The number of people exposed to irradiation is progressively rising. This is due to professions such as astronauts, diagnostic, treatment-related procedures, or accidents.

Human spaceflight began in the 1960s and since that manned spaceflight activities have been continually expanding in frequency and scope since that time, and plans are now forming for long-duration flights to deep-space destinations. However, it has been shown that space radiation which consists mainly of proton radiation is a risk factor that has the potential to negatively affect the astronauts' health during deep-space missions. Likewise, in medicine, the widely used therapeutic γ-radiation is associated with increases in the rates of several diseases. Moreover, not all symptoms appear immediately after the treatment and there might be a long latency time. To address this, proton beam therapy offers a number of potential advantages over conventional γ-radiation therapy and it has emerged as an alternative to γ-radiotherapy, at least for some types of cancer.

In both cases, space radiation and medicine, the studies about the side effects of proton radiation on human molecular pathways are still limited as are data about radiation effects on the human genetic and epigenetic landscape. So far we know that the hematopoietic system, especially Hematopoietic Stem Cells (HSCs), are highly sensitive to space radiation. Disruption of normal hematopoiesis can lead to pathologic states such as leukemia. However, **the effects of proton radiation on the hematopoietic system have yet to be fully understood**, leading to a lack of effective countermeasure strategies thus far. Therefore, understanding the biological effects of proton radiation is immediately needed. **In order to fill this gap, we plan to study the effects of proton radiation on the human biological/molecular level in the Hematopoietic stem cells (HSCs).**

Hematopoietic stem cells (HSCs) have the ability to self-renew and replenish the whole-blood system throughout the life span of the body. These cells also give rise to other blood cells like lymphocytes T, B, granulocytes, or macrophages in the process called differentiation. Many of these cells are involved in the immune response, where they protect the body against potential disease states.

In this project, we mainly focus on the molecular effects of proton radiation in Hematopoietic stem cells and their ability to differentiate after radiation. The first part of the project will be conducted in vitro on commercial Hematopoietic cell lines.

Firstly, we would like to investigate the risk of loss self-renewal of HSCs and their ability to differentiate into T cells, granulocytes, and macrophages after dose-dependent proton radiation treatment (0.5 Gy and 2.0 Gy). These combinations will allow us to study in detail the effects of radiation on the function and differentiation of HSCs.

Secondly, how these doses of radiation change the function of our DNA is not fully understood. In order to fill this gap, we plan to study chromatin conformation, its accessibility, and its gene expression profile inside the cells. These analyses may provide new insight into the molecular mechanisms on how radiation influences epigenetics alteration in HSCs.

After examining the effect of radiation on a commercial line of HSCs, we will isolate hematopoietic stem cells from female patients from the cord blood. Then, we will explore the radiation-induced changes in the differentiation and verify if the radiation effect leads to the same changes in human material.

We expect to provide new insight into the epigenetic mechanism and factors involved in the cell response after proton radiation. We believe that understanding the role of proton radiation in research could provide a molecular basis for the development of new therapies that will help protect humans from the harmful effects of this radiation. Also as a result of the project, knowledge will be completed and expanded on the potential impact of space radiation on hematopoietic stem cell differentiation in a dose-dependent manner. The data we collect will be deposited in a special database and made available to scientists for use in other research on the effects of proton radiation on the epigenome.