



p75 neurotrophin receptor (p75NTR) is a key regulator of self-renewal, proliferation and differentiation of brain tumour initiating cells

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Abstract:

Glioblastoma multiform (GBM) is the most common and aggressive brain tumor that is inevitably a fatal disease. GBM is a heterogeneous tumor consisting of tumor cells and a small population known as brain tumor initiating cells (BTICs) or glioblastoma stem-like cells. BTICs appear to drive tumor progression, underlie therapeutic resistance to current treatment and tumor relapse and have been highlighted as important therapeutic targets. The ability of glioma cells to invade into the surrounding brain parenchyma is a major clinical issue rendering glioblastoma incurable by conventional therapies. Using a large panel of GBM cells including genetically different patient-derived-BTICs we have investigated the roles of p75NTR in regulating GBM progression. Immunohistochemical studies and western blot analysis revealed that p75NTR is variably expressed on BTICs. Loss-of-function and gain-of-function studies of p75NTR revealed that p75NTR is involved in regulating self-renewal, proliferation, cell cycle progression, symmetry and asymmetry cell divisions, apoptosis, differentiation and invasion of genetically different patient-derived BTICs. Furthermore, Loss-of-function of p75NTR in these BTICs inhibited their tumorigenic behaviors in vivo and extended the survival time of mice bearing brain tumors generated by p75NTR knockdown BTICs compared to their control counterparts. These findings provide new evidence for involvement of p75NTR in regulating GBM progression and suggest p75NTR is a therapeutic target for the treatment of this devastating cancer.

Biography:

Dr Mana Alshehri, is an associate research scientist at King Abdullah International Medical Research Center in Saudi Arabia. He graduated from King Saud University with a bachelor degree in clinical laboratory sciences then he moved to England where he did his master degree in molecular medicine field from Sheffield University. After that he moved to Canada where he joined the University of Calgary to do his PhD degree and worked in the lab of Dr Stephen Robbin; the scientific director of cancer research in the Canadian Institute of health Research. During His PhD, Dr. Mana won more than 13 prizes and scholarships including a 3 years scholarship from



Arnie Charbonneau cancer institute, and a scholarship from the Canadian Institute of Health Research, and the international student scholarship from University of Calgary and others. Recently, Dr Mana won a scholarship from the Dubai Harvard Foundation for Medical Research and He is currently studying at the high impact cancer research program at Harvard Medical School, Harvard University. Dr Mana is an author on several book chapters and peer-reviewed articles published in high impact journal including Nature Communications, Biomaterials, Oncogene and others.

Publication of speakers:

- Mana Alshehri et al ; Glioma-derived IL-33 orchestrates an inflammatory brain tumor microenvironment that accelerates glioma progression, 2020 Oct 5
- Mana Alshehri et al ; cell autonomous and cell non-autonomous roles of p75 neurotrophin receptor (p75ntr) in glioma invasion, 2015 Nov 9
- Mana Alshehri et al ; Capicua regulates neural stem cell proliferation and lineage specification through control of Ets factors, 2019 May 1
- Mana Alshehri et al ; Neurons Export Extracellular Vesicles Enriched in Cysteine String Protein and Misfolded Protein Cargo, 2017 Apr 19
- Mana Alshehri et al ; A novel inhibitory effect of oxazol-5-one compounds on ROCKII signaling in human coronary artery vascular smooth muscle cells, 2016 Aug 30

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