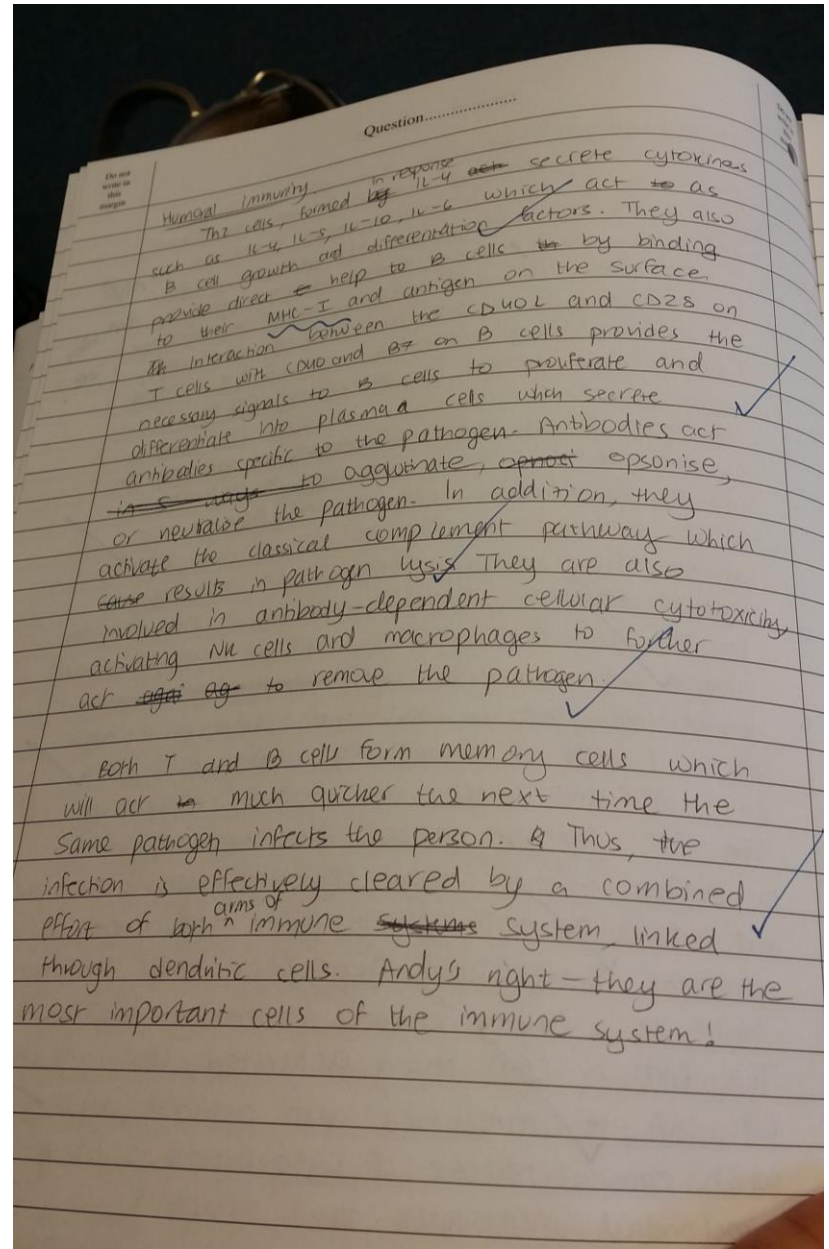
Question.....

and allows it to ~~exit~~ leave the vessel by diapedesis or transcellular migration. Neutrophils secrete many molecules which in addition to killing the pathogen also cause tissue damage. These molecules include free radicals, neutrophil elastase, neutrophil collagenase and proteases. As can be seen, the innate immune system is already underway to bring about a response to attempt to kill the pathogen. Other innate immune cells such as macrophages? and Natural killer (NK) cells also ~~make their~~ way to the site of infection. Macrophages come around 6 hours later. They phagocytose the pathogen in their attempt at clearance. ~~Phagocytosis is greatly enhanced by~~ In addition, they secrete ~~cytoki~~ pro-inflammatory cytokines such as IL-1, IL-6, and TNF-α which contribute to the recruitment of even more lymphocytes, further vasodilation, and a ~~more~~ longer lasting effect. The cytokines also act on the hypothalamus to generate fever response. NK cells also come in and attempt to kill the pathogen-infected host cell through the of granzymes or in a Fas-dependent manner, the details of which will be described in a later se

Link between innate and adaptive immunity

The link between innate and adaptive immu is provided by the DC cells. ~~These~~ There are m resident dendritic cells in the skin which const sample their environment for "danger signals" presence of pathogens. They do this by pattern receptors (PRR's) on their surface as well as intr which recognize certain molecules ~~that~~ on surfaces such as LPS ~~which~~ are called ~~are~~ pathog The most stud



Question.....

Humoral immunity

Th2 cells, formed in response to IL-4 secrete cytokines such as IL-4, IL-5, IL-10, IL-6 which act as B cell growth and differentiation factors. They also provide direct help to B cells by binding to their MHC-I and antigen on the surface. The interaction between the CD40L and CD28 on T cells with CD40 and B7 on B cells provides the necessary signals to B cells to proliferate and differentiate into plasma cells which secrete antibodies specific to the pathogen. Antibodies act to agglutinate, opsonise, or neutralise the pathogen. In addition, they activate the classical complement pathway which results in pathogen lysis. They are also involved in antibody-dependent cellular cytotoxicity activating NK cells and macrophages to further act to remove the pathogen.

Both T and B cells form memory cells which will act much quicker the next time the same pathogen infects the person. Thus, the infection is effectively cleared by a combined effort of both arms of immune system, linked through dendritic cells. Andy's right - they are the most important cells of the immune system!