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EXPLORATION OF THE THERAPEUTIC POTENTIAL OF SEMAPHORIN 5A IN HUMAN GLIOBLASTOMAS

Lee AY, Menon A, Ann Mary B, Shah Jahan FR and **Law JW**
Monash University, Malaysia

Astrocytomas are the most common form of brain tumor in human, among which glioblastoma mutliforme is highly malignant and exhibits high invasiveness and resistance to radiotherapy, leading to high recurrence rate even after radical surgical resection of the tumor and short survival after initial diagnosis. This calls for development of novel effective treatment regimens, which apparently requires a more thorough understanding of the pathoetiology at both cellular and molecular levels. Recently, accumulating evidence points to the emerging role of axon guidance molecules such as semaphorins, neuropilins and plexins in glioma progression. We have previously demonstrated the effects of semaphorin 5A (Sema5A) and its receptor plexin-B3 in inhibiting glioma cell migration, invasion and proliferation. Notably, analysis of human glioblastoma specimens revealed a marked decline in Sema5A protein level from low to high grade, suggesting a correlation between its loss of function and tumor progression. Restoration of Sema5A level by forced expression or exogenous supply of Sema5A protein in advanced grade glioblastomas successfully counteracts tumorigenicity of cancer cells. These findings provide compelling evidence that Sema5A and plexin-B3 subserve anti-tumorigenic functions, which are compromised in glioblastomas due to a downregulation of Sema5A protein expression, hence contributing to high infiltration and malignancy. In this presentation, the mechanisms of tumor suppressor effect of Sema5A and the exploration of its therapeutic potential will be discussed.

BIOGRAPHY

Lee AY obtained his PhD from the University of Hong Kong. He is currently a senior lecture at the School of Pharmacy, Monash University Malaysia. Current focus of his research is to understand the functions of axon guidance molecules semaphorins and plexins in cell migration and invasion, axon navigation, cellular differentiation, neuronal regeneration and brain tumor development. His research team has recently revealed the tumor suppressor functions of semaphorin 5A in human glioblastomas and is currently exploring its therapeutic potential. He has published his research findings in leading journals in neurosciences and cancer biology, and has served as editorial board member and reviewer in reputable journals.

alan.lee@monash.edu

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