

学位論文の要旨

論文題目 Human-biased *TMEM25* expression promotes expansion of neural progenitor cells to alter cortical structure in the developing brain

(大脳皮質発達における *TMEM25* のヒト特異的発現レベル制御による神経幹細胞の増殖促進と層構造変化)

広島大学大学院統合生命科学研究科
生命医科学プログラム

学生番号 D203862

氏名 AN BOYANG

Abstract :

Cortical expansion has occurred during human brain evolution. Accumulating evidence indicates that human-specific genes underpin cortical expansion by diversifying the number of neural progenitors (NPCs), whereas many more conserved genes showing biased expression between species should also play crucial roles in this process. By comparing human and mouse RNA-seq datasets, we found that a conserved gene, transmembrane protein 25 (*TMEM25*), was much more highly expressed in human NPCs. Overexpression of either human *TMEM25* or mouse *Tmem25* similarly promoted proliferation of mouse cortical progenitors in vitro. Mimicking human-type expression of *TMEM25* in mouse ventricular cortical progenitors accelerated proliferation of basal radial glia (bRG) (cells specifically and abundantly distributed in human subventricular zone [SVZ]) and increased the number of upper-layer neurons in vivo. By contrast, RNA-seq analysis and pharmacological assays showed that knockdown of *TMEM25* in cultured human NPCs compromised the effects of extracellular signals, leading to cell cycle inhibition via Akt repression. These data suggest that *TMEM25* can receive extracellular signals to expand bRG, a process which occurs specifically in human cortical development.