Story needs a beginning, a middle, and an end

Unfortunately many great medical advances have happened at the expense of human lives. One of this incidents happened with The Radium Girls – led to increased incidents of cancer. After the bombing of the

A significant finding that a transplantable multipotent adult bone marrow cell with clonally demonstrable hematopoietic activity with experiments showing that an intravenous transplant of normal adult mouse bone marrow cells could protect recipients from a lethal dose of radiation by replacing the destroyed blood-forming system with new and sustained source of lymphoid and myeloid cells. Over time the developmental stages of hematopoiesis became to be understand, however the transcription factors that cause this development is not well understood.

The study of transcription factors important to development has historically been carried out during the developmental stages of an organism. However, hematopoiesis is a unique setting that happens during the adult stage. The genome of an adult is typically considered closed to further development. Stem cell like cells can be induced by the addition of pioneer factors. Can the same be done for immune cells. Can immune cells be reprogrammed to other immune cell types? Do pioneer transcription factors exist in hematopoiesis?

The development of cells

PU.1 is a master regulatory of myeloid and

Place your work in the history of others so that it can be remembered. Any famous pioneer transcription factors? Any historical works in immune cell development?

The fundamental mechanism of cell development and differentiation is the coordinated action of a complex network of transcription factors. These transcription factors can bind to promoter sequences near transcription start sites to regulate transcription directly or bind to enhancer sequences thousands of base pairs from the gene they regulate. A special class of transcription factors, known as pioneer transcription factors, can bind to closed DNA sequences occluded by nucleosomes and open these stretches of DNA to commit cells to certain developmental fate decisions or even to reprogram cells. The developmental fate decisions made by these pioneer transcription factors are crucial for embryonic development to develop the zygote into the all the different cell type lineages of the adult organism. The cells in a developed adult have already been terminally differentiated with stable gene expression and are no longer under the influence of pioneer transcription factors. However, hematopoiesis is one system in which this process is happening continually throughout the lifespan of higher order eukaryotes. The presence of pioneer transcription factors during the development of immune cells could have important implications in human health and disease.

Cooperative binding of sequence-specific transcription factors in place of nucleosomes leads to an open chromatin state that allows for gene expression. These open chromatin stretches of genome are also more accessible to nucleases, and can be probed for using Next Gen Sequencing methods such as DNase I hypersensitivity or ATAC-seq. In hematopoiesis, a single progenitor, pluripotent stem cell can give rise to all the cell types found in the blood including erythrocytes, myeloid cells, and lymphoid cells. Probing these open chromatin states using next gen sequencing methods during different steps of hematopoiesis could elucidate potential binding sites of the pioneer transcription factors. Motif analysis of these DNA segments could reveal pioneer transcription factors during lymphoid development.

This universal transition represents a major reprogramming event that requires (1) chromatin remodelling to provide transcriptional competency; (2) specific activation of a new transcriptional program; and (3) clearance of the previous transcriptional program. (Lee, 2013)

A child inherits approximately 23,000 genes from her parents. This inherited genomic information is known as the “structural genome” and can be likened to computer code: a set of instructions, that when executed, perform a certain function. Sometimes environment conditions can cause chemical modifications to the genome of an individual at a critical period of development, and this pattern can be set for the rest of her life. During World War II, German blockade of the port of Amsterdam in 1944 stopped the import of food

(Find broad example). Most somatic cells may not respond as strongly to environmental pressures once past this stage of development.

However, hematopoiesis and the generation of an immune response remains one area of the body in which cells are continually development and being met with a wide range of external stimuli from infection to influence the development immune response. In cases of T cell exhaustion, persistent T cell stimulation appears to drive epigenetic changes to T cells that make it difficult to reinvigorate them even with checkpoint inhibitor blockade. Understanding the transcription factors that influence chromatin states in lymphoid cells will provide insight into the process by which lymphoid cells develop during immune responses and possibly allow us to manufacture epigenetic modifications to achieve a desired cellular fate.

The genomes of eukaryotes carry chemical marks that are added to either DNA or chromatin proteins. This epigenetic information is not uniform, but is applied regionally, and it signals or preserves local activity states, such as gene transcription or silencing