Scientific Literacy

Insight on Cell Senescence:

 Cell senescence is a permanent, stable cell cycle arrest, where cells that have reached their division limit or have undergone stress, then exit the cell cycle and enter senesscence1. This arrest state halts the division of the cell; however, the cell still maintains metabolic activities and secretes substances into the environment1. Senescent cells are associated with both protective and deleterious effects2. A category important to mention is replicative senescence. Under replicative senescence, the cells have only a short telomere left, typically uncapped1. The shortened telomere leads to DNA damage responses and triggers senescence2. Accumulated findings support stress is the main way cells enter this phase instead of apoptosis1. Majority of cells can reach this phase, and it can be understood as similar to the G0 phase of the cell cycle3. Don’t be misled though, the G0 phase is a resting state from the cell cycle and will return to division, often referred to as Quiescent 3. Cell senescence is the irreversible phase of G03.

 The irreversibility of cell senescence is where concerns lie. While senescence has the ability to avoid malignant transformation of damaged cells, the onset of the state is known to contribute to pathologies like cancer, aging tissue, and inflammatory disease2. The contribution to the pathologies lies in the secreted substances1,2. These are known as pro-inflammatory senescence-associated secretory phenotype (SASP) that communicate with the surrounding cells and immune system2. SASP is responsible for both promoting and inhibiting tumor growth2. The SASP's ability to attract immune cells to senescence cells aids in their death, acting as a tumor suppression and preventation2. However, SASP has also been found to induce tumor progression by releasing factors that stimulate angiogenesis, extracellular matrix remodeling, and epithelial-mesenchymal transition (EMT)2. Further, chronic inflammation triggered by senescence can lead to systemic immunosuppression, possibly contributing to the development of cancer2. This persistent inflammatory state not only affects immune function but may also accelerate tissue damage and aging-related degeneration as it communicates to the other cells2. From this knowledge, the complexity of cell senescence is shown along with the uncertainties it holds.

A deeper look into Transcription:

 All processes have to begin somewhere and for normal transcription that is the promoter sequence4. A promoter sequence is the kickstart of the protein coding gene to be transcribed into RNA5. The promoter sequence holds an important power, depending on the length of the sequence on each DNA, the level of control for gene-expression differs4. Combination of promoter lengths and location on DNA, help create the variety and specific purposes of each promoter sequence4. Located just upstream of the coding sequence the increased surface area of longer promoter sequences allows more proteins to bind to the promoter sequence and the range of control can be quite dramatic4. Proteins binding to the promoter sequence is specific to eukaryotes, known as transcription factors and have specific chosen DNA for every binding process.4.

Interestingly, a phenomenon can occur, interfering with the normal transcription process5. From the above paragraph, we have learned that the promoter sequence is the beginning of a normal transcription process due to its specific location on the DNA5. This process is well regulated by the cells, but sometimes a look-alike sequence fools the process5. The phenomenon is called cryptic transcription and occurs when promoter sequence look-alikes exist on other locations within the DNA5. In mammalian studies, the arise of cryptic transcription is found to increase with cell age5.

In this process of another form of transcription can occur6. Cryptic Transcription occurs in senescent cells and normal cells and can have harmful consequences5,6. RNA transcripts are produced from a short sequence that is located with individual genes6. However, how the harmful consequences of this process occurs, has been a question to scientist for years6. What we do know is Cryptic transcription has been associated with spurious behavior, meaning any at chromatin region (gene sequence), RNA polymerase II can be recruited7. This area is outside of the normal promoter sequence, and be called the cryptic promoter7.What makes this process cryptic is how the process functions within normal transcription, but creates an error-like expression in the gene when the cryptic promoter recruits the RNA polymerase7. Some studies have found Cryptic transcripts to be chromatin sensitive, allowing for a type of research to highlight the cryptic transcripts in the act, but many are still hard to detect7. A key difference between normal transcription and cryptic transcription is that normal transcription holds a strict process, while cryptic transcription sneaks into the process and changes the coding process unnoticeably until expressed,6,7.

 The Misleading Zombie:

 One could say aging is like becoming a zombie, and in the paper "Spurious intragenic transcription is a feature of mammalian cellular senescence and tissue aging8”, we will delve into the process of mammalian cells becoming a “zombie” with the topics we have just explored.

 A eukaryotic genome is transcribed into pre-mRNA and is then catalyzed by RNA polymerase8. In typical transcription once this occurs, it is crucial the chromatin structure of the replicated sequence is restored8. If not, then risk for cryptic promoter sequences increases which is known to age cells due to altering normal nucleosome arrangment8. Senescence cells attempt to prevent this damage by ceasing to replicate so they secrete soluble factors to increase immunity, but high exposure of the secretion can cause aging or damage in the still replicating, young cells8. Senescence will no longer undergo normal transcription due to risk damage or age, while normal cells carry out transcription and under senescence secretion may have a high chance of a cryptic promoter opening up and altering the RNA8. Figure g shows proliferating cells to emit a strong signal, while senescent cells barely emitted a signal8.

The researchers previous work in yeast and worms, results showed prevention of age-related intragenic cryptic transcription8. A gene body trimethylation mark on lysine 36 of histone H3 (H3K36me3) showed increased transcriptional stability, while in mice embryonic stem cells, DNA in cooperation with H3K36 methylation resulted in prevention of cryptic transcription8. In this, It was found that younger genes have a strict regulation to ensure transcription runs smoothly8.

References

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