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## Complex links between dietary lipids, endogenous endotoxins and metabolic inflammation.

Fabienne Laugerette, Cécile Vors, Noël Peretti, Marie-Caroline Michalski

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3 Mini-review

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5 **Complex links between dietary lipids, endogenous endotoxins**  
6 **and metabolic inflammation**  
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8  
9 Fabienne Laugurette,<sup>1,2,†</sup> Cécile Vors,<sup>3,4,†</sup> Noël Peretti<sup>2,6</sup> and Marie-Caroline Michalski<sup>4,5 \*</sup>  
10

11 <sup>†</sup>*FL and CV contributed equally to the work.*  
12

13 <sup>1</sup>Universite de Lyon, F-69100 VILLEURBANNE

14 <sup>2</sup>INSERM, U870, RMND, F-69621 VILLEURBANNE

15 <sup>3</sup>INSA-Lyon, IMBL, F-69621 VILLEURBANNE

16 <sup>4</sup>INRA, UMR 1235, RMND, F-69921 OULLINS

17 <sup>5</sup>CRNH Rhône-Alpes, F-69921 OULLINS

18 <sup>6</sup>Hospices Civils de Lyon, Hôpital Femme Mère Enfant, F-69500 BRON  
19

20 *\*Corresponding author:*

21 *UMR Régulations Métaboliques Nutrition et Diabète, IMBL Building, INSA-Lyon,*  
22 *11 avenue Jean Capelle, 69621 VILLEURBANNE cedex, France.*

23 *Tel : +33 4 72 43 81 12.*

24 *Fax : + 33 4 72 43 85 24.*

25 *marie-caroline.michalski@insa-lyon.fr*  
26

27 **Abstract**

28 Metabolic diseases such as obesity are characterized by a subclinical inflammatory state that  
29 contributes to the development of insulin resistance and atherosclerosis. Recent reports also indicate  
30 that (i) there are alterations of the intestinal microbiota in metabolic diseases and (ii) absorption of  
31 endogenous endotoxins (namely lipopolysaccharides, LPS) can occur, particularly during the  
32 digestion of lipids. The aim of the present review is to highlight recently gained knowledge regarding  
33 the links between high fat diets, lipid digestion, intestinal microbiota and metabolic endotoxemia &  
34 inflammation.  
35

## 1 **1. Introduction**

2 Nowadays, obesity outbreak is an important health problem due to its association with  
3 metabolic disorders such as type 2 diabetes, hyperlipidemia and hypertension. These metabolic  
4 diseases resulting of genetic, **environmental** and nutritional factors are characterized by a  
5 subclinical inflammatory state that contributes to the development of insulin resistance and  
6 atherosclerosis [1, 2]. Although the markers of chronic inflammation such as C-reactive protein  
7 predictive of the development of atherosclerosis are clearly established, the factors responsible for  
8 the initiation and maintenance of the chronic inflammation remain to be elucidated [3]. It was  
9 however noticed very recently that (i) there are alterations of the intestinal microbiota in  
10 metabolic diseases and (ii) absorption of endotoxins (namely lipopolysaccharides, LPS) can occur  
11 [4, 5]. Endotoxins, which are components of gram negative bacteria cell wall, can appear in blood  
12 circulation from intestinal microbiota via translocation [6].

13 New evidence supports the idea of a link between high fat diet and the release of endotoxins in  
14 plasma of mice and humans [4, 7, 8]. The different results suggest that a chronic fat-rich diet  
15 could result in increased endotoxemia and low-grade inflammation due to the repeated endotoxin  
16 absorption from the gut during the digestion of lipids, which in turn could increase the risk of  
17 insulin resistance and atherosclerosis. **Such endoxemia can be defined as “metabolic  
18 endotoxemia”, in contrast with other types of endotoxemia originating from exogenous bacterial  
19 infection or sepsis.** Moreover, we recently evidenced that the structure of lipids in food could be  
20 one of the determinants of LPS absorption during fat digestion in non-pathological conditions [9].

21 The present review will thus discuss the different issues relating metabolic inflammation,  
22 intestinal microbiota, endogenous endotoxin absorption and the possible modulation by lipid  
23 structure.

## 24 **2. Inflammation in metabolic diseases**

25 The low-grade inflammation is a common feature in the patho-physiology of obesity and type  
26 2 diabetes [3, 10, 11]. **Moreover, such inflammation increases the risk of insulin resistance and  
27 atherosclerosis [12-16].** The inflammatory response is characterized by the increase of pro-  
28 inflammatory cytokines as interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) in plasma  
29 [17]. Nappo et al. have reported that a high-fat meal is able to enhance these inflammatory  
30 cytokines contrary to a high carbohydrate meal [18]. It has been shown that butter and walnuts  
31 elicit postprandial activation of nuclear transcription factor kappa B (NF $\kappa$ B) in the peripheral  
32 blood mononuclear cells from healthy subjects [19]. Moreover, patients suffering from coronary  
33 diseases and **submitted** to a high fat meal present an increase of IL-6 [20]. A recent study leads by  
34 Tulk & Robinson reports that by increasing the n-3 PUFA content of a high-saturated fat meal in  
35

1 men with metabolic syndrome, inflammatory responses were not modified [21]. More recently,  
2 Magné *et al.* demonstrated a possible implication of visceral adipose tissue in the postprandial  
3 low-grade inflammation after a high-saturated fat meal in healthy rats, with a transient activation  
4 of NFkB [22]. Moreover, the pathogenesis of insulin and leptin resistance associated with the  
5 intake of high fat high carbohydrate meals can be mediated by an increase in SOCS-3 (suppressor  
6 of cytokine signaling-3) in mononuclear cells after such meals, which is concomitant with  
7 increased markers of inflammation [23].

8 However, it is still difficult to understand the mechanisms by which a high-fat diet promotes the  
9 low-grade inflammation. In this respect, new studies suggest that the quality of intestinal  
10 microbiota might be involved.

11

### 12 **3. Alterations of intestinal microbiota in metabolic diseases**

13 The intestinal microbiota, which is species specific and innate, may though be modified in some  
14 conditions [18]. Moreover, Turnbaugh *et al.* suggested that intestinal microbiota might affect  
15 energy balance [24]. A high fat diet in mother rats can influence the gut microbiota in rat pups and  
16 increase their adiposity and body weight [25]. Conversely, germ-free animals are protected from  
17 diet-induced obesity by increasing fatty acid metabolism [26, 27].

18 Several recent studies report alterations in the composition of intestinal microbiota in the course  
19 of obesity, with differences in quantity and proportion of two dominant gut bacteria: Bacteroidetes  
20 and Firmicutes [28]. For example, ob/ob mice have a 50 % reduction on Bacteroidetes and a  
21 proportional increase in Firmicutes in comparison with lean mice [29]. In human, the microbiota  
22 appears to be different between lean and obese subjects [24, 30] with a decrease of Gram negative  
23 bacteria of the phylum Bacteroidetes in obese subject [31]. However, Duncan *et al.* did not  
24 observe such differences in Bacteroidetes/Firmicutes between lean and obese subjects [32], while  
25 Zhang *et al.* report that obese subjects present greater amounts of Bacteroidetes in their  
26 microbiota compared to lean ones [33]. Therefore, the relative content of each bacterial species in  
27 different pathophysiological conditions remains a subject of debate.

28 Such alterations of the gut microbiota in obesity are important to characterize because they could  
29 trigger endogenous endotoxin (LPS) absorption from microbiota Gram negative bacteria. Indeed,  
30 recent data report the presence of low-doses of these pro-inflammatory LPS in the plasma of  
31 obese humans [10], in type 2 diabetes [34] or in patients with Crohn disease [35]. Moreover, a  
32 study by Cani *et al.* has shown that antibiotic treatment modifies the gut microbiota, reduces  
33 metabolic endotoxemia and the cecal content of LPS in both high fat-fed and ob/ob mice [5]. The  
34 quality of intestinal microbiota was correlated with intestinal barrier integrity, whose loss may  
35 lead to pro-inflammatory endotoxemia [36, 37]. It was recently shown in healthy humans that the

1 administration of probiotic-containing yoghurt may improve the gut barrier function, decreasing  
2 endotoxin release and reducing low-grade chronic inflammation [38]. Prebiotics such as  
3 oligofructose can also increase *Bifidobacteria* in mice gut, which is associated with decreased  
4 endotoxemia [39].

5 Consequently, the intestinal microbiota can be under the influence of the diet, which in turn may  
6 increase the intestinal absorption of LPS that can play a role in the low-grade-inflammation  
7 observed in obesity.

8

#### 9 **4. Proinflammatory properties of endotoxins from Gram negative bacteria (LPS)**

10 LPS, which represent about 80% of the cell wall mass of Gram negative bacteria, are toxic  
11 compounds localized on the surface of bacterial cells as a part of the outer membrane. They are  
12 constituted by an antigen-O specific chain, by a core region which represents a hetero-  
13 oligosaccharide, and by a lipid A region highly conserved and representing the toxic part of the  
14 LPS [40] (**Figure 1A**).

15

16 In pathological conditions such as infection of chronic diseases in humans, Gram negative  
17 bacteria can colonize the oral cavity and respiratory tract; they generate LPS that can lead to  
18 sepsis [41]. During a bacterial infection, LPS concentration in blood (so-called endotoxemia,  
19 normally low in healthy humans) is increased and is able to trigger the production of pro-  
20 inflammatory factors as cytokines [42, 43]. For example, the average endotoxin concentration was  
21 reported to be higher in peritoneal dialysis patients that present systemic inflammation ( $0.44$   
22  $\pm 0.18$  EU/ml), compared to healthy controls ( $0.013 \pm 0.007$  EU/ml,  $P < 0.0001$ ) [44].

23

24 Indeed, LPS are taken up by the Lipopolysaccharide Binding-Protein (LBP) a 65kDa protein  
25 produced by the liver and present in the blood at concentrations of approximately 2-20  $\mu\text{g/mL}$   
26 [45], and transferred to the glycoposphatidylinositol-linked receptor CD14 (cluster of  
27 differentiation-14) [46], expressed on the plasma membrane of various cell types, like monocytes,  
28 macrophages [47] or human intestinal epithelial cell lines [48]. Besides this membrane-bound  
29 (mCD14) state, CD14 is also found in a circulating soluble (sCD14) form [49], increasing during  
30 septic diseases [50, 51]. Moreover, sCD14 is involved in the bioactivity of circulating endotoxin,  
31 and can be considered as a potent marker of endotoxin in plasma [52]. Both forms of CD14 are  
32 able to bind the complex LPS-LBP and mediate signal transduction, including the activation of  
33 the transcription factor nuclear factor- $\kappa\text{B}$  (NF $\kappa\text{B}$ ) *via* a toll like receptor-4 (TLR4) dependant way  
34 associate with MD-2 [53]. This signalling cascade results in the release of pro-inflammatory  
35 cytokines such as Interleukin (IL)-6, or tumor necrosis factor alpha (TNF- $\alpha$ ) [54], maintaining the

1 low-grade inflammation (**Figure 1B**). These different receptors are also present on the surface of  
2 intestinal cells. Indeed, intestinal cells are able to produce, express and release molecules of LBP,  
3 CD14 and TLR4. The same series of events described above concerning immunity cells also take  
4 place at intestinal level. Epithelial cells interact with LPS, and so, are active in intestinal immune  
5 system [55].

6 However, in the case of septic shock, LBP is able to transfer LPS to plasma lipoproteins like HDL  
7 and chylomicrons, which neutralize endotoxin activity [56-59]. This neutralization results from  
8 the binding of the lipoproteins to their receptors, particularly on the liver, inducing increased  
9 biliary secretion of LPS [60, 61]. In addition to LBP, the phospholipid transfer protein (PLTP)  
10 implicated in the development of atherosclerosis [62] is able to link LPS and to detoxify the  
11 organism during septic shock [63, 64].

12

13 However, in non-pathological conditions, the healthy human body also contains numerous  
14 endogenous bacteria ( $\sim 10^{14}$ ) [6]. In this case, Gram negative bacteria reside as a majority in the  
15 gut in which they constitute, together with Gram positive bacteria, the intestinal microbiota.  
16 Intestinal absorption of endogenous LPS from this microbiota would result in the same pro-  
17 inflammatory mechanisms as described above, though to a much lesser extent: low-grade  
18 inflammation or so-called metabolic inflammation as observed in obesity.

19

## 20 **5. Links between high fat diets, inflammation and endotoxemia**

21 Extrinsic factors such as the diet can affect the inflammatory response to exogenous LPS. For  
22 example, mice submitted to a high saturated fat and cholesterol diet increase their sensitivity to  
23 LPS injection [65]. However, very recent studies also support the concept that dietary fats can  
24 induce absorption of endogenous LPS from the intestinal microbiota and subsequent  
25 inflammatory response.

26 The pioneering article by Cani et al. (2007) reported that a four-week high fat diet in mice (72%  
27 energy as fat) increases plasma endotoxin levels (endotoxemia) in comparison with a control diet,  
28 and that chronic low-dose infusion of LPS leads to weight gain and insulin resistance [4]. In turn  
29 CD14-KO mice resisted to increased weight gain, endotoxemia and insulin resistance induced by  
30 a high fat diet [4]. [Importantly, Shi et al. have also shown that TLR4-KO mice are protected from](#)  
31 [NFkB-induced inflammation and development of insulin resistance \[66\]. Both works thus show a](#)  
32 [link between innate immunity and lipid-induced insulin resistance. Moreover,](#) the increase in  
33 plasma LPS is lower when mice are submitted to a diet containing 35% energy as fat compared  
34 with mice fed a high-fat diet [7]. In humans, Amar et al. found a link between food intake and  
35 plasma endotoxin, with a positive correlation between energy intake and endotoxemia [7].

1 On an acute basis, Erridge *et al.* showed in humans that an acute high fat bolus (50 g butter on  
2 toast) was sufficient to promote a transient increase in endotoxemia, 30 min after ingestion, in  
3 lean to obese occasional smokers [8]. Because these authors considered that smoking could  
4 contribute to elevation of plasma endotoxin via the absorption of LPS by lung [67], they examined  
5 endotoxemia for 4 hours in men receiving no meal, a high-fat meal, no meal and 3 cigarettes, or a  
6 high-fat meal and 3 cigarettes [8]. Fat was found to be the only significant parameter impacting on  
7 postprandial endotoxemia [8]. Consistently, Ghoshal *et al.* show in mice that forced feeding with  
8 triolein leads to an increase of endotoxemia after 90 minutes [68]. Conversely, feeding with  
9 tributyrin or chemically preventing chylomicron secretion blunted postprandial endotoxemia [68].  
10 Most recently, we have shown in healthy non-smoking humans that the digestion of a mixed  
11 breakfast, containing various types of lipids (animal, vegetal) in emulsified and non-emulsified  
12 forms, results in a transient elevation of endotoxin in plasma and an increase of sCD14 [9]. This  
13 can explain the significant peak of inflammatory cytokine IL-6 that we observed 2 h after the  
14 mixed meal (**Figure 2A**). Moreover, LPS appeared to be partly transported by chylomicrons  
15 (**Figure 2A**), as observed by endotoxemia measurements and LPS immunogold labelling on  
16 purified chylomicrons [9].

17 Altogether, these results show that high fat diet can result in increased endotoxemia, which in turn  
18 could be triggered by repeated ingestions of single high fat meals. Indeed, lipid digestion and  
19 chylomicrons secretion can promote intestinal absorption of LPS from gut microbiota [9, 68],  
20 which could contribute to postprandial inflammatory responses [69, 70] and thus to the onset and  
21 maintenance of chronic low-grade inflammation.

22

## 23 **6. New insights: where dietary fat properties and lipid absorption kinetics might impact on** 24 **endotoxemia and inflammation**

25 Elevated postprandial lipemia, due to postprandial chylomicron concentration, is known to  
26 have a deleterious impact on cardiovascular risk [71]. Particularly, new interest has recently arisen  
27 in the literature regarding the metabolic importance of the kinetics of lipid absorption during  
28 digestion, which can be modulated by dietary fat structure [72, 73]. In food products, most fatty  
29 acids are esterified in the form of triacylglycerols (TAG) that are digested in the stomach and in  
30 the small intestine through the action of specific lipases [74-76]. After the pancreatic lipolysis,  
31 free fatty acids and 2-monoacylglycerols are released, which are mainly absorbed by enterocytes.  
32 In the latter, lipolysis products are re-esterified as TAG, secreted into lymph and further released  
33 in the bloodstream in chylomicrons [74, 77].

34 The recent findings about postprandial endotoxemia and inflammation suggest a new role of  
35 the lipid digestion/chylomicron secretion phase, in promoting an immune response. Very recently,

1 we have shown that the postprandial lipemia of rats was increased when fed a fine emulsion of  
2 sunflower oil with lecithin as emulsifier, compared to unemulsified sunflower oil [9]. This finding  
3 was consistent with another recent report in humans showing that the absorption of *n*-3 PUFA was  
4 higher from an emulsion than from the originate oil [78]. Most importantly, our results show that  
5 postprandial endotoxemia was increased after emulsion vs oil feeding, with AUC of LPS being  
6 correlated with AUC of TAG during digestion (**Figure 2B**, [9]). This correlation appears to be  
7 due to the role of chylomicrons in postprandial LPS transport [9, 68].

8 Now, it appears that the kinetics of postprandial lipemia and chylomicron secretion can be  
9 modified by dietary fat properties. Regarding fatty acid composition of dietary fat, Mekki *et al.*  
10 observed that butter in a meal resulted in (i) lower postprandial lipemia and chylomicron  
11 accumulation and (ii) smaller chylomicrons, than emulsified vegetable oil [79]. Regarding TAG  
12 molecular structure, dietary fats that contain mostly SFA at the *sn*-2 position of their TAG are  
13 reported to induce a higher and more prolonged postprandial lipemia [80]. Moreover, obese  
14 subjects can be more sensitive than lean ones regarding the modulation of postprandial lipemia by  
15 different TAG structures [81]. In general, long chain saturated fatty acids esterified to the *sn*-1 and  
16 *sn*-3 positions are less prone to be absorbed, due to their possible saponification as calcium soaps  
17 in the gastrointestinal tract that are excreted in stools [82-84]. Moreover, long chain saturated fatty  
18 acids present a higher solid proportion (so-called solid fat content, SFC) at 37°C, which is  
19 reported to play an important role in limiting fat absorption [85, 86], especially in obese humans  
20 [81]. Some studies have also shown that differently emulsified lipids [87-90] and differently  
21 structured dairy products [91-95] result in different lipolysis and lipemia profiles, as previously  
22 reviewed [72, 96, 97]. We may thus wonder whether the biochemical and physicochemical  
23 properties of dietary fats could contribute to modulate LPS absorption during digestion, due to  
24 their effects on overall lipid absorption and chylomicron secretion.

25 In induced septic endotoxemia in animal models, the composition of dietary lipids was  
26 reported to affect inflammatory response and even death outcomes. For example in mice, it was  
27 shown, that a high saturated fat and cholesterol diet increased the sensitivity of mice to LPS, and  
28 the release of IL-6 and TNF- $\alpha$  [65]. Rats fed medium-chain TAG during 1 week presented a higher  
29 survival score and lower liver alterations after intravenous infusion of a dose of LPS than their  
30 counterparts fed with corn oil presenting 100% death and acute liver alterations by infiltration &  
31 activation of K $\ddot{u}$ pffer cells [98]. During digestion, short- and medium chain fatty acids are  
32 absorbed directly by the portal vein to be oriented towards  $\beta$ -oxidation in the liver [74, 99].  
33 Moreover, other recent results in rats show that medium chain TAG would protect against  
34 lipotoxicity and insulin resistance induced by high fat diet, compared to long chain saturated TAG  
35 that are usually reported to be deleterious [100]. Dietary phospholipids may also present



1 nutritional benefits in the regulation of lipemia and chronic metabolic outcomes in the context of  
2 high fat diets [72, 101].

3 Consequently, **choosing** adapted molecular lipid formulations (fatty acid profile, PL vs TAG)  
4 and modifying the kinetics of lipid absorption and chylomicron secretion can be possible  
5 strategies to reduce postprandial endotoxin absorption and/or the metabolic consequences  
6 regarding low-grade inflammation (**Figure 3**).

7

## 8 **7. Conclusion**

9 The relationship between fat-rich diets and endotoxemia is an emerging concept, which could  
10 explain the onset and maintenance of the subclinical inflammatory state that enhances the  
11 development of insulin resistance. Recent results support the concept that the digestion of  
12 dispersed dietary lipids can enhance absorption of endogenous endotoxins. The long-term  
13 consequences of such postprandial endotoxemia in the context of high fat diets in humans, and the  
14 underlying mechanisms, remain to be further explored. Moreover, adapted lipid formulations and  
15 their physical structuration can change both the extent and kinetics of postprandial endotoxemia.  
16 Therefore, optimizing the quantity, composition, physicochemical properties and emulsification  
17 state of dietary fats can be possible strategies to limit postprandial endotoxemia, with the aim of  
18 preventing low-grade inflammation. In the current context of obesity and cardiovascular disease  
19 outbreak, the links between dietary lipid properties, inflammation and interactions with intestinal  
20 microbiota appear to be complex, thus justifying the need for interdisciplinary studies in the  
21 future.

22

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2 **References**

- 3 [1] C. Bouchard, Current understanding of the etiology of obesity: genetic and nongenetic  
4 factors, *The American journal of clinical nutrition* 53 (1991) 1561S-1565S.
- 5 [2] S.U. Raymond, S. Leeder, H.M. Greenberg, Obesity and cardiovascular disease in  
6 developing countries: a growing problem and an economic threat, *Current opinion in clinical  
7 nutrition and metabolic care* 9 (2006) 111-116.
- 8 [3] R. Ross, Atherosclerosis is an inflammatory disease, *Am Heart J* 138 (1999) S419-420.
- 9 [4] P.D. Cani, J. Amar, M.A. Iglesias, M. Poggi, C. Knauf, D. Bastelica, A.M. Neyrinck, F.  
10 Fava, K.M. Tuohy, C. Chabo, A. Wage, E. Delmee, B. Cousin, T. Sulpice, B. Chamontin, J.  
11 Ferrieres, J.F. Tanti, G.R. Gibson, L. Casteilla, N.M. Delzenne, M.C. Alessi, R. Burcelin,  
12 Metabolic endotoxemia initiates obesity and insulin resistance, *Diabetes* 56 (2007) 1761-1772.
- 13 [5] P.D. Cani, R. Bibiloni, C. Knauf, A. Wage, A.M. Neyrinck, N.M. Delzenne, R. Burcelin,  
14 Changes in gut microbiota control metabolic endotoxemia-induced inflammation in high-fat diet-  
15 induced obesity and diabetes in mice, *Diabetes* 57 (2008) 1470-1481.
- 16 [6] R.D. Berg, The indigenous gastrointestinal microflora, *Trends in Microbiology* 4 (1996)  
17 430-435.
- 18 [7] J. Amar, R. Burcelin, J.B. Ruidavets, P.D. Cani, J. Fauvel, M.C. Alessi, B. Chamontin, J.  
19 Ferrieres, Energy intake is associated with endotoxemia in apparently healthy men, *Am J Clin  
20 Nutr* 87 (2008) 1219-1223.
- 21 [8] C. Erridge, T. Attina, C.M. Spickett, D.J. Webb, A high-fat meal induces low-grade  
22 endotoxemia: evidence of a novel mechanism of postprandial inflammation, *American Journal of  
23 Clinical Nutrition* 86 (2007) 1286-1292.
- 24 [9] F. Laugerette, C. Vors, A. Geloën, M.A. Chauvin, C. Soulage, S. Lambert-Porcheron, N.  
25 Peretti, M. Alligier, R. Burcelin, M. Laville, H. Vidal, M.C. Michalski, Emulsified lipids increase  
26 endotoxemia: possible role in early postprandial low-grade inflammation, *Journal of Nutritional  
27 Biochemistry* doi:10.1016/j.jnutbio.2009.11.011 (2010).
- 28 [10] P. Libby, P.M. Ridker, A. Maseri, Inflammation and atherosclerosis, *Circulation* 105  
29 (2002) 1135-1143.
- 30 [11] A.S. Greenberg, M.S. Obin, Obesity and the role of adipose tissue in inflammation and  
31 metabolism, *The American journal of clinical nutrition* 83 (2006) 461S-465S.
- 32 [12] R. Ross, The pathogenesis of atherosclerosis: a perspective for the 1990s, *Nature* 362  
33 (1993) 801-809.
- 34 [13] P. Libby, Inflammation in atherosclerosis, *Nature* 420 (2002) 868-874.
- 35 [14] S.E. Shoelson, L. Herrero, A. Naaz, Obesity, inflammation, and insulin resistance,  
36 *Gastroenterology* 132 (2007) 2169-2180.
- 37 [15] G. Tarantino, P. Colicchio, P. Conca, C. Finelli, M.N.D. Di Minno, M. Tarantino, D.  
38 Capone, F. Pasanisi, Young adult obese subjects with and without insulin resistance: what is the  
39 role of chronic inflammation and how to weigh it non-invasively?, *Journal of Inflammation-  
40 London* 6 (2009) -.
- 41 [16] K. Park, M. Steffes, D.H. Lee, J.H. Himes, D.R. Jacobs, Association of inflammation with  
42 worsening HOMA-insulin resistance, *Diabetologia* 52 (2009) 2337-2344.
- 43 [17] G.C. Burdge, P.C. Calder, Plasma cytokine response during the postprandial period: a  
44 potential causal process in vascular disease?, *The British journal of nutrition* 93 (2005) 3-9.
- 45 [18] F. Nappo, K. Esposito, M. Cioffi, G. Giugliano, A.M. Molinari, G. Paolisso, R. Marfella,  
46 D. Giugliano, Postprandial endothelial activation in healthy subjects and in type 2 diabetic  
47 patients: role of fat and carbohydrate meals, *Journal of the American College of Cardiology* 39  
48 (2002) 1145-1150.
- 49 [19] C. Bellido, J. Lopez-Miranda, L.M. Blanco-Colio, P. Perez-Martinez, F.J. Muriana, J.L.  
50 Martin-Ventura, C. Marin, P. Gomez, F. Fuentes, J. Egido, F. Perez-Jimenez, Butter and walnuts,  
51 but not olive oil, elicit postprandial activation of nuclear transcription factor kappaB in peripheral

- 1 blood mononuclear cells from healthy men, *The American journal of clinical nutrition* 80 (2004)  
2 1487-1491.
- 3 [20] P. Lundman, S. Boquist, A. Samnegard, M. Bennermo, C. Held, C.G. Ericsson, A.  
4 Silveira, A. Hamsten, P. Tornvall, A high-fat meal is accompanied by increased plasma  
5 interleukin-6 concentrations, *Nutr Metab Cardiovasc Dis* 17 (2007) 195-202.
- 6 [21] H.M. Tulk, L.E. Robinson, Modifying the n-6/n-3 polyunsaturated fatty acid ratio of a  
7 high-saturated fat challenge does not acutely attenuate postprandial changes in inflammatory  
8 markers in men with metabolic syndrome, *Metabolism: clinical and experimental* 58 (2009) 1709-  
9 1716.
- 10 [22] J. Magne, F. Mariotti, R. Fischer, V. Mathe, D. Tome, J.F. Huneau, Early postprandial  
11 low-grade inflammation after high-fat meal in healthy rats: possible involvement of visceral  
12 adipose tissue, *The Journal of nutritional biochemistry* (2009).
- 13 [23] H. Ghanim, S. Abuaysheh, C.L. Sia, K. Korzeniewski, A. Chaudhuri, J.M. Fernandez-  
14 Real, P. Dandona, Increase in Plasma Endotoxin Concentrations and the Expression of Toll-like  
15 Receptors and Suppressor of Cytokine Signaling-3 in Mononuclear Cells After a High-Fat, High-  
16 Carbohydrate Meal Implications for insulin resistance, *Diabetes Care* 32 (2009) 2281-2287.
- 17 [24] P.J. Turnbaugh, R.E. Ley, M.A. Mahowald, V. Magrini, E.R. Mardis, J.I. Gordon, An  
18 obesity-associated gut microbiome with increased capacity for energy harvest, *Nature* 444 (2006)  
19 1027-1031.
- 20 [25] S. Mozes, D. Bujnakova, Z. Sefcikova, V. Kmet, Developmental changes of gut microflora  
21 and enzyme activity in rat pups exposed to fat-rich diet, *Obesity (Silver Spring, Md)* 16 (2008)  
22 2610-2615.
- 23 [26] F. Backhed, R.E. Ley, J.L. Sonnenburg, D.A. Peterson, J.I. Gordon, Host-bacterial  
24 mutualism in the human intestine, *Science (New York, N.Y)* 307 (2005) 1915-1920.
- 25 [27] F. Backhed, H. Ding, T. Wang, L.V. Hooper, G.Y. Koh, A. Nagy, C.F. Semenkovich, J.I.  
26 Gordon, The gut microbiota as an environmental factor that regulates fat storage, *Proceedings of  
27 the National Academy of Sciences of the United States of America* 101 (2004) 15718-15723.
- 28 [28] R. Burcelin, E. Luche, M. Serino, J. Amar, The gut microbiota ecology: a new opportunity  
29 for the treatment of metabolic diseases?, *Front Biosci* 14 (2009) 5107-5117.
- 30 [29] R.E. Ley, F. Backhed, P. Turnbaugh, C.A. Lozupone, R.D. Knight, J.I. Gordon, Obesity  
31 alters gut microbial ecology, *Proceedings of the National Academy of Sciences of the United  
32 States of America* 102 (2005) 11070-11075.
- 33 [30] M. Bajzer, R.J. Seeley, Physiology: obesity and gut flora, *Nature* 444 (2006) 1009-1010.
- 34 [31] R.E. Ley, P.J. Turnbaugh, S. Klein, J.I. Gordon, Microbial ecology - Human gut microbes  
35 associated with obesity, *Nature* 444 (2006) 1022-1023.
- 36 [32] S.H. Duncan, G.E. Loblely, G. Holtrop, J. Ince, A.M. Johnstone, P. Louis, H.J. Flint,  
37 Human colonic microbiota associated with diet, obesity and weight loss, *Int J Obes (Lond)* 32  
38 (2008) 1720-1724.
- 39 [33] H. Zhang, J.K. DiBaise, A. Zuccolo, D. Kudrna, M. Braidotti, Y. Yu, P. Parameswaran,  
40 M.D. Crowell, R. Wing, B.E. Rittmann, R. Krajmalnik-Brown, Human gut microbiota in obesity  
41 and after gastric bypass, *Proceedings of the National Academy of Sciences of the United States of  
42 America* 106 (2009) 2365-2370.
- 43 [34] S.J. Creely, P.G. McTernan, C.M. Kusminski, M. Fisher, N.F. Da Silva, M. Khanolkar, M.  
44 Evans, A.L. Harte, S. Kumar, Lipopolysaccharide activates an innate immune system response in  
45 human adipose tissue in obesity and type 2 diabetes, *American journal of physiology* 292 (2007)  
46 E740-747.
- 47 [35] O. Pastor Rojo, A. Lopez San Roman, E. Albeniz Arbizu, A. de la Hera Martinez, E.  
48 Ripoll Sevillano, A. Albillos Martinez, Serum lipopolysaccharide-binding protein in endotoxemic  
49 patients with inflammatory bowel disease, *Inflammatory bowel diseases* 13 (2007) 269-277.
- 50 [36] P.D. Cani, N.M. Delzenne, Interplay between obesity and associated metabolic disorders:  
51 new insights into the gut microbiota, *Curr Opin Pharmacol* 9 (2009) 737-743.

- 1 [37] P.D. Cani, S. Possemiers, T. Van de Wiele, Y. Guiot, A. Everard, O. Rottier, L. Geurts, D.  
2 Naslain, A. Neyrinck, D.M. Lambert, G.G. Muccioli, N.M. Delzenne, Changes in gut microbiota  
3 control inflammation in obese mice through a mechanism involving GLP-2-driven improvement  
4 of gut permeability, *Gut* 58 (2009) 1091-1103.
- 5 [38] E.J. Schiffrin, A. Parlesak, C. Bode, J.C. Bode, M.A. van't Hof, D. Grathwohl, Y. Guigoz,  
6 Probiotic yogurt in the elderly with intestinal bacterial overgrowth: endotoxaemia and innate  
7 immune functions, *The British journal of nutrition* 101 (2009) 961-966.
- 8 [39] P.D. Cani, A.M. Neyrinck, F. Fava, C. Knauf, R.G. Burcelin, K.M. Tuohy, G.R. Gibson,  
9 N.M. Delzenne, Selective increases of bifidobacteria in gut microflora improve high-fat-diet-  
10 induced diabetes in mice through a mechanism associated with endotoxaemia, *Diabetologia* 50  
11 (2007) 2374-2383.
- 12 [40] M.J. Osborn, S.M. Rosen, L. Rothfield, L.D. Zeleznick, B.L. Horecker,  
13 Lipopolysaccharide of the Gram-Negative Cell Wall, *Science* 145 (1964) 783-789.
- 14 [41] L.L. Stoll, G.M. Denning, N.L. Weintraub, Potential role of endotoxin as a  
15 proinflammatory mediator of atherosclerosis, *Arterioscler Thromb Vasc Biol* 24 (2004) 2227-  
16 2236.
- 17 [42] T. Goto, S. Eden, G. Nordenstam, V. Sundh, C. Svanborg-Eden, I. Mattsby-Baltzer,  
18 Endotoxin levels in sera of elderly individuals, *Clin Diagn Lab Immunol* 1 (1994) 684-688.
- 19 [43] J.C. Marshall, Lipopolysaccharide: an endotoxin or an exogenous hormone?, *Clin Infect*  
20 *Dis* 41 Suppl 7 (2005) S470-480.
- 21 [44] C.C. Szeto, B.C. Kwan, K.M. Chow, K.B. Lai, K.Y. Chung, C.B. Leung, P.K. Li,  
22 Endotoxemia is related to systemic inflammation and atherosclerosis in peritoneal dialysis  
23 patients, *Clin J Am Soc Nephrol* 3 (2008) 431-436.
- 24 [45] P. Gallay, C. Barras, P.S. Tobias, T. Calandra, M.P. Glauser, D. Heumann,  
25 Lipopolysaccharide (LPS)-binding protein in human serum determines the tumor necrosis factor  
26 response of monocytes to LPS, *J Infect Dis* 170 (1994) 1319-1322.
- 27 [46] E. Hailman, H.S. Lichenstein, M.M. Wurfel, D.S. Miller, D.A. Johnson, M. Kelley, L.A.  
28 Busse, M.M. Zukowski, S.D. Wright, Lipopolysaccharide (LPS)-binding protein accelerates the  
29 binding of LPS to CD14, *J Exp Med* 179 (1994) 269-277.
- 30 [47] P.S. Tobias, R.J. Ulevitch, Lipopolysaccharide binding protein and CD14 in LPS  
31 dependent macrophage activation, *Immunobiology* 187 (1993) 227-232.
- 32 [48] D.P. Funda, L. Tuckova, M.A. Farre, T. Iwase, I. Moro, H. Tlaskalova-Hogenova, CD14 is  
33 expressed and released as soluble CD14 by human intestinal epithelial cells in vitro:  
34 lipopolysaccharide activation of epithelial cells revisited, *Infect Immun* 69 (2001) 3772-3781.
- 35 [49] V. Bazil, J.L. Strominger, Shedding as a mechanism of down-modulation of CD14 on  
36 stimulated human monocytes, *J Immunol* 147 (1991) 1567-1574.
- 37 [50] S. Bas, B.R. Gauthier, U. Spenato, S. Stingelin, C. Gabay, CD14 is an acute-phase protein,  
38 *J Immunol* 172 (2004) 4470-4479.
- 39 [51] M.J. Fenton, D.T. Golenbock, LPS-binding proteins and receptors, *Journal of leukocyte*  
40 *biology* 64 (1998) 25-32.
- 41 [52] N. Hiki, D. Berger, M.A. Dentener, Y. Mimura, M.A. Buurman, C. Prigl, M. Seidelmann,  
42 E. Tsuji, M. Kaminishi, H.G. Beger, Changes in endotoxin-binding proteins during major elective  
43 surgery: Important role for soluble CD14 in regulation of biological activity of systemic  
44 endotoxin, *Clinical and Diagnostic Laboratory Immunology* 6 (1999) 844-850.
- 45 [53] H.M. Kim, B.S. Park, J.I. Kim, S.E. Kim, J. Lee, S.C. Oh, P. Enkhbayar, N. Matsushima,  
46 H. Lee, O.J. Yoo, J.O. Lee, Crystal structure of the TLR4-MD-2 complex with bound endotoxin  
47 antagonist Eritoran, *Cell* 130 (2007) 906-917.
- 48 [54] S.J. van Deventer, H.R. Buller, J.W. ten Cate, L.A. Aarden, C.E. Hack, A. Sturk,  
49 Experimental endotoxemia in humans: analysis of cytokine release and coagulation, fibrinolytic,  
50 and complement pathways, *Blood* 76 (1990) 2520-2526.
- 51 [55] J.E. Tomlinson, A.T. Blikslager, Interactions between lipopolysaccharide and the intestinal  
52 epithelium, *Journal of the American Veterinary Medical Association* 224 (2004) 1446-1452.

- 1 [56] E.B. Eichbaum, H.W. Harris, J.P. Kane, J.H. Rapp, Chylomicrons can inhibit endotoxin  
2 activity in vitro, *J Surg Res* 51 (1991) 413-416.
- 3 [57] T.E. Read, C. Grunfeld, Z. Kumwenda, M.C. Calhoun, J.P. Kane, K.R. Feingold, J.H.  
4 Rapp, Triglyceride-rich lipoproteins improve survival when given after endotoxin in rats, *Surgery*  
5 117 (1995) 62-67.
- 6 [58] A.C. Vreugdenhil, C.H. Rousseau, T. Hartung, J.W. Greve, C. van 't Veer, W.A. Buurman,  
7 Lipopolysaccharide (LPS)-binding protein mediates LPS detoxification by chylomicrons, *J*  
8 *Immunol* 170 (2003) 1399-1405.
- 9 [59] M.M. Wurfel, S.T. Kunitake, H. Lichenstein, J.P. Kane, S.D. Wright, Lipopolysaccharide  
10 (LPS)-binding protein is carried on lipoproteins and acts as a cofactor in the neutralization of LPS,  
11 *The Journal of experimental medicine* 180 (1994) 1025-1035.
- 12 [60] H.W. Harris, C. Grunfeld, K.R. Feingold, T.E. Read, J.P. Kane, A.L. Jones, E.B.  
13 Eichbaum, G.F. Bland, J.H. Rapp, Chylomicrons alter the fate of endotoxin, decreasing tumor  
14 necrosis factor release and preventing death, *J Clin Invest* 91 (1993) 1028-1034.
- 15 [61] H.W. Harris, D.C. Rockey, P. Chau, Chylomicrons alter the hepatic distribution and  
16 cellular response to endotoxin in rats, *Hepatology* 27 (1998) 1341-1348.
- 17 [62] X.C. Jiang, S. Qin, C. Qiao, K. Kawano, M. Lin, A. Skold, X. Xiao, A.R. Tall,  
18 Apolipoprotein B secretion and atherosclerosis are decreased in mice with phospholipid-transfer  
19 protein deficiency, *Nat Med* 7 (2001) 847-852.
- 20 [63] T. Gautier, A. Klein, V. Deckert, C. Desrumaux, N. Ogier, A.L. Sberna, C. Paul, N. Le  
21 Guern, A. Athias, T. Montange, S. Monier, F. Piard, X.C. Jiang, D. Masson, L. Lagrost, Effect of  
22 plasma phospholipid transfer protein deficiency on lethal endotoxemia in mice, *J Biol Chem* 283  
23 (2008) 18702-18710.
- 24 [64] R.S. Munford, Sensing gram-negative bacterial lipopolysaccharides: a human disease  
25 determinant?, *Infect Immun* 76 (2008) 454-465.
- 26 [65] H. Huang, T. Liu, J.L. Rose, R.L. Stevens, D.G. Hoyt, Sensitivity of mice to  
27 lipopolysaccharide is increased by a high saturated fat and cholesterol diet, *J Inflamm (Lond)* 4  
28 (2007) 22.
- 29 [66] H. Shi, M.V. Kokoeva, K. Inouye, I. Tzamelis, H. Yin, J.S. Flier, TLR4 links innate  
30 immunity and fatty acid-induced insulin resistance, *Journal of Clinical Investigation* 116 (2006)  
31 3015-3025.
- 32 [67] J.D. Hasday, R. Bascom, J.J. Costa, T. Fitzgerald, W. Dubin, Bacterial endotoxin is an  
33 active component of cigarette smoke, *Chest* 115 (1999) 829-835.
- 34 [68] S. Ghoshal, J. Witta, J. Zhong, W. de Villiers, E. Eckhardt, Chylomicrons promote  
35 intestinal absorption of lipopolysaccharides, *Journal of lipid research* 50 (2009) 90-97.
- 36 [69] P. Lundman, S. Boquist, A. Samnegard, M. Bennermo, C. Held, C.G. Ericsson, A.  
37 Silveira, A. Hamsten, P. Tornvall, A high-fat meat is accompanied by increased plasma  
38 interleukin-6 concentrations, *Nutrition Metabolism and Cardiovascular Diseases* 17 (2007) 195-  
39 202.
- 40 [70] N.N. Mehta, F.C. McGillicuddy, P.D. Anderson, C.C. Hinkle, R. Shah, L. Pruscino, J.  
41 Tabita-Martinez, K.F. Sellers, M.R. Rickels, M.P. Reilly, Experimental Endotoxemia Induces  
42 Adipose Inflammation and Insulin Resistance in Humans, *Diabetes* (2009).
- 43 [71] M. Lefevre, P.M. Kris-Etherton, G. Zhao, R.P. Tracy, Dietary fatty acids, hemostasis, and  
44 cardiovascular disease risk, *Journal of the American Dietetic Association* 104 (2004) 410-419.
- 45 [72] M.C. Michalski, Specific molecular and colloidal structures of milk fat affecting lipolysis,  
46 absorption and postprandial lipemia, *Eur J Lipid Sci Technol* 111 (2009).
- 47 [73] H. Singh, A. Ye, D. Horne, Structuring food emulsions in the gastrointestinal tract to  
48 modify lipid digestion, *Progress in Lipid Research* (2009).
- 49 [74] H.L. Mu, C.E. Hoyt, The digestion of dietary triacylglycerols, *Progress in Lipid Research*  
50 43 (2004) 105-133.
- 51 [75] M. Armand, Lipases and lipolysis in the human digestive tract: where do we stand?,  
52 *Curr.Opin.Clin.Nutr.Metab.Care* 10 (2007) 156-164.

- 1 [76] N. Miled, S. Canaan, L. Dupuis, A. Roussel, M. Rivišre, F. Carrišre, A. de Caro, C.  
2 Cambillau, R. Verger, Digestive lipases - from three dimensional structure to physiology,  
3 *Biochimie* 82 (2000) 973-986.
- 4 [77] V. Petit, I. Niot, H. Poirier, P. Besnard, Absorption intestinale des acides gras: faits et  
5 incertitudes, *Nutrition Clinique et Metabolisme* 21 (2007) 38-45.
- 6 [78] I. Garaiova, I.A. Guschina, S.F. Plummer, J. Tang, D. Wang, N.T. Plummer, A  
7 randomised cross-over trial in healthy adults indicating improved absorption of omega-3 fatty  
8 acids by pre-emulsification, *Nutrition Journal* 6 (2008) 4-13.
- 9 [79] N. Mekki, M. Charbonnier, P. Borel, J. Leonardi, C. Juhel, H. Portugal, D. Lairon, Butter  
10 differs from olive oil and sunflower oil in its effect on postprandial lipemia and triacylglycerol-  
11 rich lipoproteins after single mixed meals in healthy young men, *J.Nutr.* 132 (2002) 3642-3649.
- 12 [80] S.E.E. Berry, T.A.B. Sanders, Influence of triacylglycerol structure of stearic-rich fats on  
13 postprandial lipemia, *Proceedings of the Nutrition Society* 64 (2005) 205-212.
- 14 [81] D.M. Robinson, N.C. Martin, L.E. Robinson, I. Ahmadi, A.G. Marangoni, A.J. Wright,  
15 Influence of Interesterification of a Stearic Acid-Rich Spreadable Fat on Acute Metabolic Risk  
16 Factors, *Lipids* (2009).
- 17 [82] J.K. Lorenzen, S. Nielsen, J.J. Holst, I. Tetens, J.F. Rehfeld, A. Astrup, Effect of dairy  
18 calcium or supplementary calcium intake on postprandial fat metabolism, appetite, and  
19 subsequent energy intake, *American Journal of Clinical Nutrition* 85 (2007) 678-687.
- 20 [83] N. Boon, G.B. Hul, J.H. Stegen, W.E. Sluijsmans, C. Walle, D. Langin, N. Viguerie, W.H.  
21 Sarris, An intervention study of the effects of calcium intake on faecal fat excretion, energy  
22 metabolism and adipose tissue mRNA expression of lipid-metabolism related proteins,  
23 *International Journal of Obesity* 31 (2007) 1704-1712.
- 24 [84] N.T. Bendsen, A.L. Hother, S.K. Jensen, J.K. Lorenzen, A. Astrup, Effect of dairy calcium  
25 on fecal fat excretion: a randomized crossover trial, *International Journal of Obesity* (2009).
- 26 [85] S.E.E. Berry, G.J. Miller, T.A.B. Sanders, The solid fat content of stearic acid-rich fats  
27 determines their postprandial effects, *American Journal of Clinical Nutrition* 85 (2007) 1486-  
28 1494.
- 29 [86] L. Bonnaire, S. Sandra, T. Helgason, E.A. Decker, J. Weiss, D.J. McClements, Influence  
30 of lipid physical state on the in vitro digestibility of emulsified lipids, *Journal of Agricultural and*  
31 *Food Chemistry* 56 (2009) 3791-3797.
- 32 [87] P. Borel, M. Armand, B. Pasquier, M. Senft, G. Dutot, C. Melin, H. Lafont, D. Lairon,  
33 Digestion and absorption of tube-feeding emulsions with different droplet sizes and compositions  
34 in the rat, *J.Parenteral Enteral Nutr.* 18 (1994) 534-543.
- 35 [88] P. Borel, M. Armand, P. Ythier, G. Dutot, C. Melin, M. Senft, H. Lafont, D. Lairon,  
36 Hydrolysis of emulsions with different triglycerides and droplet sizes by gastric lipase in vitro.  
37 Effect on pancreatic lipase activity, *Journal of Nutritional Biochemistry* 5 (1994) 124-133.
- 38 [89] G. Favé, T.C. Coste, M. Armand, Physicochemical properties of lipids: new strategies to  
39 manage fatty acid bioavailability, *Cell.Mol.Biol.* 50 (2004) 815-831.
- 40 [90] S. Mun, E.A. Decker, D.J. McClements, Influence of emulsifier type on in vitro  
41 digestibility of lipid droplets by pancreatic lipase, *Food Research International* 40 (2007) 770-781.
- 42 [91] G. Clemente, M. Mancini, F. Nazzaro, G. Lasorella, A. Riviaccio, A.M. Palumbo, A.A.  
43 Rivellese, L. Ferrara, R. Giacco, Effect of different dairy products on postprandial lipemia,  
44 *Nutr.Metab.Cardiovasc.Dis.* 13 (2003) 377-383.
- 45 [92] K.M. Sanggaard, J.J. Holst, J.F. Rehfeld, B. Sandstrom, A. Raben, T. Tholstrup, Different  
46 effects of whole milk and a fermented milk with the same fat and lactose content on gastric  
47 emptying and postprandial lipaemia, but not on glycaemic response and appetite, *British Journal*  
48 *of Nutrition* 92 (2004) 447-459.
- 49 [93] T. Tholstrup, C.E. Hoy, L. Normann Andersen, R.D.K. Christensen, B. Sandström, Does  
50 fat in milk, butter and cheese affect blood lipids and cholesterol differently?, *J.Am.Coll.Nutr.* 23  
51 (2005) 169-176.

- 1 [94] M.C. Michalski, V. Briard, M. Desage, A. Geloën, The dispersion state of milk fat  
2 influences triglyceride metabolism in the rat - A (CO<sub>2</sub>)-C-13 breath test study, *European Journal*  
3 *of Nutrition* 44 (2005) 436-444.
- 4 [95] M.C. Michalski, A.F. Soares, C. Lopez, N. Leconte, V. Briard, A. Geloën, The  
5 supramolecular structure of milk fat influences plasma triacylglycerols and fatty acid profile in the  
6 rat, *European Journal of Nutrition* 45 (2006) 215-224.
- 7 [96] M.C. Michalski, On the supposed influence of milk homogenization on the risk of CVD,  
8 diabetes and allergy, *British Journal of Nutrition* 97 (2007) 598-610.
- 9 [97] M.C. Michalski, C. Januel, Does homogenization affect the human health properties of  
10 cow's milk?, *Trends in Food Science & Technology* 17 (2006) 423-437.
- 11 [98] H. Kono, H. Fujii, M. Asakawa, M. Yamamoto, M. Matsuda, A. Maki, Y. Matsumoto,  
12 Protective effects of medium-chain triglycerides on the liver and gut in rats administered  
13 endotoxin, *Annals of surgery* 237 (2003) 246-255.
- 14 [99] D.M. Small, The effects of glyceride structure on absorption and metabolism,  
15 *Annu.Rev.Nutr.* 11 (1991) 413-434.
- 16 [100] S. Wein, S. Wolffram, J. Schrezenmeir, D. Gasperikova, I. Klimes, E. Seb'kova, Medium-  
17 chain fatty acids ameliorate insulin resistance caused by high-fat diets in rats, *Diabetes*  
18 *Metab.Res.Rev.* 25 (2009) 185-194.
- 19 [101] E. Wat, S. Tandy, E. Kapera, A. Kamili, R.W. Chung, A. Brown, M. Rowney, J.S. Cohn,  
20 Dietary phospholipid-rich dairy milk extract reduces hepatomegaly, hepatic steatosis and  
21 hyperlipidemia in mice fed a high-fat diet, *Atherosclerosis* (2009).

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1 **Figure caption**

2 Figure 1. (A) Typical structure of bacterial endotoxins (lipopolysaccharides, LPS). (B)  
3 Proinflammatory cascade induced by LPS.  
4 LBP: Lipopolysaccharide-binding protein; mCD14: membrane cluster of differentiation 14;  
5 TLR4: toll-like receptor 4; MD2: myeloid differentiation protein-2; NFkB: nuclear factor kB; IL6:  
6 interleukin-6 (inflammatory cytokine).

7  
8 Figure 2. (A) Digestion of a mixed breakfast with 33 g lipids induces postprandial increase in  
9 plasma LPS, sCD14 and IL-6 in healthy humans; LPS being partly adsorbed onto chylomicrons  
10 (adapted from Laugerette *et al.* [9]).  
11 (B) Postprandial endotoxin accumulation (AUC of endotoxemia during 6 h of digestion) depends  
12 on dietary fat presence and emulsification state in force fed lean rats (adapted from Laugerette *et*  
13 *al.* [9]).

14  
15 Figure 3. Possible impact of dietary lipids on postprandial lipid and LPS absorption and metabolic  
16 outcomes.

17 Obesity and Type 2 Diabetes are characterized by altered profile of intestinal microbiota and by  
18 altered lipid metabolism.

19 During lipid digestion, endotoxins from microbiota are absorbed along with lipids and can be  
20 vehicled by chylomicrons.

21 In a healthy pattern, lipids are mostly oxidized and endotoxins are cleared by the liver.

22 In a metabolic dysfunction pattern (obesity, type 2 diabetes), lipids are more oriented towards  
23 storage in the adipose tissue and more circulating endotoxins contribute to generate low-grade  
24 inflammation.

25