Contractile responses to perivascularfat from rat thoracic aorta

Perivascular fat (PVAT) is now considered an active endocrine and paracrine organ that modulates vascular reactivity. Many of the studies have focused on its anti-contractile effect through the release of perivascular-derived relaxing factors(1). However, we have recently demonstrated that PVAT from thoracic aorta impairs endothelium-dependent relaxation under physiological conditions, and thus represents a pro-contractile action (2). In this study, we investigated whether or not PVAT can directly induce vasocontractions.

Male Wistar rats (10-12 weeks) were killed by cervical dislocation and thoracic aortae, or small mesenteric arteries, were isolated for isometric tension recording. Contractility of aortic segments with (+PVAT) and without (-PVAT) were compared. In some experiments, PVAT was dissectedfrom aortae, homogenised and then added to isolated aortae or mesenteric arteries. Data are shown as mean±sem (n≥4) and analysed by two-way or one-way analysis of variance, or Student *t*-test, where appropriate.

In the aorta, the presence of PVAT had no effect on 60 mMKClcontraction (-PVAT: 16±1mN; +PVAT:14±2mN) but slightly enhanced the concentration-dependent response to methoxamine, an α1-adrenoceptor agonist (contraction to 10μM methoxamine, +PVAT: 135±15% vs -PVAT: 89±18% of KCl contraction; $P<0.05$). In -PVAT aorta, PVAT homogenate induced contractions (55±22% of KCl contraction) that were not significantly affected by losartan (1μM, AT_1 receptor antagonist: 3±11% inhibition) butabolished by prazosin (1μM; α1-adrenoceptor antagonist: 104±14%; $P<0.01$). This PVAT contraction did not require the presence of an endothelium (data not shown). On the other hand, tyramine, which is known to stimulate catecholamine release, induced concentration-dependent contraction only in the presence of aortic PVAT (contraction to 100μM tyramine,+PVAT: 54±19%; -PVAT: 3±1%of KCl contraction). This tyramine-induced contraction was reduced by prazosin (1μM; 84±20% inhibition).In contrast, aortic PVAT homogenate or tyramine had no contractile effect in small mesenteric arteries.

To conclude, these data are consistent with a pro-contractileeffect ofaortic PVAT. It can induce aortic contractions, probably through the release of catecholamines which then activate α1-adrenoceptors in the vascular wall.

(1) Gollasch M (2012). *Br J Pharmacol* **165**: 633-642

(2) Xue Y *et al*. (2014). Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol12Issue3abst094P.pdf