Impact of Exercise Intervention on DNA Methylation of *FKBP5* in Obese, Insulin Resistant South African Women

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Abstract

Background: Obesity and insulin resistance are modifiable risk factors which present opportunities for type 2 diabetes prevention and intervention. We previously showed that DNA methylation of FK506-binding protein (FKBP5) is altered in subcutaneous adipose tissue (SAT) from obese compared to normal-weight South African women, and significantly associated with adiposity and insulin resistance. The aim of this study was to explore the effect of a 12-week exercise intervention on FKBP5 methylation in obese, insulin resistant (OBIR) South African women.

Methods: OBIR South African women (n=35) were randomized into an exercise (n=20) or control (n=15) group. The exercise group underwent aerobic and resistance training for 12-weeks, while participants from the control group continued their normal daily activities. FKBP5 methylation was measured in gluteal SAT (GSAT) and abdominal SAT (ASAT) by pyrosequencing and the presence of the FKBP5 rs1360780 polymorphism was evaluated using quantitative real-time PCR.

Results: Two CpG dinucleotides within FKBP5 intron 7 were hypermethylated in ASAT (CpG542: 28% vs 41%, p=0.001; CpG543: 28% vs 41%, p=0.003), but not GSAT in response to exercise training. When stratified based on genotype, carriers of the T allele presented higher FKBP5 methylation after exercise training when compared to baseline in GSAT (CpG542, 29% vs 37%, p=0.033; CpG543, 31% vs 38%, p=0.028), while no DNA methylation differences were observed in individuals with the C/C genotype. In TSAT, both genotypes displayed FKBP5 hypermethylation post exercise intervention compared to baseline (CC: CpG542, 25% vs 37%, p=0.008; CpG543, 26% vs 36%, p=0.013; C/T: CpG542, 32% vs 47%, p=0.022; CpG543, 32% vs 49%, p=0.023).

Conclusion: Exercise training induces FKBP5 hypermethylation in OBIR South African women, which occurs in a genotype and SAT depot-specific manner. These findings highlight epigenetic changes that can be modulated by exercise during obesity and may aid in appropriate interventions to reduce the surging impact of this disease.

Recent Publications

Willmer, T., Dias, S., Louw, J., Goedecke, J., Pheiffer, C. (2020) DNA methylation of *FKBP5* in South African women: associations with BMI and insulin resistance. Clinical Epigenetics, 12(141). DOI: 10.1186/s13148-020-00932-3

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Bleloch, J. S., Ballim, R. D., Kimani, S., Parkes, J., Panieri, E., Willmer, T., and Prince, S. (2017) Managing sarcoma: where have we come from and where are we going? Ther Adv Med Oncol, 9(10), 637–659. DOI: 10.1177/1758834017728927.

Willmer, T., Cooper, A., Peres, J., Omar, R and Prince, S. (2017) The T-Box Transcription Factor 3 in Development and Cancer. BioScience Trends. DOI: 10.5582/bst.2017.01043.

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Biography (150 word limit)

Tarryn Willmer is Senior Scientist in the Biomedical Research and Innovation Platform at the South African Medical Research Council. She is also a extraordinary senior lecturer in the Department of Medical Physiology, Stellenbosch University, South Africa. She holds a BSc, BSC (Hons) and MSc in Biochemistry from Rhodes University and a PhD in Cell Biology from the University of Cape Town.

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Notes/Comments: