Insulin-Like Growth Factor System Alters The Differentiation of Placental Mesenchymal Stem Cells into Skeletal Muscle

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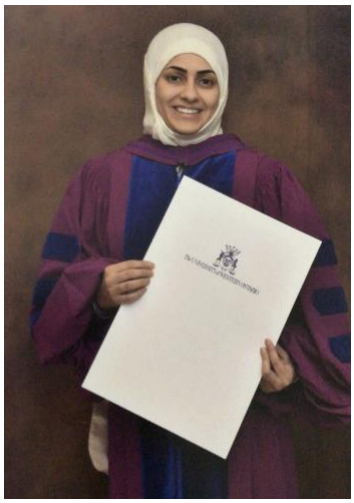
Abstract:

Insulin-like growth factors are major components of the stem cell niche, as they regulate proliferation and differentiation of many tissues including skeletal muscle. Insulin-like growth factor binding protein-6 (IGFBP-6) is expressed in developing muscle cells and is the main regulator of IGF-II (fetal IGF). To date, no previous studies have been reported relating placental mesenchymal stem cells (PMSCs), muscle differentiation, and IGFBP-6. We **hypothesized** that IGFBP-6 regulates the maintenance of pluripotency of PMSCs and promotes their differentiation into muscle. **OBJECTIVES: 1)** to investigate the capacity of PMSCs to differentiate into muscle; and **2)** to evaluate the intracellular and extracellular actions of IGFBP-6 on PMSCs muscle differentiation. **METHODS:** Chorionic villi were collected from preterm placenta and stem cell identity was verified. Cells were then differentiated into muscle for 14 days and the impact of IGFBP-6 was investigated by adding IGFBP-6 or silencing it using siRNA. **RESULTS:** Isolated cells differentiated into muscle cells, forming multi-nucleated fibers expressing muscle markers with increased levels of IGFBP-6 and decreasing levels of pluripotency markers. Additionally, extracellular addition of IGFBP-6 significantly increased protein levels of muscle commitment maker Pax3/7, with an increase at the earlier time points for muscle markers that goes down by time. Interestingly, both SOX2 and OCT4 levels correlate with IGFBP-6. On the other hand, silencing IGFBP-6, significantly decreased both pluripotency and differentiation markers at the earlier time points. we identified the signal transduction mechanisms of IGFBP-6 on muscle differentiation by placental mesenchymal stem cells (PMSCs). We also showed that muscle differentiation required activation of both AKT and MAPK pathways. Interestingly, we demonstrated that IGFBP-6 could compensate for IGF-2 loss and help enhance the muscle differentiation process by triggering predominantly the MAPK pathway independent of activating either IGF-1R or the insulin receptor (IR). These findings indicate the complex interactions between IGFBP-6 and IGFs in PMSC differentiation into the skeletal muscle and that the IGF signaling axis, specifically involving IGFBP-6, is important in muscle differentiation. **CONCLUSION:** IGFBP-6 regulates PMSC differentiation into muscle, with more prominent effects at the beginning of the differentiation process when PMSCs commit to muscle formation.

PUBLICATIONS

1. **Aboalola D**, Han V KM. Insulin-Like Growth Factor Binding Protein-6 Promotes the Differentiation of Placental Mesenchymal Stem Cells into Skeletal Muscle Independent of Insulin-Like Growth Factor Receptor-1 and Insulin Receptor. Stem Cells International 2019; vol.2019, Article ID 9245938.
2. **Aboalola D**, Han V KM. Different Effects of Insulin-Like Growth Factor- 1 and Insulin-Like Growth Factor-2 on Myogenic Differentiation of Human Mesenchymal Stem Cells. Stem Cells International 2017; vol.2017, Article ID 8286248.
3. **Aboalola D**, Han V KM. Insulin-Like Growth Factor Binding Protein-6 Alters the Myogenic Differentiation of Human Mesenchymal Stem Cells. Stem Cells International 2017, Article ID 2348485.
4. Youssef A, **Aboalola D**, Han V KM. The Roles of Insulin-Like Growth Factors in Mesenchymal Stem Cell Niche. Stem Cells International 2017; vol.2017, Article ID 9453108.

Photo:



Doctor of Philosophy, Anatomy and Cell Biology – Stem Cells

The University of Western Ontario London Ontario, Canada *2012-2017*

Master of Science, Anatomy and Cell Biology – Stem Cells

The University of Western Ontario London Ontario, Canada *2009- 2011*

Bachelor degree in Science, Biology

King AbdulAziz University Jeddah, Saudi Arabia *2003- 2007*

AWARDS:
Sheikh Hamdan Bin Rashid Al Maktoum Award for Medical Science for best oral presentation (First Place) - MEMBS
Abu Dhabi, UAE – 2017

Travel award from Till & McCulloch Stem Cell Meeting
Toronto, Ontario, Canada – 2015

Best Poster- Gabriel G. Altmann Research Award
London, Ontario, Canada – 2014

Travel award from Gordon Research Conference
Ventura, California, USA – 2013

Best Poster/Basic Science – Paediatrics Research Day
London, Ontario, Canada – 2013

Travel award from 6th International Congress of GRS & IGF
Munich, Germany – 2012

Lab Experience:

- Isolating and characterizing mesenchymal stem cells from the chorionic villi of preterm human placenta
- Cell culture, molecular biology, flow-cytometry, Immunocytochemistry, and cell imaging
- Protein biochemistry techniques (Western blotting and ELISA)
- Cell biology (mammalian cell transfection and immunoprecipitation)

Work:
Post-Doctoral Researcher Scientist (2017 – Present)
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