Resistance training increases total AKT, but decreases basal AS160 phosphorylation in individuals with clusters of metabolic risk factors

C.A. Goodman,[1] I. Levinger,[1] K.F. Howlett,[2] J. Peake,[3] A. Garnham,[2] D.L. Hare,[4] G. Jerums[5] and S. Selig,[1]
[1]School of Human Movement, Recreation and Performance, Victoria University, Melbourne, VIC 8001, Australia, [2]School of Exercise and Nutrition Sciences, Deakin University, Melbourne, VIC 3125, Australia, [3]School of Human Movement Studies, University of Queensland, Brisbane, QLD 4072, Australia, [4]Department of Cardiology, Austin Health, University of Melbourne, VIC 3084, Australia and [5]Department of Endocrinology, Austin Health, University of Melbourne, VIC 3084, Australia.

An increased risk profile and levels of inflammatory markers may lead to abnormal glucose homeostasis, insulin resistance and type 2 diabetes. Studies have reported that obesity and diabetes impairs the phosphatidylinositol 3- kinase (PI3-K) pathway, partly by reducing phosphorylation and activity of the insulin signalling proteins Akt and Akt substrate of 160kDa (AS160) (Krook *et al.*, 2004; Krook *et al.*, 1998; Karlsson *et al.*, 2005). Aerobic training has been shown to improve insulin signalling protein phosphorylation and improve insulin sensitivity. The effect of resistance training (RT) on insulin signalling proteins however is less clear. Howlett *et al*. (2007) recently reported that AS160 phosphorylation decreases immediately after an acute bout of resistance exercise. To date, no studies have examined the effect of prolonged resistance training on basal AS160 phosphorylation. Also, limited data exist concerning the association between inflammatory markers, metabolic risk factors and total and phosphorylated forms of Akt and AS160. Therefore, this study investigated the effects of RT, as a single intervention, on total and phosphorylated forms of Akt and AS160 in individuals with clusters of metabolic risk factors, and the correlation between these proteins, metabolic risk factors and inflammatory markers in this population.

Twenty-one untrained men (n = 13) and women (n = 8) aged 51.2 ± 1.5 (Mean ± SEM; range 40-69 yr), who had two or more risk factors for metabolic syndrome (International Diabetes Federation; Zimmet *et al.,* 2005) were randomly allocated to training (n = 10) or non-exercise control (n = 11) groups. Randomisation was stratified according to sex. RT was performed 3 days a week for 10 weeks with a gradual increase in intensity from 40-50% of one repetition maximum (1RM) to 80-85% of 1RM (see Levinger *et al.,* (2007) for details). Before and after the RT, anthropometric measurements were conducted, resting muscle biopsies (*vastus lateralis*) were obtained, and blood samples were collected for inflammatory markers (IL-1β, IL-6, IL-8, IL-10 & TNF-α). To obtain 'basal' levels of Akt/AS160 phosphorylation and systemic markers of inflammation, the post-training muscle biopsy and blood samples were taken 4-5 days after the last training bout to minimise any acute changes due to the last training stimulus. Muscle samples were analysed for total and phosphorylated forms of Akt and AS160 by Western blotting and for muscle glycogen content. Results are Mean ± SEM.

Pre-training (baseline), the two groups did not differ significantly in terms of sex, age, anthropometric measurements or metabolic risk factors. At baseline, with all participants combined, there were positive correlations between total Akt and total AS160 (r = 0.48, p = 0.03) and the phosphorylated forms of Akt (Ser^{473}) and AS160 (r = 0.65, p < 0.01). RT significantly increased total Akt from 172.8 ± 15.9 to 215.8 ± 27.1 arbitrary units (or 22.5 ± 8.2 % increase; p < 0.01 compared to pre-training value and p = 0.06 compared to controls) and reduced basal AS160 phosphorylation from 95.1 ± 18.2 to 71.5 ± 13.9 arbitrary units (or 19.9 ± 12.3 % decrease; p = 0.02 compared to pre-training data and p = 0.01 compared to controls). RT did not significantly alter basal Akt (Ser^{473}) phosphorylation or total AS160 protein content. Also, these proteins did not change in the Control group. RT did not alter the plasma levels of inflammatory markers. RT tended to increase glycogen stores (27.4 ± 10.9%, p = 0.06). The percentage change in phosphorylated AS160 was negatively correlated with the number of metabolic risk factors (r = 0.81, p < 0.01) and with plasma HbA1c (r = 0.74, p = 0.02).

In summary, 10 wks of RT increased total Akt protein content and reduced the basal levels of AS160 phosphorylation in middle aged people with high increased numbers of metabolic risk factors. The implications of this result for insulin signaling and glucose homeostasis remain to be determined.

Howlett KF, Sakamoto K, Garnham A, Cameron-Smith D & Hargreaves M. (2007) *Diabetes*, **56:** 1608-14.
Karlsson HK, Zierath JR, Kane S, Krook A, Lienhard GE & Wallberg-Henriksson H. (2005) *Diabetes*, **54:** 1692-97.
Krook A, Roth RA, Jiang XJ, Zierath JR & Wallberg-Henriksson H. (1998) *Diabetes*, **47:** 1281-6.
Krook A, Wallberg-Henriksson H & Zierath JR. (2004) *Medicine and Science in Sports and Exercise*, **36:** 1212-17.
Levinger I, Goodman C, Hare DL, Jerums G & Selig S. (2007) *Diabetes Care*, **30:** 2205-10.
Zimmet PZ, Alberti KG & Shaw JE. (2005) *Medical Journal of Australia*, **183:**175-176.