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PERSPECTIVE

Retroviral legacies: An evolutionary perspective towards endogenous retroviruses and myelin formation

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The myelin sheath, an insulating layer enveloping axons in both the central and peripheral nervous systems, enables efficient propagation of action potentials via saltatory conduction. This occurs through periodic depolarization at the nodes of Ranvier, where essential ion channels are densely aggregated. A recent study delved into the evolutionary origins and functionality of RNLTR12-int, a retroviral retrotransposon that influences myelin sheath synthesis by aiding the binding of SOX-10 to the myelin basic protein gene's promoter region.[1] This interaction is critical for myelin compaction, a characteristic prevalent across jawed vertebrates, enhancing the structural complexity of their central nervous systems.[1]

The study highlights how endogenous retroviruses (ERVs), particularly ERV1, have integrated into the human genome, some of which remain functionally active, influencing myelin synthesis and showcasing the evolutionary benefits conferred by ancient viral genes. For example, RNLTR12-int plays a pivotal role in the maturation of oligodendrocytes and the myelination process in the central nervous system and affects Schwann cell functionality in the peripheral nervous system.[1] The inhibition of RNLTR12-int transcription significantly reduces myelin content in peripheral axons, suggesting a critical role in myelin development, which is believed to have emerged simultaneously in the central and peripheral nervous system.[1]

The concept of "retromyelin" sequences in jawed vertebrates related to myelin evolution points to convergent evolution. Whether these sequences, which first appeared in cartilaginous fishes, are derived from a common ancestor or multiple retroviral infections after speciation is debated. Studies involving 22 species to construct a phylogenetic tree indicated that retromyelin's structural similarities across different species support the hypothesis of separate retroviral invasions postspeciation.[1]

Additionally, the vertebrate genome's myriad extinct ERV elements underscore the interplay between viruses and vertebrate evolution. Although some viral elements, such as retromyelin, did not become established in jawless vertebrates and invertebrates, leading to their genomic extinction, those retained in jawed vertebrates have been instrumental in evolutionary advancements such as myelin development.[1] Beyond structural benefits, certain ERV envelope proteins in the mammalian genome serve as barriers against exogenous retroviral infections and contribute to vital functions crucial for maintaining pregnancy viability, such as placental tissue protection and trophoblast cell fusion.[2,3]

In conclusion, the evolutionary interdependence between vertebrates and ancestral viruses has been pivotal in shaping cellular morphology and enhancing survival through innovations such as myelin. The continued exploration of these relationships is crucial for understanding the intricate mechanisms of cellular function in mammalian evolution. Research on this subject not only enriches our knowledge of genetic

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and evolutionary biology but also illustrates the profound impact of viral elements on vertebrate development. Further studies are essential to unravel more about these complex interactions and their broader implications.

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