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Ins2 gene expression and function in the mouse brain

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Insulin deficiency and insulin resistance has both been reported in Alzheimer's disease. This study was designed to examine whether insulin protein or markers of insulin promoter activity can be observed in the mouse brain and to also determine the effects of brain-specific insulin gene (*Ins2*) knockout on behaviour to ascertain the possible role of insulin produced locally in the brain. We have employed germline *Ins2* knockout mice (*Ins2*-/-), heterozygous mutant mice ($Ins2^{+/-}$), and their wildtype littermate controls ($Ins2^{+/+}$), as well as cell type specific *Ins2* knockout mice derived by crossing NesCre, SynCre, or CamkCre mice with mice harboring a floxed *Ins2* allele (on the Ins1-/- background). Mice were genotyped using PCR. Insulin mRNA analysis using qPCR confirmed the deletion of the Ins2 gene in the germline knockout animals, but revealed a paradoxical increase in *Ins2* mRNA in many brain regions of the $Ins1^{-/-}$:$Ins2^{f/f}$:NesCre, $Ins1^{-/-}$:$Ins2^{f/f}$:SynCre, $Ins1^{-/-}$:$Ins2^{f/f}$:CamkCre, relative to their littermate controls, suggesting an upregulation of Ins2 production from non-neuronal cell types within the brain. Indeed, analysis of *Ins2* gene activity using $Ins2^{GFP}$ knock-in mice suggested the presence of *Ins2* in non-neuronal cell types surrounding the ventricles. Interestingly, preliminary behavioural studies (Y-maze, open field test, familiar object test, and Morris water maze) identified differences in learning and memory in mice lacking *Ins2* expression in the brain. Collectively, these results suggest that *Ins2* is expressed in both neuronal and non-neuronal cell types within the brain, where it has complex roles modulating behavior. This work may shed light on the role of insulin in Alzheimer's disease.

Biography

Sunday A. Ajayi completed his PhD at Obafemi Awolowo University, Ile-Ife, Nigeria in 2012 and moved to University of KwaZulu-Natal, Durban South Africa between 2013 and 2015 for Postdoctoal Fellowship. In 2016 he relocated to Vancouver, Canada where he is presently a Postdoctoral Fellow sponsored by IBRO-ISN Research Fellowship in the Laboratory of Professor James D. Johnson at the University of British Columbia.

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