Progression And Formation Of Cancer

Cancer is a leading cause of deaths worldwide, with so many new kinds of cancers still developing, it is vital to understand what is happening within the molecular structures of cells. It is estimated that 1 in every 3 people will develop a form of cancer and with a survival rate estimate of 5 years, it is crucial to continue research and studies into this form of disease. The Carcinogenesis progress itself as a basic understanding is the multistage development in which one abnormal cell mutates and grows resulting in a malignant tumour, which then has the means to travel throughout the body and attacking healthy body tissue (Mader and Windelspecht 2017). This essay will provide an overview into the cell's development and how these tumours form through mutation via overactivity oncogenes or substantial loss of tumour suppressor genes, the cell division cycle focusing on asymmetric or symmetric divisions and polarity, and finalizing with how cancer cells escape apoptosis as well as further invasion means and cell survival and continuous progression within the human body. Taking an in-depth look into Hanahan and Weinburg's (2000) hallmarks of cancer.

Cancer formation is the process in which there is a disruption to normal cell division and behaviour. Furthermore, the unregulated cell division stems from either the deactivation of tumour suppressor genes which ordinarily acts a way to stop the cell division at a specific point or if a proto-oncogene mutates becomes an oncogene which leaves the cell to be continuously active, these factors can change how the pathways are structured, with resulting effect being the beginning development of carcinogenesis (Mader and Windelspecht 2017). Firstly, looking at the transformation of a proto-oncogene to a dominate oncogene which initiates the production of tumours through overactivity. There are several mechanisms that activate this change in the cells, starting with the introduction of retroviruses insertion and their ability to disrupt the regulation of the coding sequence disruption the stability of mRNA or chromosol translocation, which is a process in which an inactive gene caused by disruption fuses with a second regulated gene encoding fusion proteins, such proteins as BRC-ABL can be created through this balanced translocation (Schulz 2007). Another pathway that can cause malignant tumours is the inhibitory activity of tumour suppressor genes, which are usually a means of stopping the cells from receiving new DNA after a specific number of replicates so if there is a lacking amount of tumour suppressor genes this inactivity allows the cells to continue to replicate causing unregulated growths (Pecorino 2008). Looking further into this is understanding, there are implications when there is a loss of the tumour suppressor molecule p53, which usually plays a role in the triggering or activation of apoptosis, stopping cell cycles and allowing the DNA to repair, thus without this gene carcinogenesis begins to activate, though the relevance of this gene in its entirety towards cancers or other autoimmune diseases are still in the early stages of understanding (Johannes and Irun 2007). The mutation of this gene is very common in the diagnosis of cancer, with over half of cancers in humans containing the inactivity of this gene, this gene is only triggered to activate when the cells have been damaged or stressed, giving a form of protection to the organisms which therefore it is understandable to find the inactive form of this gene in types of cancers (Vogelstein et al. 2000). To further understand how these genes become mutated, allow the growth or deactivate and allow the continuous life of cancer cells, critical examination into the cell cycle and cell division pathways is a high means of progress in the understanding of the development of various types of cancers.

Progress has been made in identifying that asymmetric cell division allows the stem cells to renew themselves through producing two daughter cells that contain different cell fates, whereas only one daughter cell will retain the ability to refer back to cell self-renewal (Knoblich 2008). However, after a certain point, this continuous regenerating of the cells can start to pose a threat in developing forms of Cancer as the overactivity can cause those mutations to arise. Looking at an ordinary fruit fly for an example, the Drosophila neuroblast cells will divide asymmetrically to the daughter cell that will differentiate, but in the cases where the asymmetric divisions are unregulated and interrupted, the end result is neuroblasts dividing symmetrically which causes the beginning of tumour formations (Morrison and Kimble 2006). There is a feasible relationship between cancer and cell polarity which justifies an in depth look into this hypothesis Cauussinin, and Gonzalez (2005) transplanted a form of mutated genes from a Drosophila melanogaster larval neuroblasts into a healthy adult host, this mutated gene was designed to affect the control mechanisms in asymmetric cell division. The resulting tumours that formed during this experiment showed that due to the unsettled functions that control asymmetric cell vision, the tumours were structurally unable to be distinguished between each other, this shows that hyperproliferation of stem cells has likely occurred, leading to a progression in the development of cancer (Cauussinin, and Gonzalez 2005). The drosophila as seen are an exception model organism for recognizing the changes in cell polarity and causes of tumorigenesis, providing the first example of a gene where loss of polarity caused the formation of a tumour with an efficient example focusing on the neuroblastoma, a solid malignant neoplasm (Wodarz, and Gonzalez 2006). This furthers the understanding on how this loss of epithelial cell polarity aids in the formation of tumorigenesis and its effect on the pathways within the cells. Typically, this loss can be seen through the unregulated and mutated proteins tumour suppressor and proto oncoproteins and their contribution to the loss of control in asymmetric cell divisions, allowing self-renewal of abnormal cells to develop (Martin-Belmonte and Perez-Moreno 2012). There is a need for future research into the complexity of cell polarity and aids in understanding further progression and survival of cancer cells, including the avoidance of apoptosis and beginning of mitosis.

The process that is apoptosis refers to an organism’s ability to destroy cells in a fast and effectively controlled manner, due to signalled damage to the DNA through the mitochondria. However, the connection between apoptosis and cancer in that the mutated cancerous cells will not respond to these signals even when the cancer cells DNA is damaged which allows for continuous cell replicates to divide, and so therefore never actually reach the cell suicide stage (Mader and Windelspecht 2015). Apoptosis is also crucial in maintaining homeostasis of tissues, when the cells become destressed from the damage or breakage of DNA double-strands, signals are sent resulting in the apoptic stage being induced one example of this is the activation of the TP53 and the induced signals to the pro-apoptic BCL-2 proteins to begin apoptosis (Schulz 2007). Other compelling evidence suggests that apoptosis can be initiated through other ontogenetic change that in turn has produce pressure to override the apoptosis stage during carcinogenesis. One example of this can be seen with the mechanisms of the FAS/CD95 receptors that would ordinarily control cell numbers by destroying cells as other cells begin to re-new, if this pathway is obstructed then overactivity of cells become a role in diagnoses of lymphoproliferative disorders, which includes various forms of leukaemia as well as other cancers (Lowe et al. 2000). Apoptosis, however, is not the only effective way to eliminate cells, various other ways include passive methods such as necrosis and motoric catastrophe, which can induce cell death. Furthermore, in recent studies it has been shown that these passive methods have evidence to be genetically regulated and result from specific kinds of DNA damage. However, motoric catastrophe can only be considered a trigger for apoptosis

due to a failure in the cell division as judged by cell fusion (Brown and Attardi 2005).

Another outlook on the mechanisms of Apoptosis is that though this process is in fact a contributing factor to the development of cancers, it is also feasible that the mechanisms of Apoptosis can aid in the treatment of cancer (Pecorino 2008). There are possibilities that apoptosis pathways can be restored with many treatment strategies in place to view if this is evidentially true, these include targeting the Bcl-2 family or silencing the anti-apoptic proteins and genes of the Bcl-2 family such as the use of the Bcl-2 antisense oblimer drug known as obilmersen sodium (Wong 2011). This is a targeting agent to Bcl-2 and has shown signs that tumour cells can become more sensitive to the effects of chemotherapy, aiding in the survival of patients. Another study focusing on how siRNA specific for Bcl-2 can be contributing a positive effect on the treatment for pancreatic cancer when 2 regions of the Bcl-2 were introduced to pancreatic cancer cells, resulting in pro-apoptic effects being observed within the tumour cells (Ocker et al. 2005). There is literature suggesting that apoptosis can aid in treatment of cancer however, many questions still arise from the results in these studies, therefore, continuous preclinical studies are necessary in further focus of apoptosis effects in both causes and treatments of tumour cells.

Due to a failure of apoptosis, the following areas to examine are how cancer cells are able to continuously re-new and replicate the cells within the tumour growth, followed by the cells being able to grow their own blood vessels finishing with the stage of metastasis. Firstly, looking into the ability to replicate continuously, specifically looking into the use of Telomeres and telomerase activity (Pecorino 2008). Ordinarily, a normal cell can only be allowed a specific number of replications during the DNA sequence before they cease to grow due to the shortening of chromosomal ends referred to as Telomers. However, cancer cells will continue to maintain the length of their telomeres, thus allowing the DNA cycle to replicate with no limit (Hanahan and Weinberg 2000). Further studies outline that cancer cells do in fact have relatively short telomeres, but high telomerase activity and there is evidence showing that when there are shorter telomeres due to a lacking RNA gene, the people with this genetic disorder are at a higher risk of many forms of cancers (Shammas 2011). These cancerous cells possess more than this ability, they themselves are also capable of building their own blood vessels, which aid in their survival and further ability of growth this is known as angiogenesis. As an example of how this process begins, think of this stage as a switch that can be turned on and off, and when there is balance between pro and anti-angiogenic molecules, the switch remains off. However, when the molecules become disrupted or imbalanced, the cancerous cells can begin to formulate their own blood vessels, keeping the cells alive by providing oxygen and nutrients, this ability to survive leads the cells to begin the next stage: metastasis (Carmeliet and Jain 2000). The final stage in the cancer progression is metastasis, the ability to move and create new tumours away from the original source. Somehow these cells are able to avoid the mechanics that leave other cells in place, and so, they are able to travel through blood and lymphatic vessels where the cells can begin their attack on healthy tissue, forming new tumours, therefore activating angiogenesis and feeding the tumours with those oxygen and nutrients that are in fact taken from normal tissue, causing severe damage to the DNA structures (Mader & Windelspect 2017).

In conclusion, the progression and formation of cancer is a very complex disruption to DNA structures and has various abilities in order to survive and grow. The continuous unregulated cell divisions through mutations and overactivity, as well as the loss of tumour suppressor genes are the starting process in which tumours are formed. This continues on to the processes in

which these cells have adapted certain abilities within the body that allow continuous growth, avoidance of dead cell mechanisms and movement throughout the body thereby attacking the body and robbing healthy tissue of its nutrients. The resulting focus on future research should be evident in many areas, though there is still a lot unknown information on how cancer is formed and how it has such ways of surviving in the body through the structures of the cells. Though all of the above is relevant in how cancer is formed, it is also crucial in increased understanding on how treatment can be aided through further studies and preclinical practices.