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Biology 293

Leukemia Research Paper

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Within my research and reading on the recent discoveries on possible treatments for acute myeloid leukemia, AML, made by Israeli scientist I was fascinated by the amount of attention to details when it comes to cell division. Although this is something that we study in spades as biology students it is rarely in that much detail. The amount of energy focused on replication as well as the countless man hours to understand the process of cell division allowed the scientist studying AML to test six drugs and potentially discovery a cure for this cancer. Understanding the process of cell division is crucial to understanding the solution that was created by these scientists for the problem that has had scientist stumped for the past 40 years (Minzel).

At the beginning of cell division, the key enzyme is CK1 alpha. It is this enzyme that is responsible for the phosphorylation of the protein p53. This protein responses to damaged cells which need to be killed, apoptosis, essentially acting as a pathway during cell replication. It is the change in H2AX to H2AX gamma that is recognized by p53 which indicates whether the DNA is damaged. Once this happens BAX, a pro-apoptosis protein, will signal the mitochondria to release c- chromatin into cytoplasm to combine with Apaf-1 which will allow the formation of apoptosomes. This gives way to the movement of damaged cells towards apoptosis p53 and the activation of caspase 3. The job of breaking down the damaged cells is caspase 3’s responsibility (Samarasinghe). The ideal behind the experiment in which we are studying was to find a drug that would inhibit the growth of leukemia by increasing apoptosis in damaged cells. In damaged cells without treatment the CK1 phosphorylates beta-catenin in Ser 45 which increases the proliferation with buildup. This is done by means of transcription after the relocation into the nucleus (Steel). This causes the leukemia.

To test the effectiveness of each drug, six in total, in this experiment mice were used. These mice were infected with AML and then analyzed for data. There are many ways the scientists used to test these drugs including if it would produce p53 with different concentrations. They also studied the death and survival rates once the drug was administered. If there was any binding affinity that it may induce production of CK1 alpha. Most importantly they studied the amount of leukemia cells in each mouse before and after exposure to the drugs. Within this research paper they used different diagrams to display their data including a western blot test, binding affinity charts, and tissue histology (Minzel).

After careful analysis of the research the two inhibitors that show the most promise A51 and A86. This conclusion came from the ample data that was provided in the research. In the case of both inhibitors it was most effective in the pathways CDK1 alpha and the CDK7/9 SE regulated. In the CDK1 alpha pathway damaged DNA induced the proper response from p53. Allowing this pathway to prevent damaged cells from transcription by apoptosis. In the CDK 7/9 SE regulated pathway quickened the rate of function in the p53 and by doing so it increased the rate of apoptosis. The data collected will confirm these results and I will explain them in further detail (Minzel).

In the line graph depicted in as figure 2A, indicates that in both A51 and A86 there was the most Annexin V at certain concentrations, which is a protein that indicates apoptosis has occurred (Steel). The data also shows that A51 and A86 have a stronger binding affinity with CDK7 as per figure 4E and a stronger binding affinity with CDK9 as per figure 4D. These two binding affinities inhibit the transcription of the leukemia cells and decreases the proliferation. It is in figure 1F that the data shows that both inhibitors had a strong effect on both p53 and gamma H2AX.Although that both inhibitors have proven that they have effects on certain pathways, they also demonstrated the increase of apoptosis which improved the mice lives. Those with successful treatment lived longer and healthier. This was depicted in figure 3G (Minzel).

Going into this I did not know what to expect. I knew that leukemia was a serious thing that takes the lives of many. These researchers set out to find a cure for leukemia. Did they meet their goals? Maybe. I don’t know if they cure AML, but the signs are positive for a potential drug treat. I think more testing needs to be done before introducing it to a human trial, but I would not rule out the possible of eventual human testing.

References

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