Life Cycle of Neurons

Nabiha Javed

Neurons are one of the most important cells in the human body; they are used to signal other parts of our body to start or stop processes vital for sustaining life. Despite all of our somatic cells being bound to the process that is the cell cycle, the life cycle of neurons is something that is quite different from other cells in the human body. Our somatic cells go through the life cycle of becoming differentiated, carrying out their respective jobs, and then undergoing apoptosis once they are worn out or damaged. The majority of neurons we have in our brains are present by the time of birth, however there is evidence that neurogenesis is a lifelong process, which is a belief contrasting starkly to the previous thought that humans are born with all the neurons they were going to ever have.

Once cells in our body die, they are destroyed and are consequently replaced by new cells. Neurogenesis replaces neurons that have died, however, are not replaced by new cells in the way that other specialized cells in our body are. Neurons are limited in their capacity to proliferate. When neurons die unnaturally, the brain suffers ramifications, making way for neurological and neurodegenerative diseases such as types of dementias. In order to better understand the causes and effects of such neurological and neurodegenerative disorders, we must examine the life cycle of a neuron, from neurogenesis to death. We must also understand what the structure and function of a neuron is, and why neurons are so important to the human brain and the human body at large.

The majority of cells undergo these cycles, on average, 40 to 60 times in their lifetime; this is quite different from neurons, who often remain in a phase known as G0. G0 is a nondividing and nonreIn order to understand what the life cycle of a neuron is, it is fundamental to first acknowledge the cell cycle and its implications on the neuron's development and eventual death. The cell cycle has four main phases: G1, S, G2, and M (1). In eukaryotes, somatic cells undergo mitosis, which is where the parent cell duplicates its genetic material and splits into two subsequent daughter cells identical to its initial composition. This creates two new cells that are genetically identical to the mothering cell. Mitosis consists of 4 phases: prophase, metaphase, anaphase, and cytokinesis. After all four steps of mitosis are complete, the two resulting daughter cells are functional and complete. plicating phase of the cell cycle. Progression through the cell cycle is closely monitored by checkpoints resulting from the activation of different signalling pathways, leading to inhibition of CDK (2) and cyclin complexes. Each cell must complete the phases in order before progressing to the next one. If any defect is detected by proteins involved in regulating the cell cycle, the proteins halt the progression of the cycle until this defect is addressed. This makes it nearly impossible for a defective cell to make it past the cell cycle without being corrected, if possible, or sent into programmed cell death if the defect is too extensive to be fixed.

The central nervous system, composed of the brain and spinal-cord, is made up of 2 basic cell types, one of these types being neurons. In order to understand the functions of a neuron, it is necessary to understand the structure of a neuron. Neurons vary in their morphology depending on what variety of neuron they are, however, they all have basic structure similarities with one another. All neurons contain four distinct regions: the cell body, dendrites, axon, and axon terminals. All four of these regions serve distinct and different purposes that are vital to the function of a neuron in terms of it being a messenger cell. The cell body of a neuron, also known as the soma, contains the nucleus, which is the control center and the 'brain' of the neuron. Essentially all neuronal proteins and membranes are synthesized in the nuclei of neurons. From this cell body, the dendrites and axon branch out from the left and right, respectively. In order to communicate with each other, neurons send messages across the synapse, a gap between one neuron's dendrites and the other's axon. Most neurons have multiple dendrites, which serve to receive chemical signals originating from the axon terminals of other nearby neurons. Neurons' axons do not contain any ribosomes, and thus do not synthesize proteins. Axons are the channel by which action potential travels over a neuron, from the dendrites all the way to the end of the axon terminals of a neuron. Neurons are the cells that help our central nervous system relay messages all over our body. This makes our organ systems do what they do, and helps us respond to our environment in the ways we react.

Despite there being the previous belief of neurons dying off and not being replaced by subsequent neurons after the fact, there is now evidence neurogenesis does happen over the span of a person's lifetime. Neurogenesis, or the birth of neurons, is the process by which new neurons are created and introduced into the human body for use. Neurons are born in areas in the brain rich with neural stem cells; neural stem cells have the ability to create most, if not all, of the varieties of neurons and glial cells found in the brain and spinal cord.

After the birth of a neuron, migration occurs. Migration is the process by which neurons go to parts of the braion or spinal cord that need their services. Migration is the part of a neuron's life cycle where a lot of neurons do end up dying off, despite neurons being the longest living cells in the human body. Scientists speculate that only a third of neurons make it to their destination.

Once a neuron reaches its destination, it will differentiate in order to become a specialized neuron specific to the job it will be carrying out. Neurons are responsible for the uptake of neurotransmitters, chemicals that relay messages to the brain, and thus differentiation is an important component of a neuron's function. Unlike most other cells, neurons are believed to lose their ability to proliferate once.

This means that neurons cannot divide and make more of themselves after they have undergone the process of differentiation.

Differentiation is the process by which neurons become specialized to do specific jobs around the brain and nervous system. The ramifications of adult neurons dying leads to many neurological and neurodegenerative diseases we see, such as varieties of dementias or Parkinson's disease. Although neurogenesis is indeed a lifelong process, adult neurons have challenges in proliferating and being replaced after dying in development and migration. Neurons can die in a variety of ways, but the unnatural neuronal death that occurs occasionally in a human brain can lead to diseases and disorders. The progressive death of specific neuron populations is what is characteristic of neurodegenerative disorders. For example, Alzheimer's disease, the most common cause of dementia, is characterized by neurons reentering the cell cycle. Research has further suggested that Alzheimers involves a dysfunction in this cell cycle reentry, leading to what is known as the two-hit hypothesis of Alzheimer's disease. The first hit in this hypothesis is abnormal cell cycle reentry, typically resulting in neuronal apoptosis and thus a prevention of Alzheimer's disease in the brain. The second hit, however, involves chronic oxidative damage that prevents apoptosis of the neurons, leading to the plaques and tangles characteristic of an Alzheimer's brain. Neurons are quite apt to oxidative stress as a result of the high oxidative metabolism rate in the brain, which explains this chronic damage. Oxidative stress is also seen as a major damage to genetic material. Cells with extensively damaged DNA often will be destroyed via apoptosis to prevent complications from arising, as seen by neuronal apoptosis in the first hit in the two hit hypothesis. Other unnatural causes of neuronal death are stress, head trauma, strokes, or physical illnesses. Glucocorticoids are hormones that are released when we are stressed, and extended exposure to these substances can damage the brain, making our neurons more exposed to neurological injuries. Preventing stress in day to day life may make our brains more resistant to strokes, forms of dementias, and other types of neurological disorders.

The brain is made up of tissues, composed of various kinds of cells. Of these cells are neurons, which are the messengers and signal relayers of our brain. From birth, migration, differentiation, to death, a neuron carries out several important tasks for our wellbeing, such as taking up neurotransmitters and signaling other parts of the body on when to start and stop processes vital to the processes of living.

References

1. Barrio-Alonso,8 E et al. "Cell cycle reentry triggers hyperploidization and synaptic dysfunction followed by delayed cell death in differentiated cortical neurons." Scientific reports vol. 8,1 14316. 25 Sep. 2018, doi:10.1038/s41598-018-3270-4

2. Brain Basics: The Life and Death of a Neuron. www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Life-and-death-Neuron.

3.6. Frade, J., 2015. Neuronal Cell Cycle: The Neuron Itself And Its Circumstances. [online] Taylor & Francis. Available at: https://www.tandfonline.com/doi/full/10.1080/15384101.2015.1004937> [Accessed 18 September 2020].

4. Fricker, Michael et al. "Neuronal Cell Death." Physiological reviews vol. 98,2 (2018): 813-880. doi:10.1152/physrev.00011.2017

5. Jellinger, Kurt A., and Christine Stadelmann. "Problems of cell death in neurodegeneration and Alzheimer's Disease." Journal of Alzheimer's disease : JAD vol. 3,1 (2001): 31-40. doi:10.3233/jad-2001-3106

6. 10. Krantic, S., Mechawar, N., Reix, S. and Quirion, R., 2020. Apoptosis-Inducing Factor: A Matter Of Neuron Life And Death.

7. Kruman, Inna I. Why Do Neurons Enter the Cell Cycle? 5 Apr. 2004, www.tandfonline.com/doi/abs/10.4161/cc.3.6.901?src=recsys.

8. Lodish H, Berk A, Zipursky SL, et al. Molecular Cell Biology. 4th edition. New York: W. H. Freeman; 2000. Section 21.1, Overview of Neuron Structure and Function. https://www.ncbi.nlm.nih.gov/books/NBK21535/

9. Moh C., Kubiak J.Z., Bajic V.P., Zhu X., Smith M.A., Lee H. (2011) Cell Cycle Deregulation in the Neurons of Alzheimer's Disease. In: Kubiak J. (eds) Cell Cycle in Development. Results and Problems in Cell Differentiation. Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-642-19065-0_23

10. Neary, D., Snowden, J., Mann, D., Northen, B., Goulding, P. and Macdermott, N., 1990. Frontal lobe dementia and motor neuron disease. Journal of Neurology, Neurosurgery & Psychiatry, 53(1), pp.23-32.

11. Sapolsky, R. M. (1992). Stress, the aging brain, and the mechanisms of neuron death. The MIT Press.