



Official Journal of TESMA

# Regenerative Research

www.regres.tesma.org.my  
E-ISSN 2232-0822

Tissue Engineering  
and Regenerative  
Medicine Society of  
Malaysia

Regenerative Research 7(1) 2018 147

## INSIDE-OUT EFFECTS OF TYPE 2 DIABETES MELLITUS (T2DM) ON DIABETIC TENDINOPATHY: *IN VIVO* & *IN VITRO* STUDIES

Hui-Yee Tan<sup>1</sup>, Sik-Loo Tan<sup>1</sup>, Hak Savatey<sup>1</sup>, Mun-Peak Nyon<sup>2</sup>, Tunku Kamarul<sup>1,\*</sup>

<sup>1</sup>Tissue Engineering Group (TEG), NOCERAL, Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, MALAYSIA.

<sup>2</sup>Clinical Investigation Center (CIC), Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, MALAYSIA.

### ARTICLE INFO

Published: 26<sup>th</sup> August 2018

\*Corresponding author:

Tunku Kamarul

Email:

tkzrea@um.edu.my

### KEYWORDS

Orthopaedics;  
Type II Diabetes;  
Obesity;  
Tendon

### SUMMARY

**Introduction:** Among the diabetic cases, more than 95% of them are Type 2 Diabetes Mellitus (T2DM), which is characterized by insulin resistance (IR). Diabetes had been reported to be associated with musculoskeletal diseases, eg: diabetic tendinopathy. However, the downstream signalling of IR on tendon remains largely to be discovered. The objectives of this study are (i) to determine the effect of IR on tendon microstructure and total collagen expression in tendon *in vivo* (ii) to determine the effect of IR on tenocytes (tendon cells) homeostasis. **Materials and methods:** In *in vivo* study, 16 Sprague-Dawley rats were randomly divided into 3 groups: Group 1 (G1) with normal diet, Group 2 (G2) and Group 3 (G3) were both fed with high fat diet and induced with Streptozotocin (STZ). G3 was then treated with Metformin while G2 did not. The Achilles tendons (AT) were collected for total collagen assay (TCA), histology analysis and immunofluorescence (IF) staining. In the *in vitro* study, the primary human tenocytes were induced with tumor necrosis factor-alpha (TNF- $\alpha$ ) to develop IR model. At 24 hours, the glucose uptake activity and total collagen assay were performed. **Results:** H&E histology showed no apparent changes in the tendon microstructure, while IF staining evidenced the presence of insulin receptor on AT of all the groups. TCA of AT showed significantly lower total collagen content in G2 and G3 compared to G1. *In vitro* analysis showed significantly reduced of glucose uptake in IR model tenocytes. **Discussion:** Previous studies had been reported that T2DM clinically reduce the tendon biomechanics in diabetic tendinopathy patients. This can be explained by the reduction of total collagen contents in IR-induced groups. Reduction of glucose uptake in IR tenocyte models also showed the negative impact of IR signalling on glucose transporter type 4 (GLUT4) activities. **Conclusion:** IR significantly reduced the total collagen content in AT *in vivo*, and significantly suppressed the glucose uptake in tenocytes *in vitro*.

### Acknowledgement

Supported by HIR-MOHE research grant initiative and University of Malaya Fundamental Research Grant Scheme (FRGS: FP004-2015A and FP031-2015A).