Glycated proteins inhibit K^+ channels in isolated vascular smooth muscle cells

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Fibronectin (FN) has been shown to enhance K^+ channel activity *via* an integrin-mediated mechanism. As vascular smooth muscle (VSM) K^+ channels mediate vasodilation, we investigated whether advanced glycation of fibronectin (as occurs in diabetes and renal failure) alters the normal stimulatory effect of this matrix protein on these channels. Under sterile conditions, FN (1mg/ml) was glycated (gFN) for 5 days in the presence of methylglyoxal (50mM) or glycolaldehyde (50mM). Albumin, a non-matrix protein, was similarly glycated as a control. VSM cells were enzymatically isolated from rat cerebral arteries for K^+ channel activity studies *via* whole cell patch clamp. The inhibitors, iberiotoxin (0.1μM) and 4-aminopyridine (1mM), were used to identify contributions of large conductance, Ca^{2+}-activated, K^+ channels and voltage-gated K^+ channels, respectively. While native FN enhanced whole cell K^+ current (1.8 fold), gFN caused a 56% inhibition of current compared to baseline. Furthermore, native albumin did not enhance basal K^+ current but when glycated caused inhibition (61%; $p < 0.05$). Inhibitor studies indicated a predominant effect of gFN on the Kv component of total K^+ current. These studies provide a potential mechanism by which advanced glycated proteins impair VSM function and adversely impact arteriolar vasodilation.