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Human adiponectin binds to bacterial lipopolysaccharide

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Abstract

Adiponectin has anti-inflammatory and anti-atherogenic properties in addition to its acknowledged roles in insulin sensitivity and energy homeostasis. These properties include the suppression of lipopolysaccharide [LPS]-mediated inflammatory events. We demonstrated that both recombinant and native adiponectin directly bind LPS derived from three different bacteria. The interaction occurred at pH 5.0–6.0 and was inhibited by the presence of Ca^{2+} and Mg^{2+}, but enhanced by the sequestration of these cations. Maximal binding occurred at pH 6.0 in the presence of ethylenediaminetetraacetic acid. Lipid A and C1q were not inhibitory, although LPS, heparin, zymosan, and individual sugars all inhibited the reaction. Periodate-mediated deglycosylation of adiponectin, and reduction and alkylation also inhibited binding. Since adiponectin infiltrates into [relatively] acidic sites of inflammation, it may act as a scavenging anti-inflammatory agent in atherosclerosis and vascular damage where LPS [and other pro-inflammatory molecules] are present.

Keywords: Adiponectin; Lipopolysaccharide; Glycosylation; pH; Endotoxin; Binding

It has been proposed that adiponectin, an adipose-specific glycoprotein circulating in high concentration, has an important role in insulin sensitivity and energy homeostasis. Adiponectin knockout mice have delayed clearance of plasma fatty acids [1], and may exhibit a moderate to severe degree of insulin resistance [1,2]. Supplementation of adiponectin in vivo leads to a reduction in serum glucose in the absence of increased insulin secretion [3]. Furthermore, treatment of mice with a globular fragment of adiponectin significantly decreases the elevated levels of plasma-free fatty acids caused by administration of a high fat test meal [4].

However, recent attention has turned to its apparent anti-inflammatory and anti-atherogenic properties. Inflammatory events in blood vessels, which can be mimicked by subcutaneous inoculation of lipopolysaccharide [LPS], contribute to coronary artery disease. Thus, LPS stimulated an up-regulation of adhesion molecules, cytokines, and chemokines in locally infected sites [5]. However, adiponectin inhibited LPS-induced NFκB activation and IL-6 production in adipocytes [6] and suppressed expression of adhesion molecules in endothelial cells [7]. Supplementation in vivo ameliorated atherosclerosis in apo-E-deficient mice [8,9] and protected the heart from ischaemia–reperfusion injury via AMPK- and COX-2-dependent pathways [10]. Adiponectin-deficient mice showed increased neointimal thickening and proliferation of vascular smooth muscle cells in mechanically injured arteries [11]. When the endothelium is damaged, adiponectin infiltrates the area and binds to vascular matrix proteins such as collagens I, III, and IV [12].

While receptors have been described which are specific for various forms of the protein [9], direct binding by adiponectin of platelet-derived growth factor [PGDF] BB obviated the need for receptor interaction to suppress the proliferation of smooth muscle cells [13]. Other growth factors were also shown to bind to adiponectin with distinct affinities, thus controlling their bioavailability and inflammatory potential at a pre-receptor level [14].

The molecule is subjected to significant post-translational modification, forming hexameric and larger isoforms

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that show biological activities not observed in smaller trimeric species [15]. Indeed, mutant forms of adiponectin with impaired ability to multimerize have been linked to diabetes [16]. The protein is also variably glycosylated with disialic acid [17] and glucosylgalactosyl [18] moieties. The role of these modifications on the activity of the molecule remains to be fully elucidated, although when the glycosylated lysine residues were substituted with arginines, which remain unmodified, the protein had greatly diminished insulin-sensitizing activity [18].

Given the anti-inflammatory role described for adiponectin, particularly in relation to LPS, we investigated whether adiponectin behaves like the related molecule C1q and other members of the collectin family of molecules in the ability to bind LPS. We also investigated factors controlling this interaction including the role of pH, divalent cations, and glycosylation, and demonstrated binding of LPS by both recombinant and native adiponectin from human serum.

Methods

Adiponectin. Carrier-free recombinant human adiponectin expressed in a mouse myeloma cell line was purchased from R&D [Minneapolis, MN].

Biotinylation of LPS. LPS was treated with 20 mM metaperiodate in 0.1 M acetate buffer, pH 5.0, and biotinylated with biotin hydrazide following the manufacturer's instructions [Pierce, Rockford, IL].

Periodate oxidation. Immobilized adiponectin was treated with 20 mM metaperiodate in 0.1 M acetate buffer, pH 5.0, overnight at 4 °C. The reaction was then quenched with glycerol, and in some experiments the aldehyde groups reacted with 1 mg/ml sodium borohydride.

ELISAs. Antigenic levels of adiponectin in column fractions were determined by a commercial sandwich ELISA [R&D] following the manufacturer's instructions.

To examine the interaction of adiponectin with LPS, the protein was coated at 1 μg/ml in phosphate-buffered saline on Nunc Maxisorp wells. Non-specific binding sites were quenched by incubation with 3% bovine albumin, and biotinylated LPS in 0.1 M acetate buffer was allowed to interact with adiponectin for 60 min at room temperature. After washing with PBS containing 0.1% Tween 20, bound LPS was detected by the addition of avidin-peroxidase, followed after washing by tetramethylbenzidine substrate. Colour development occurred for 5–60 min, and OD readings were taken at 450 nm after the addition of sulphuric acid.

The effect of various substances on this interaction was determined by their preincubation for 30 min with biotinylated LPS before addition of the mixture to the ELISA well. All sugars, zymosan, inulin, and lipid A were from Sigma [St. Louis, MO], while heparin was purchased from Merck [Whitehouse Station, NJ] and C1q from Calbiochem [San Diego, CA].

In other experiments, LPS was coated onto Nunc Maxisorp wells in phosphate buffer at 100 μg/ml. Non-specific binding was prevented by bovine albumin as before, and the amount adiponectin bound on subsequent incubation determined by the addition of a biotinylated monoclonal antibody to adiponectin [R&D], followed by avidin-peroxidase, and tetramethylbenzidine substrate.

The binding of LPS to C1q was determined by coating C1q at 10 μg/ml on Nunc wells. Non-specific binding was again prevented by the addition of bovine albumin, and the binding of biotinylated LPS was determined as before.

The binding of LPS to adiponectin from human sera was determined by capturing the protein from serum diluted 1/50 with a monoclonal antibody [R&D]. Biotinylated LPS was then added in acetate buffer containing albumin and detected as before. Seven individual sera were used: four from control subjects with normal insulin sensitivity and three from patients with end stage renal disease on dialysis. The latter had significantly higher levels of adiponectin, but reduced insulin sensitivity.

Enzyme digestion. To investigate any effect on protein structure induced by pH or ethylenediaminetetraacetic acid [EDTA], adiponectin was incubated for up to 16 h at 37 °C with 0.1–0.5 mg/ml trypsin [Sigma] or Glu C [Sigma] enzyme in acetate buffer, pH 5.0, or at pH 6.0 with the addition of 10 mM EDTA. The resulting fragments were analysed by reducing SDS analysis, followed by blotting onto nitrocellulose. This was probed with a polyclonal goat antibody to adiponectin [Santa Cruz, Ca], which was detected by a peroxidase-conjugated polyclonal antibody and chemiluminescence.

Reduction and alkylation of adiponectin. To investigate the role of multimer formation on LPS binding, the protein was incubated with 0.1 M dithiothreitol [DTT] in phosphate-buffered saline for 60 min at 37 °C before the addition of 0.2 M iodoacetamide.

Superose column chromatography. Adiponectin in plasma was resolved by chromatography on an FPLC Superose 12 column [Pharmacia, Piscataway, NJ] equilibrated with phosphate-buffered saline.

Results

Characterization of adiponectin–LPS interaction

Preliminary experiments showed that while biotinylated LPS from *Escherichia coli* 0111:B4 bound to immobilized adiponectin in acetate and bis-tris buffers, phosphate buffer inhibited binding. Acetate gave satisfactory buffering capacity over the pH range in which binding occurred. While binding of biotinylated LPS to adiponectin was maximal at pH 5.0, it increased further in the presence of EDTA, and the pH optimum was shifted to pH 6.0 (Fig. 1). This effect of EDTA was specific for the immobilized adiponectin, as shown by an experiment where EDTA was added to adiponectin for 60 min, then removed and biotinylated LPS added. In the reverse experiment, adiponectin bound to LPS immobilized on polystyrene wells, with maximal binding occurring at pH ~ 6.5.

Binding of adiponectin to LPS was also saturable, with half maximal binding occurring at 0.5 μg/ml (Fig. 2A). The binding of biotinylated LPS to adiponectin was also

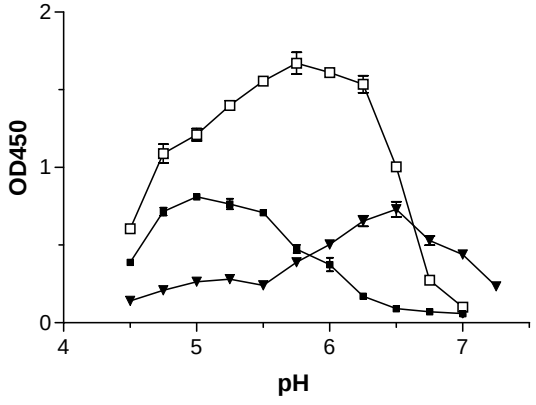

Fig. 1. The effect of pH on the binding of biotinylated LPS from *E. coli* 0111:B4 to solid-phase recombinant human adiponectin in the presence [□] and absence [■] of EDTA. The influence of pH on the binding of recombinant adiponectin to solid-phase LPS from *E. coli* 0111:B4 is also shown [▼]. Data represent means ± SEM in a representative experiment. Results are representative of at least three independent experiments.

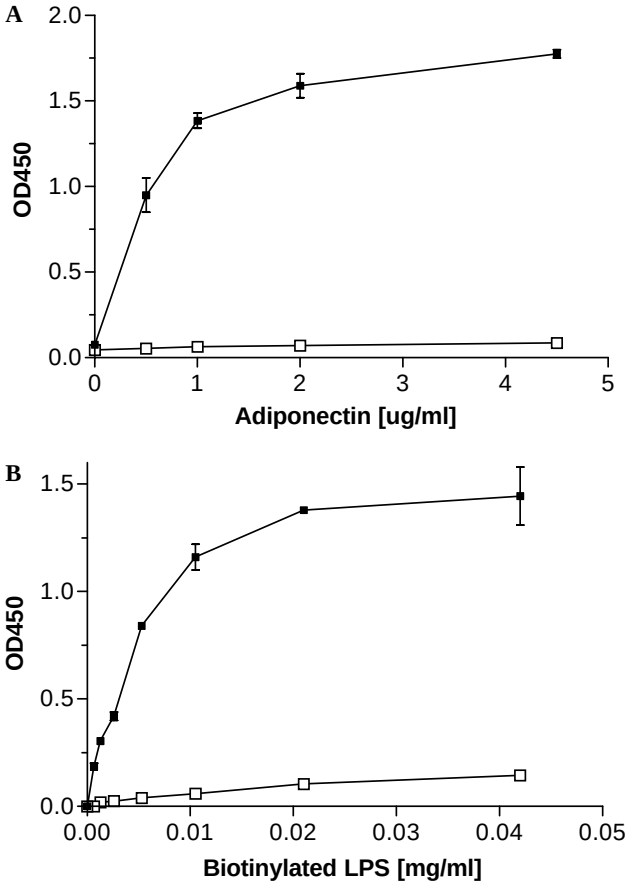

Fig. 2. (A) The binding of recombinant human adiponectin to LPS from *E. coli* 0111:B4 [■], or to bovine albumin [□]. (B) The binding of biotinylated LPS from *E. coli* 0111:B4 to solid-phase recombinant human adiponectin [■], or to bovine albumin [□]. Data represent means ± SEM in a representative experiment. Results are representative of at least three independent experiments.

saturable, with half maximal binding occurring at ~50 μg/ml LPS (Fig. 2B). In both cases, there was little binding to albumin-coated wells.

The role of the structure of adiponectin on binding LPS

The effect of incubation at pH 5 and at pH 6 in the presence of EDTA on the structure of adiponectin was examined by investigating the susceptibility of the protein to either trypsin or Glu C enzymes. Up to five different fragments were detected with various incubation times. However, there was no change in the pattern of fragmentation [not shown].

FPLC analysis [19] of recombinant adiponectin revealed that most of the preparation was of high molecular weight; i.e., up to 1000 kDa. The size distribution of the adiponectin species that bound immobilized LPS was similar. To further investigate the potential for low molecular weight [trimeric] species to bind LPS, recombinant adiponectin was reduced by incubation with 0.1 M DTT, coated on to ELISA wells, and subsequently alkylated with 0.2 M iodoacetamide. Alternatively, bound adiponectin was reduced and alkylated in situ. In each case, no binding to LPS was detected, although detection of polystyrene-bound adiponectin with a monoclonal antibody [BD, San Jose, CA] confirmed that reduction and alkylation had not significantly affected the quantity of adiponectin bound.

The effect of cations on the interaction of adiponectin and LPS

We investigated the effect of cations at both pH optima. At pH 5.0 the addition of up to 0.4 M NaCl to biotinylated LPS inhibited adiponectin binding, while binding at pH 6.0 in the presence of EDTA was stimulated several fold in the presence of up to 0.2 M NaCl, although 0.4 M NaCl was inhibitory (Fig. 3).

Given the stimulation of binding obtained in the presence of EDTA, we further investigated the role of divalent cations in the binding of LPS to adiponectin. The effect of ethylene glycol-bis-*N*,*N*′-tetraacetic acid [EGTA] was similar to that of EDTA, with stimulation of binding at pH 6.0 (Fig. 4). However, the addition of divalent cations such as Ca^{2+} and Mg^{2+} was inhibitory at both pH 5.0 and pH 6.0. When Mg^{2+} was added to EGTA to determine the role of Ca^{2+} in the interaction, the effect was inhibitory at both pH 5 and pH 6.

The effect of potential inhibitors on the interaction of adiponectin and LPS

We further investigated the binding between adiponectin and LPS in the presence of potentially interfering substances at both pH optima. As expected, the addition of 17 μg/ml of unlabelled LPS reduced binding to background levels. C1q also interacts with LPS [20,21], and we confirmed this reaction occurred at both pH values in our buffer system [not shown]. Nevertheless, the addition of

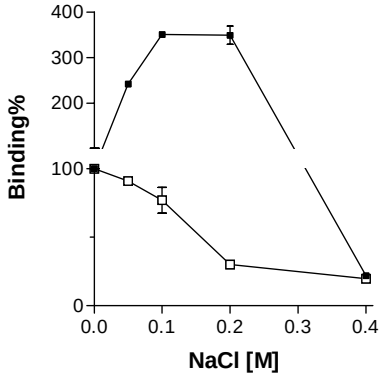

Fig. 3. The effect of the concentration of NaCl on the binding of biotinylated LPS from *E. coli* 0111:B4 to solid-phase recombinant human adiponectin at pH 6.0 in the presence [■] of EDTA, and at pH 5.0 in the absence of EDTA [□]. Data represent means ± SEM in a representative experiment. Results are representative of at least three independent experiments.

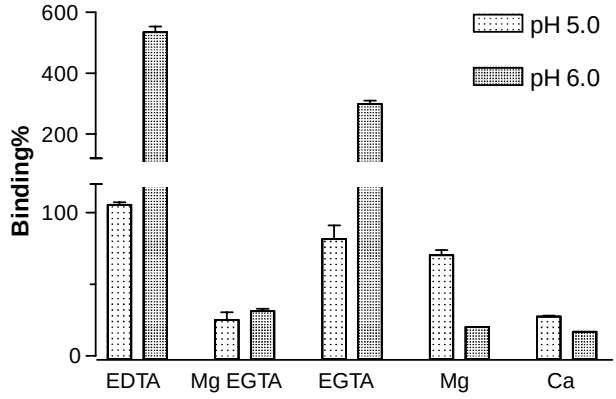

Fig. 4. The effect of the addition or removal of divalent cations at pH 5.0 or pH 6.0 on the binding of biotinylated LPS from *E. coli* 0111:B4 to solid-phase recombinant human adiponectin. Data represent means ± SEM in a representative experiment, normalized to the binding observed in acetate buffer alone. Results are representative of at least three independent experiments.

C1q [up to 17 μg/ml] had no effect on the interaction of LPS with adiponectin (Fig. 5). In contrast, the addition of the same amount of the glucose polymer zymosan inhibited the interaction at pH 5.0 and 6.0, while the fructose polymer inulin was inhibitory only at pH 5.0. Endotoxin-free heparin was strongly inhibitory at 12 μg/ml. Lipid A, beyond a titratable effect attributable to the dimethyl sulphoxide used to solubilize the mixture, was not inhibitory at up to 17 μg/ml (Fig. 5).

The role of sugar residues on the interaction between adiponectin and LPS

As adiponectin is a glycoprotein, we also investigated the role of sugar residues on its interaction with LPS. ELISA well-bound adiponectin preincubated for 16 h at 4 °C with acetate buffer containing 20 mM periodate was

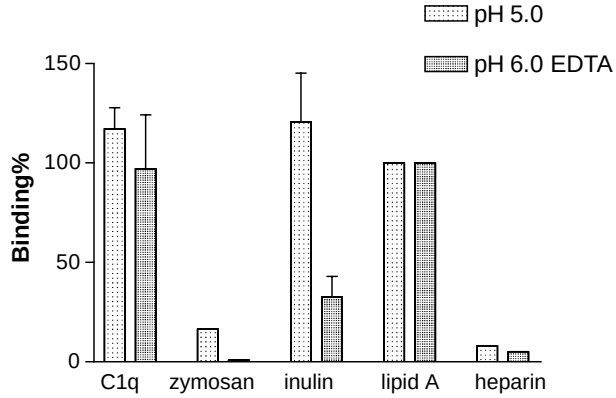

Fig. 5. The effect of selected potential inhibitors on the binding of biotinylated LPS from *E. coli* 0111:B4 to solid-phase recombinant human adiponectin at pH 5.0 in the absence of EDTA, and at pH 6.0 in the presence of EDTA. Data represent means ± SEM in a representative experiment, normalized to the binding observed in acetate buffer alone. Results are representative of at least three independent experiments.

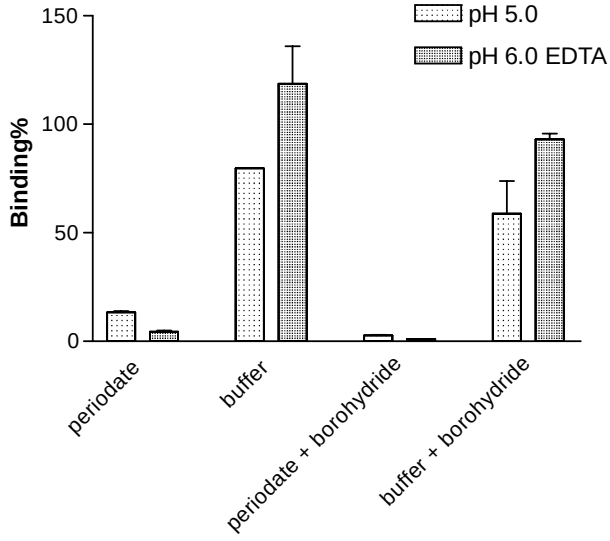

Fig. 6. The effect of periodate on the binding of biotinylated LPS from *E. coli* 0111:B4 to solid-phase recombinant human adiponectin at pH 5.0 in the absence of EDTA, and at pH 6.0 in the presence of EDTA. In some experiments, periodate incubation was followed by incubation with sodium borohydride. Data represent means ± SEM in a representative experiment, normalized to the binding observed in acetate buffer alone. Results are representative of at least three independent experiments.

inhibited from binding LPS at both pH 5, and at pH 6 in the presence of EDTA (Fig 6). This inhibitory effect was retained when the aldehyde groups produced by periodate were removed by incubation with borohydride. Both acetate and borohydride treatment alone had minimal effect on the binding reaction, and the pH optimum was reassessed and shown not to be affected by modification of the carbohydrate moieties [not shown]. Reaction of bound adiponectin so modified with a biotinylated monoclonal anti-adiponectin [R&D] confirmed that both the antigenicity and quantity of adiponectin bound to the ELISA well remained unaltered [not shown].

To further examine the role of sugar moieties in the interaction between adiponectin and LPS, and to establish that this interaction was a general property of adiponectin, three different preparations of LPS were biotinylated and the effect of the addition of various sugars was investigated (Table 1). These were LPS produced by *E. coli* 0111:B4, *E. coli* 0127:B8, and *Salmonella abortus equi*. Both the latter bound adiponectin in a saturable manner similar to that presented in Fig. 2B for *E. coli* 0111:B4 [not shown]. Sugars such as glucose had little effect on the interaction of all three preparations with adiponectin, while others such as *N*-acetyl mannosamine and fucose were strongly inhibitory at 150 mM, but only on the interaction with LPS from *Salmonella abortus equi* (Table 1).

The interaction of native adiponectin with LPS

To ensure that the interaction observed with recombinant purified adiponectin was representative of that which occurs in vivo, the binding of LPS to human serum

Table 1
The influence of sugars on the binding of biotinylated LPS to adiponectin

	LPS 1		LPS 2		LPS 3	
	0.45 M	0.15 M	0.45 M	0.15 M	0.45 M	0.15 M
Glucose	73		76		87	
Sucrose	38	74	63		51	
N-Acetyl glucosamine	59		57		40	63
Lactose	17	49	42	54	77	
Deoxyglucose	60		62		45	54
Galactose	114		68		37	53
Fucose	33	49	58		29	31
N-Acetyl mannosamine	93		86		18	23

The influence of sugars on the binding of biotinylated LPS from *E. coli* 0111:B4 [LPS 1], *E. coli* 0127:B8 [LPS 2], and *Salmonella abortus equi* [LPS 3] to recombinant human adiponectin at pH 5.0. Where binding was <50% on the addition of 0.45 M sugar, binding in the presence of 0.15 M sugar was also determined. Data represent means of duplicate points in a representative experiment, normalized to the binding% observed in acetate buffer alone. At least two additional experiments were performed.

adiponectin was investigated. The maximal interaction of LPS and adiponectin captured from saturating levels of serum by a monoclonal antibody was determined to occur at pH 6.0 in the presence of EDTA. Control wells in which sera were incubated with either bovine albumin or with a monoclonal specific for mouse, rather than human, adiponectin, showed minimal binding [OD450 $\sim$ 0.05 for LPS 1 and LPS 2, and $\sim$0.1 to 0.2 for LPS 3]. This background was subtracted from the data from individual sera presented in Fig. 7. There was a significant interaction with each LPS preparation, particularly that from *Salmonella*. However, the interaction observed was significantly less than that seen with the recombinant adiponectin preparation, applied as a positive control at 0.25 μg/ml, and less than that obtained via the interaction of LPS with immobilized recombinant adiponectin.

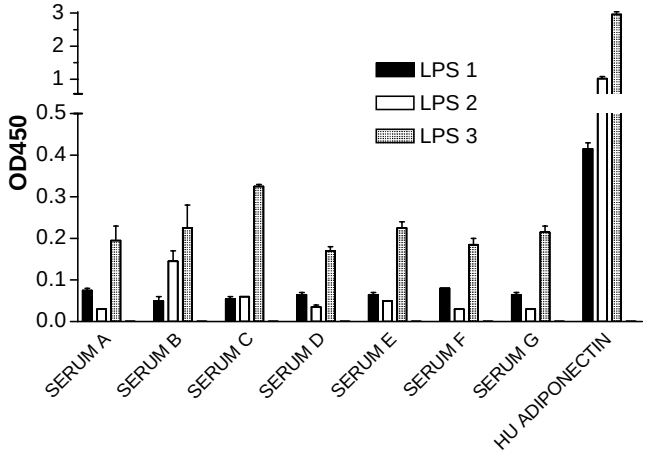

Fig. 7. The binding of biotinylated LPS from *E. coli* 0111:B4 [LPS 1], *E. coli* 0127:B8 [LPS 2], and *Salmonella abortus equi* [LPS 3] to human adiponectin captured from seven individual human sera, or recombinant human adiponectin, by a monoclonal antibody. Incubations were performed at pH 6.0 in the presence of EDTA. Data represent means ± SEM in a representative experiment. The binding for each LPS preparation is significantly greater than background binding to bovine albumin [Wilcoxon non-parametric test; $p < 0.01$]. Results are representative of at least three independent experiments.

Discussion

Adiponectin is known to affect LPS-mediated inflammatory events. It inhibits LPS-induced NFκB activation and IL-6 production, and increases PPARγ2 expression in adipocytes [6], while in macrophages it suppressed both LPS-induced TNFα and IL-6 production [22]. This was associated with an attenuation of the translocation of NFκB to the nucleus. However, the mechanisms of these interactions are believed to occur within the cell, whereas our results suggest that adiponectin may have anti-inflammatory potential by directly binding to LPS.

Adiponectin is known to bind selectively to platelet-derived growth factor [PDGF]-BB. This strongly suppressed proliferation and migration in smooth muscle cells, and inhibited growth factor-stimulated ERK signalling, suggesting that adiponectin acts as a modulator for vascular remodelling [13]. The various oligomeric complexes of adiponectin were also shown to bind selectively to PDGF-BB, basic fibroblast growth factor [FGF] and heparin binding epidermal growth factor [HB EGF] with distinct affinities, thereby controlling their bioavailability and inflammatory potential at a pre-receptor level [14]. Thus, basic FGF preferentially interacted with the HMW form, whereas HB EGF bound all isoforms. Each appeared to have distinct binding sites. These direct interactions obviate the need for binding the recognized receptors [9] before a physiological response can be induced.

The binding of LPS to immobilized adiponectin was enhanced, and the pH optimum raised by the addition of EDTA, suggesting that the removal of divalent cations such as Ca^{2+} and/or Mg^{2+} was affecting the structure of the molecule. The pH optimum for the interaction of adiponectin with immobilized LPS, or of LPS with monoclonal-captured adiponectin, had a similar, raised pH. It is known that cations affect the structure and apparent size of LPS [23]. However, it was shown this effect on the pH optimum was due to cations present in the preparation of adiponectin, since an identical effect was seen in experiments where EDTA was added, then removed before the addition of LPS. EGTA strongly interacts with

Ca^{2+} rather than Mg^{2+}, and it also increased the interaction with LPS, whereas binding was inhibited by the addition of either Ca^{2+} or Mg^{2+}. The fact that a mixture of Mg^{2+} and EGTA [allowing selective removal of Ca^{2+}] was also inhibitory suggests that either Mg^{2+} or Ca^{2+} can bind to adiponectin and decrease its affinity for LPS. A possible explanation lies in the tertiary structure of adiponectin, which may itself depend on calcium: the globular domain has different structures in its Ca^{2+}-bound and Ca^{2+}-free forms [24,25]. The differential effects of NaCl on the binding of LPS by adiponectin at pH 5.0, or at pH 6.0 in the presence of EDTA also suggest it is the structure of adiponectin, rather than that of the LPS, which is being altered by the addition of cations. The higher concentration of NaCl necessary to disrupt the interaction at pH 6.0 suggests, along with the enhanced binding at this pH, that the affinity of the interaction is higher at pH 6.0 in the absence of divalent cations. The effect of cation concentration on this interaction was also seen in the related molecule C1q, which bound more tightly to LPS from the Re form of *Salmonella* than to the S form at physiological cation concentrations [26,27]. Since the fragmentation pattern of adiponectin was unchanged by different pH, it is not likely that major structural changes occurred as a result of this environmental modification.

The interaction between the two molecules was saturable, and half-maximal binding of adiponectin to LPS occurred at 0.5 μg/ml, a physiological concentration. The preparation of recombinant adiponectin consisted largely of HMW isoforms by FPLC analysis, and the binding of LPS paralleled the concentration of adiponectin of each isoform. However, reduction and alkylation, which collapses the protein into the trimer, led to a complete loss of binding. This suggests, as was the case for the interaction of adiponectin with various growth hormones [14], that the quaternary structure of the protein is vital to its function. This result also offers an explanation for the lower binding of LPS by monoclonal-captured native adiponectin as compared with the recombinant molecule. The former is present in a range of isoforms, including the trimer [19], and may also differ in the degree and type of glycosylation present.

Adiponectin is extensively modified post-translationally into multiple isoforms of different p*I*, and 6 out of 8 of these were glycosylated. These modifications occurred in the collagenous domain on four glycosylated lysine residues. The modifying group was likely to be glucosylgalactosyl in nature, and it contributed to the insulin sensitizing effect of adiponectin [18,28]. Other modifications include the presence of disialic acid [17]. Our data show that gentle periodate-mediated destruction of sugar residues on adiponectin led to a loss of binding. While this might suggest they interact with LPS directly, sugars are also thought to increase the stability of the collagen helix [29], and so periodate may indirectly interfere with the interaction with LPS.

Other evidence that sugars are important for the interaction between the molecules was provided by the ability of fucose, lactose and *N*-acetyl mannosamine to inhibit the interaction of adiponectin with all three LPS preparations examined. Given the differences in degrees of inhibition between these LPS varieties, however, it seems likely that the sugar residues and their arrangement on the LPS are also important in determining the specificity of interaction between LPS and adiponectin. Lactose, a disaccharide that consists of glucose and galactose, strongly inhibited only the binding of LPS from *E. coli* 0111:B4 to adiponectin, but this individual sugar may not model the avidity and conformation of glucosylgalactosyl-modified adiponectin [18].

We confirmed that complement subcomponent C1q bound to LPS [20], and showed that C1q did not inhibit the interaction of LPS with adiponectin, suggesting C1q and adiponectin have different binding specificities for LPS. LPS itself inhibited the binding of the biotinylated molecule to adiponectin, but Lipid A was not inhibitory, suggesting that the polysaccharide side-chains of LPS are responsible for binding. Interaction between C1q and bacterial LPS occurred via the collagen-like moiety [20] through interaction with Lipid A [30,31], which supports our findings.

Zymosan, a complex carbohydrate-containing cell wall preparation from yeast, was inhibitory at both pH values, but the plant carbohydrate inulin, comprised mainly of fructose units, was inhibitory at pH 5.0 only. C1q binds the mucopolysaccharide heparin via the collagenous region [32], and heparin also strongly inhibited the binding of LPS to adiponectin, suggesting a competition for binding sites between the molecules.

Hypoxic environments such as wound beds, tumours, and sites of inflammation have an extracellular pH which may be as low as 6, and it has been reported that a low pH binding optimum has been exploited to regulate the interaction of vascular endothelial growth factor and C-reactive protein to fibronectin [33,34]. Adiponectin, which has pH optima for binding with LPS of 5.0–6.0, may behave in an analogous fashion. When the endothelium is damaged, adiponectin infiltrates into the subendothelial space of the vascular wall, and binds to vascular matrix proteins such as collagens I, III, and IV [12]. It may therefore act as a scavenging anti-inflammatory agent in atherosclerosis and vascular damage where LPS or other pro-inflammatory molecules are present. One could speculate that the exacerbation in type 2 diabetes of cardiovascular inflammation [5] may be linked to the decreased levels of total, and decreased proportion of high molecular weight adiponectin [35].

Thus, like C1q and other members of the collectin family of molecules, both recombinant and native adiponectin bind LPS. Although it shares little sequence homology, adiponectin is similar in structure and some functions to surfactant proteins including SP-A and SP-D, which have collagen-like and lectin domains that

are able to interact with carbohydrate regions of LPS. SP-A and SP-D also modulate LPS-induced production of pro-inflammatory mediators in leukocytes by interaction with LPS or with leukocyte receptors [36]. Whether the ability of adiponectin to interact with LPS or other molecules affects its biological behavior or receptor interactions remains to be determined.

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