Changes of Fatty Acid Composition in Incubated Rat Pancreatic Islets
Evidence for Fatty Acid Release

EF Martins¹, CK Miyasaka², P Newsholme³, R Curi⁴, AR Carpinelli⁴

S U MMARY

Objective: The hypothesis that changes in fatty acid composition of pancreatic islets occur during incubation was investigated.

Methods: The content and composition of fatty acids (FA) from rat pancreatic islets and culture medium after incubation for 1 and 3 hours in the absence or in the presence of 5.6, 8.3, or 16.7 mM glucose were determined by HPLC analysis.

Results: The FA content of pancreatic islets was reduced after 1 hour incubation in the absence of glucose. However, the total FA content was restored by incubating in the presence of 5.6 mM glucose and exceeded by incubating in the presence of 8.3 mM or 16.7 mM glucose. Saturated FA contributed a substantially greater proportion of the total FA increase in comparison to unsaturated FA, being palmitic and stearic acids the most important. The total lipid content of pancreatic islets was not increased if the period of incubation in the presence of glucose was extended to 3 hours. A substantial amount of FA was found in the medium after 1 hour incubation in the absence of glucose: 141 ng per 80 islets for saturated and 75 ng per 80 islets for unsaturated. The release of FA from islets is increased in the presence of glucose.

Conclusion: The release of FA from islets is a novel finding and may be related to modulation of B-cell function.

Key-words: Fatty acid composition · Fatty acid release · Glucose · Pancreatic islets.

RéSUMÉ

 Modifications de la composition en acides gras dans des îlots pancréatiques de rat en culture.
 Arguments en faveur d’une libération d’acides gras

Objectif : Cette étude a testé l’hypothèse selon laquelle la mise en culture d’îlots pancréatiques modifie leur composition en acides gras.

Méthodes : Le contenu et composition en acides gras (AG) d’îlots pancréatiques de rats a été mesuré par HPLC dans l’îlot et le milieu de culture après incubation pendant 1 et 3 heures en absence ou en présence de glucose 5.6, 8.3, ou 16.7 mM.

Résultats : Le contenu en AG des îlots pancréatiques était réduit après 1 heure d’incubation en absence de glucose. Cependant, le contenu total en AG était restauré par incubation en présence de 5.6 mM glucose et augmenté par incubation en présence de glucose 8.3 mM ou 16,7 mM. Les AG saturés contribuaient de façon prédominante à l’augmentation totale des AG par comparaison aux AG insaturés, avec au premier rang l’acide palmitique et l’acide stéarique. Le contenu lipidique total des îlots pancréatiques n’était pas augmenté si la période d’incubation en présence de glucose était prolongée jusqu’à 3 heures. Une quantité substantielle d’AG a été trouvée dans le milieu après 1 heure d’incubation sans glucose : 141 ng pour 80 îlots pour les AG saturés et 75 ng pour 80 îlots pour les AG insaturés. La libération d’AG par les îlots est augmentée en présence de glucose.

Conclusion : La libération d’AG par les îlots est une nouvelle notion, qui peut être mise en relation avec une modulation de la fonction B-cellulaire.

Mots-clés : Composition en acides gras · Libération d’acides gras · Glucose · Îlots pancréatiques.

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The process of insulin secretion from pancreatic B-cells is stimulated by an increase in glucose metabolism subsequent to an increase in extracellular glucose concentration. An increase in the ATP/ADP ratio results inhibition of K⁺_ATP channels [1, 2], thus depolarising the cell membrane, which results activation of VDCC, an elevation in intracellular Ca²⁺ and stimulation of insulin release [3]. However, several potentiating events (involving mitochondrial metabolism and/or activation of protein kinases) also occur which modulate insulin secretion [4-6].

FA are important regulators of glucose-induced insulin secretion [7-11]. Acute lowering of plasma FA levels lowers basal insulin secretion [11], whereas increased levels of free FA in fasted mice stimulates in vivo beta-cell electrical activity [12], which is associated with enhanced intracellular calcium concentration and thus insulin secretion. Circulating FA are essential for an efficient glucose induced stimulation of insulin secretion after prolonged fasting in humans [9]. FA have been postulated to activate signalling proteins in pancreatic islets such as protein kinase C, that can potentiate the mechanism of glucose-induced insulin secretion [13, 14].

Intracellular glucose metabolism may additionally promote changes in the phospholipid composition of pancreatic islets [15-17]. Evidence has been accumulated for the synthesis of FA in insulin producing cells [18]. Glucose provides glycerol-phosphate for esterification of FA [9, 19, 20]. Glucose may also be metabolised to citrate in the mitochondria and after being exported to the cytosol may be cleaved to oxaloacetate and acetyl CoA by ATP-citrate lyase. Acetyl CoA carboxylase provides malonyl CoA from acetyl CoA, the starting point for FA synthesis [21, 22]. In spite of this, however, changes in FA composition of pancreatic islets incubated in the absence and in the presence of glucose were not investigated yet. In this study, rat pancreatic islets were incubated for 1 hour in the absence or in the presence of 5.6, 8.3, or 16.7 mM glucose. The content and composition of FA in the islets and culture medium were then determined by HPLC analysis. The persistence of the changes was evaluated by extending the incubation period to 3 hours.

Material and methods

Animals

Wistar rats (weighing 200 ± 20 g) obtained from the Department of Physiology and Biophysics, Institute of Biomedical Sciences, USP, were used. The animals were kept in cages in groups of five rats and housed under a light-dark cycle of 12/12 h at 23 ± 2 °C. The rats were fed ad libitum a diet containing 45.5% carbohydrate, 18% protein and 4% lipid and had free access to water. The protocol for utilization of animals was certified on n.174/2001, with the Ethical Principles for Animal Research adopted by the Brazilian College of Animal Experimentation and was approved by the Institute of Biomedical Sciences São Paulo University — Ethical Committee for Animal Research.

Incubation of pancreatic islet

Rat pancreatic islets were isolated as described by Lacy and Kostianovsky [23]. This method is described with details in our previous publications [4, 24, 25]. Batches of 80 islets were incubated in 2 mL of Krebs-Henseleit buffer (in mM: 139 Na⁺, 5 K⁺, 1 Ca²⁺, 1 Mg²⁺, 124 Cl⁻, and 24 HCO₃⁻) at 37 °C for 1 or 3 hours in the absence or in the presence of 5.6, 8.3, and 16.7 mM glucose. After incubation, the medium and islets were removed for analysis.

Lipid extraction and High performance liquid chromatographic analysis of FA

The lipids were obtained from the pancreatic islets and culture medium as previously described [26]. The lipids were saponified using 2 mL of an alkaline methanol solution (1 mol/L NaOH in 90% methanol) at 37 °C, for 2 hours, in a shaking water bath. Afterwards, the alkaline solution was acidified to pH 3 with HCl solution 1 mol/L. FA were then extracted 3 times with 2 mL hexane. After the extraction procedure and saponification [27-29], the FA were derivatized with 4-bromomethyl-7-coumarin [30] and the analysis performed in a liquid chromatograph Shimadzu model LC-10A. The samples were eluted using a C8 column (25 cm × 4.6 id, 5 μm of particles) with pre-column C8 (2.5 cm × 4.6 id, 5 μm of particles), 1 mL per minute of acetonitrile/water (77: 23, by vol) flow and fluorescence detector (325 nm excitation and 395 nm emission) [29]. The FA used as standards were obtained from Sigma Chemical Co. (St. Louis, MO, USA): lauric (C12: 0), myristic (C14: 0), palmitic (C16: 0), palmitoleic (C16: 1ω6); stearic (C18: 0); oleic (C18: 1ω9), linoleic (C18: 2ω6), linolenic (C18: 3ω6), arachidonic (C20: 4), eicosapentaenoic (C20: 5ω3) (EPA), docosahexaenoic (C22: 6ω3) (DHA), and margaric (C17: 0) acids. This latter FA was used to calculate recovery and quantification.

For quantification of FA, we determined the capacity factor (K'), elution sequence, linearity, recovery, precision,
Unsaturation index 2033.18 1045.56 1352.60 1363.81 1323.45

12: 0 Lauric acid 82.34
Fatty acids Freshly obtained none 5.6 mM 8.3 mM 16. mM

Results

Statistical analysis

Polyunsaturated/saturated (P/S) FA ratio

Unsaturation index

The unsaturation index of the FA present in pancreatic islets and culture medium was calculated [31]. The quantity of each FA was multiplied by the number of double bonds present. The total summation was determined and the values are presented in Tables I and II.

Table I

High performance liquid chromatographic analysis of fatty acids composition of freshly obtained and 1 hour-incubated pancreatic islets. The incubation were carried out in the absence and in the presence of different glucose concentrations. The values in ng per 80 islets expressed as mean ± SEM were from four independent experiments using pool of islets from 3 rats each.

<table>
<thead>
<tr>
<th>Fatty acids</th>
<th>Freshly obtained</th>
<th>none</th>
<th>5.6 mM</th>
<th>8.3 mM</th>
<th>16. mM</th>
</tr>
</thead>
<tbody>
<tr>
<td>12: 0 Lauric acid</td>
<td>82.34 ± 2.13</td>
<td>84.31 ± 6.41</td>
<td>117.65 ± 7.89</td>
<td>111.85 ± 0.88</td>
<td>162.40 ± 23.09a, b</td>
</tr>
<tr>
<td>14: 0 Myristic acid</td>
<td>30.84 ± 1.25</td>
<td>32.15 ± 5.49</td>
<td>54.85 ± 0.81a</td>
<td>54.33 ± 6.93</td>
<td>65.63 ± 3.62a, b</td>
</tr>
<tr>
<td>16: 0 Palmitic acid</td>
<td>247.99 ± 11.48</td>
<td>56.09 ± 15.76a</td>
<td>326.99 ± 14.13b, b</td>
<td>348.83 ± 6.69b</td>
<td>378.80 ± 14.78b</td>
</tr>
<tr>
<td>16: 1 Palmitoleic acid</td>
<td>2.27 ± 0.20</td>
<td>19.81 ± 0.15a</td>
<td>34.63 ± 2.29b, b</td>
<td>34.61 ± 0.82b, b</td>
<td>24.70 ± 3.82a</td>
</tr>
<tr>
<td>18: 0 Stearic acid</td>
<td>239.64 ± 4.61</td>
<td>65.38 ± 11.77a</td>
<td>346.69 ± 26.41b</td>
<td>402.36 ± 17.48a b c</td>
<td>473.96 ± 10.76a b c</td>
</tr>
<tr>
<td>18: 1 Oleic acid</td>
<td>119.55 ± 5.98</td>
<td>109.19 ± 8.31</td>
<td>157.01 ± 22.94</td>
<td>178.64 ± 7.11</td>
<td>165.94 ± 16.31</td>
</tr>
<tr>
<td>18: 2 Linoleic acid</td>
<td>202.27 ± 0.58</td>
<td>141.45 ± 14.01</td>
<td>174.03 ± 23.13</td>
<td>230.37 ± 18.49</td>
<td>182.24 ± 19.16</td>
</tr>
<tr>
<td>18: 3 γ Linolenic acid</td>
<td>7.94 ± 0.81</td>
<td>9.92 ± 0.89</td>
<td>15.21 ± 1.96</td>
<td>17.91 ± 0.01b, b</td>
<td>17.35 ± 0.46b</td>
</tr>
<tr>
<td>20: 4 Arachidonic acid</td>
<td>320.31 ± 9.98</td>
<td>120.44 ± 4.64a</td>
<td>149.56 ± 5.33a</td>
<td>124.84 ± 7.02a</td>
<td>136.50 ± 14.32a</td>
</tr>
<tr>
<td>20: 5 EPA</td>
<td>13.35 ± 0.95</td>
<td>9.26 ± 0.38</td>
<td>15.99 ± 2.22</td>
<td>13.01 ± 0.48</td>
<td>13.71 ± 0.19</td>
</tr>
<tr>
<td>22: 6 DHA</td>
<td>22.50 ± 1.63</td>
<td>12.64 ± 0.19a</td>
<td>14.84 ± 1.34a</td>
<td>11.94 ± 1.58a</td>
<td>14.95 ± 0.68</td>
</tr>
</tbody>
</table>

Unsaturation index 2033.18 1045.56 1352.60 1363.81 1323.45

Statistical analysis was performed using ANOVA and Tukey’s test for \( p < 0.01 \), where (a) different as compared to freshly obtained islets; (b) different as compared to the condition without glucose (none); (c) different as compared to 5.6 mM glucose. EPA — Eicosapentaenoic acid. DHA — Docosahexaenoic acid.

interference, and limit of detection. The minimum limit of quantification of the FA ranged from 1 to 10 pg. We obtained one curve of calibration for each standard, determining coefficients of correlation and regression.

Unsaturation index

The unsaturation index of the FA present in pancreatic islets and culture medium was calculated [31]. The quantity of each FA was multiplied by the number of double bonds present. The total summation was determined and the values are presented in Tables I and II.

Polyunsaturated/saturated (P/S) FA ratio

The P/S ratios of the total FA present in the pancreatic islets and medium were calculated as previously described [32].

Statistical analysis

All results are expressed as the mean and standard error of the mean (SEM), whose applicable. For statistical analysis, ANOVA was used to detect differences among the groups and Tukey’s test was employed to indicate statistical significance at \( p < 0.01 \).

Results

Preliminary experiments were performed to determine insulin secretion by the pancreatic islets after 1 hour incubation in the presence of glucose. The values expressed as µU per islet in hour were \( 60 ± 4 \) for 5.6 mM, 118 ± 9 for 8.3 mM, and \( 447 ± 19 \) for 16.7 mM glucose concentrations (mean ± SEM of 8 determinations). Insulin was determined as previously described [33]. However, the pancreatic islets used in this study are a mixture of various cell types in which B cells represent 60% to 80% of the total. Therefore the changes observed might not reflect exclusively changes in B-cell.

Changes in FA composition of incubated pancreatic islets

The total lipid content of pancreatic islets was substantially reduced after 1 hour incubation in the absence of glucose (Fig 1A). The total lipid content was restored by incubating islets in the presence of 5.6 mM glucose and exceeded by incubating in the presence of 8.3 mM or 16.7 mM glucose. Saturated FA provided a substantially greater proportion of the total lipid in comparison to unsaturated FA (Fig 1A).

Palmitic and stearic acids were quantitatively the most important saturated FA increased while linoleic and oleic acids were quantitatively the most important unsaturated FA present over 3 hours. The values in ng per 80 islets were quantitatively the most important unsaturated FA increased while linoleic and oleic acids were quantitatively the most important unsaturated FA.

The total lipid content was restored by incubating islets in the presence of 5.6 mM glucose concentrations (mean ± SEM of 8 determinations). Insulin was determined as previously described [33]. However, the pancreatic islets used in this study are a mixture of various cell types in which B cells represent 60% to 80% of the total. Therefore the changes observed might not reflect exclusively changes in B-cell.

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Palmitic and stearic acids were quantitatively the most important saturated FA increased while linoleic and oleic acids were quantitatively the most important unsaturated FA.

The total lipid content of pancreatic islets was not significantly increased if the period of incubation in the presence of glucose was extended to 3 hours compared to 1 hour of incubation (Fig 1B). Likewise the proportion of saturated and unsaturated FA over 3 hours was similar to 1 hour of incubation.
Table II
High performance liquid chromatographic analysis of fatty acid composition of the medium pancreatic islets incubated for 1 hour with different glucose concentrations. The values in ng per 500µl expressed as mean ± SEM were obtained from four independent experiments using pool of islets from 3 rats each.

<table>
<thead>
<tr>
<th>Fatty acids</th>
<th>None</th>
<th>5.6 mM</th>
<th>8.3 mM</th>
<th>16.7 mM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
<td>Mean ± SE</td>
</tr>
<tr>
<td>12: 0 Lauric acid</td>
<td>56.44 ± 1.00</td>
<td>52.91 ± 2.52</td>
<td>55.17 ± 1.94</td>
<td>54.54 ± 2.53</td>
</tr>
<tr>
<td>14: 0 Myristic acid</td>
<td>15.03 ± 0.75</td>
<td>28.98 ± 2.01 &lt;sup&gt;b&lt;/sup&gt;</td>
<td>27.01 ± 0.34 &lt;sup&gt;b&lt;/sup&gt;</td>
<td>29.61 ± 1.28 &lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>16: 0 Palmitic acid</td>
<td>37.61 ± 2.87</td>
<td>128.60 ± 1.84 &lt;sup&gt;b&lt;/sup&gt;</td>
<td>117.74 ± 1.82 &lt;sup&gt;b&lt;/sup&gt;</td>
<td>116.48 ± 1.61 &lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>16: 1 Palmitoleic acid</td>
<td>5.91 ± 0.43</td>
<td>10.73 ± 1.68</td>
<td>9.94 ± 0.78</td>
<td>10.97 ± 0.50 &lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>18: 0 Stearic acid</td>
<td>31.84 ± 1.13</td>
<td>172.95 ± 2.13 &lt;sup&gt;b&lt;/sup&gt;</td>
<td>156.64 ± 5.13 &lt;sup&gt;b&lt;/sup&gt;</td>
<td>156.66 ± 4.46 &lt;sup&gt;b,c&lt;/sup&gt;</td>
</tr>
<tr>
<td>18: 1 Oleic acid</td>
<td>32.65 ± 1.42</td>
<td>44.04 ± 4.87</td>
<td>67.51 ± 0.29 &lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>67.15 ± 2.50 &lt;sup&gt;b,c&lt;/sup&gt;</td>
</tr>
<tr>
<td>18: 2 Linoleic acid</td>
<td>27.75 ± 1.26</td>
<td>41.46 ± 4.47</td>
<td>79.64 ± 9.02 &lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>72.11 ± 7.32 &lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>18: 3 γ-Linolenic acid</td>
<td>4.30 ± 0.39</td>
<td>5.66 ± 0.61</td>
<td>9.96 ± 1.04 &lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>7.72 ± 0.15 &lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>20: 4 Arachidonic acid</td>
<td>&lt;0.01</td>
<td>0.42 ± 0.01</td>
<td>0.67 ± 0.11</td>
<td>0.60 ± 0.03</td>
</tr>
<tr>
<td>20: 5 EPA</td>
<td>4.56 ± 0.13</td>
<td>6.46 ± 0.28</td>
<td>7.71 ± 0.93 &lt;sup&gt;b&lt;/sup&gt;</td>
<td>7.21 ± 0.39 &lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>22: 6 DHA</td>
<td>&lt;0.01</td>
<td>4.40 ± 0.71</td>
<td>5.48 ± 0.31</td>
<td>6.28 ± 0.54</td>
</tr>
</tbody>
</table>

Unsaturation index 129.76 215.06 340.71 321.60

Statistical analysis was performed using ANOVA and Tukey’s test for p < 0.01, where (b) different as compared to the condition without glucose (none); (c) different as compared to 5.6 mM group. EPA — Eicosapentaenoic acid. DHA — Docosahexaenoic acid.

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...tion (Fig 1B). Palmitic and stearic acids were also quantitatively the most important saturated FA, whereas linoleic and arachidonic acids were quantitatively the most important unsaturated FA found after 3 hours (data not shown).

It is interesting to note that the P/S ratio of pancreatic islets cultivated in the absence of glucose was markedly reduced after 3 hours in comparison to 1 hour incubation; from 1.78 to 0.57.

Release of FA from pancreatic islets

During 1 h incubation, pancreatic islets released a substantial amount of FA to the medium either in the absence or presence of glucose (Fig 2A). In the absence of glucose, the total amount of FA released reached up to 216 ng per 80 islets. The proportion of FA released was: 141 ng per 80 islets for saturated and 75 ng per 80 islets for unsaturated FA. The rank order of the amount of FA released to the medium in the absence of glucose was: lauric > palmitic > oleic = stearic > linoleic > myristic > palmitoleic > EPA ≥ linolenic. The release activity of FA from the islets was more pronounced after 3 hours incubation (Fig 2B). The total amount of FA released reached 296 ng per 80 islets after 3 hours incubation. The relative amount of the FA released was also modified after 3 hours incubation: stearic > palmitic ≥ oleic > myristic = lauric > palmitoleic = linoleic > arachidonic = γ-linolenic = EPA ≥ DHA.

The addition of glucose to incubated islets caused a significant increase of the content of FA in the medium. After 1 hour incubation, the addition of 5.6 mM glucose raised the medium content of palmitic (3.4-fold) and stearic (5.4-fold) acids as compared to islets incubated in the absence of glucose (Tab II). In addition to the increase of these FA, 8.3 mM glucose raised also oleic (2.1-fold), linoleic (2.9-fold), and γ-linolenic (2.3-fold) acids, and EPA (1.7-fold). High glucose (16.7 mM) caused a significant increase in the medium content of FA including palmitoleic acid (1.9-fold). Therefore, the addition of glucose provoked a significant release of all FA, except for arachidonic acid and DHA. The total content of FA in the medium was raised by 2.4-fold when 5.6 mM glucose was added. This increase was mainly due to release of saturated FA and it was not modified when glucose concentration was raised to 8.3 and 16.7 mM.

The changes in the composition of FA in the medium became more pronounced when the period of incubation was increased to 3 hours (data not shown). In particular, 5.6 mM glucose raised the medium concentration of palmitic and stearic acids. 16.7 mM glucose further increased the release of most FA especially palmitic and stearic acids.

Discussion

Pancreatic B cell glucose metabolism results in an increased rate of production of key metabolites, including citrate, which is exported from the mitochondria to the cytosol and acts as a precursor of malonyl CoA synthesis [34]. An increase in malonyl CoA concentration can inhibit carnitine palmitoyl transferase I, leading to a reduction in beta-oxidation [35]. There is consequently a rise in concentration...
of acyl-CoA, which has been proposed to modulate insulin secretion [21, 36]. There is evidence that in addition to inhibition of free FA oxidation, glucose-induced insulin secretion is also associated with increased free FA esterification, and complex lipid synthesis by pancreatic B cells [37]. Significant increases have been reported in the total mass of diacylglycerol (DAG) [38], triacylglycerol [39], and phosphatidic acid (PA) [40]. Evidence is presented herein that marked changes of FA composition occur in incubated pancreatic islets. In the absence of glucose FA content decreases, whereas in the presence of glucose, FA content is restored. A significant increase of stearic acid in pancreatic islets was observed after 1 hour incubation in the presence of glucose that remained for up to 3 hours.

In the absence of glucose it is possible that endogenous FA oxidation is increased. As mentioned above, malonyl-CoA produced from glucose metabolism is a potent inhibitor of CPT-1 activity and so FA oxidation [35]. Thus, uninhibited FA oxidation may explain the marked reduction in FA content of pancreatic islets incubated in the absence of glucose. The reduction of polyunsaturated FA was more pronounced than that of saturated FA as indicated by P/S ratio. The precise reason for this observation remains to be clarified. Glucose metabolism therefore preserves the FA content of the islets. Although the mechanism for FA-induced insulin secretion is not fully known, a number of putative mechanisms have been proposed [8]. The role of FA in the pancreatic B-cell includes production of acyl-CoA, phospholipids, DAG, PA, and other signaling metabolites.

Saturated FA with 16 and 18 carbons can markedly enhance glucose stimulated insulin secretion from the perfused pancreas of fasted rats [10]. For example, addition of stearate caused a 21-fold enhancement of insulin release in comparison to 12.5 mM glucose alone. The mechanism for the potent...
enhancing effect of saturated long-chain FA on glucose stimulated insulin secretion is not known. Evidence is presented that a quantitatively important increase of saturated FA (myristic, palmitic, and stearic) in the incubation medium is observed when islets are incubated in the presence of glucose at all concentrations. FA release from a variety of cell types has previously been described, e.g. adipocytes, cells of the immune system where release is related to cell function (provision of lipid fuel and modulation of the immune response respectively) [41]. The significance of FA release for pancreatic B-cell function remains to be elucidated.

In this study evidence is provided for change in FA composition and content in pancreatic islets incubated in the absence or in the presence of glucose. The changes observed probably reflect changes in content of intracellular triacylglycerol, phospholipid, cholesterol ester, DAG and PA. The process of release of FA from islets reported in this paper is a novel finding and may relate to modulating of B-cell function. Taking into account that a mixture of various cell types is present in pancreatic islets, FA may mediate the interaction between different cells.

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