Serum and adipocyte resistin in polycystic ovary syndrome with insulin resistance

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BACKGROUND: The aim of this study was to investigate the relationship between resistin and insulin resistance in patients with polycystic ovary syndrome (PCOS). METHODS: We compared serum resistin levels in 17 PCOS women and 10 lean, healthy, age-matched non-PCOS women and also compared levels of insulin receptor (IR), phosphatidylinositol-3 kinase (PI3-kinase), glucose transporter 4 (GLUT4) protein and resistin mRNA in adipocytes isolated from the omental adipose tissue of five of the PCOS patients and five age- and weight-matched, non-PCOS controls, to look for local defects in insulin action in PCOS. RESULTS: The PCOS group was hyperinsulinaemic and displayed an impaired insulin response in a 75 g oral glucose tolerance test and an abnormal homeostasis model insulin resistance index. Serum resistin levels were similar in PCOS patients and controls; however, resistin mRNA levels were 2-fold higher in adipocytes from PCOS patients. No correlation was found between serum resistin levels and either the BMI or testosterone levels. Western blot analysis showed that adipocyte levels of insulin receptor, PI3-kinase, and GLUT4 were respectively decreased by 56, 39.4 and 54% in PCOS patients compared with controls. CONCLUSIONS: These results suggest that overexpression of the resistin gene in adipocytes may be a local determinant factor in the pathogenesis of PCOS.

Key words: adipose tissue/LH/PCOS/resistin/signal transduction

Introduction

Polycystic ovary syndrome (PCOS) is a heterogeneous syndrome characterized by oligomenorrhoea or amenorrhoea, hyperandrogenism, and multiple small subcapsular cystic follicles in the ovary on ultrasonography (Franks, 1995). It affects ~5–10% of women of reproductive age (Dunaif, 1997), and ~16–80% of the affected women are obese (Dunaif, 1992). PCOS is frequently associated with insulin resistance accompanied by compensatory hyperinsulinaemia and obesity (Burghen et al., 1980). Insulin resistance is thought to play an important role in the aetiology of PCOS (Chang et al., 1983; Shoupe et al., 1983). In vitro and in vivo studies have shown that, in women with PCOS, the sensitivity of insulin to glucose metabolism is subnormal and that moderate hyperinsulinaemia prevails (Dunaif et al., 1991). The administration of insulin sensitizing agents, such as metformin, may increase insulin sensitivity and thus induce ovulation (Nestler et al., 1998).

Several studies have investigated the possible cellular mechanism underlying insulin resistance in PCOS employing the major insulin target tissue, the adipocyte. Marsden et al. (1994) reported decreased numbers of insulin receptors and severe impairment of insulin action in adipocytes from amenorrhoeic women with PCOS. Ciaraldi (1997) showed that adipocytes from PCOS patients have low levels of adenosine. Rosenbaum et al. (1993) found that the decrease in the maximal rate of adipocyte glucose uptake is secondary to a significant decrease in GLUT4 glucose transporter protein.

These results suggest that insulin resistance in PCOS represents post-binding defects in signal transduction and may involve defects in more than one step in the signalling pathway.

The hormone resistin, a novel 12.5 kDa cysteine-rich protein, also known as resistin-like molecule (RELM) or ‘found in inflammatory zone’ (FIZZ), is secreted by adipocytes (Steppan et al., 2001). Serum resistin levels are significantly increased in insulin-resistant mice and genetic or diet-induced obese mice (Steppan et al., 2001). In addition, neutralization of endogenous resistin with antibodies significantly suppresses hyperglycaemia in diet-induced obese mice by improving insulin sensitivity (Steppan et al., 2001). Furthermore, resistin gene expression in obese mice is down-regulated by...
thiazolidinedione (TZD) compounds, a new class of antidiabetic drugs with an insulin-sensitizing action. These results suggest that resistin may be an important link between increased fat mass and insulin resistance.

In an animal study, resistin mRNA levels were found to be decreased in insulin-resistant rats (Juan et al., 2001), while human studies have shown resistin mRNA levels to be very low in freshly isolated adipocytes and undetectable in pre-adipocytes, endothelial cells and vascular smooth muscle cells (Nagaev and Smith, 2001; Savage et al., 2001; Sentinelli et al., 2002). McTernan (2002) also reported that resistin mRNA was detectable in human adipocytes and that its levels were 4-fold higher in adipocytes from abdominal tissue depots than in those from the thigh. Thus, resistin may serve as a hormone link between central obesity and insulin resistance in humans and may regulate insulin sensitivity and glucose tolerance.

This study was performed to compare serum levels of resistin in women with PCOS and normal controls, and to detect its expression in human adipocytes using the semi-quantitative RT–PCR. We also examined whether the decreased adipocyte insulin response seen in PCOS patients might be attributable to local defects of insulin action in the signal transduction pathway, including defects in the insulin receptor, phosphatidylinositol 3-kinase (PI3-kinase), and the GLUT4 glucose transporter.

Materials and methods

Subjects

Seventeen women (10 obese and seven lean: obesity defined as BMI ≥ 27 kg/m², lean as BMI < 27 kg/m²) who fulfilled the inclusion criteria for PCOS given below were enrolled in this study. All were in good health and had not taken oral contraceptives within the last 3 months. The protocol was reviewed and approved by the Institutional Review Board of both the Shin Kong Wu Ho-Su Memorial Hospital and Taipei Veteran General Hospital. All patients entered this study only after informed written consent was obtained.

PCOS was defined by clinical, laboratory and ultrasound criteria. The clinical criteria included oligomenorrhea (menstrual interval >6 weeks) or amenorrhea (no menstrual loss for >6 months) dating from menarche. All subjects were hirsute with a score of >10 on the Ferriman–Gallwey score (Ferriman and Gallwey, 1961). None of the subjects had acanthosis nigricans. The biochemical criteria were an increased LH concentration (> 6 mIU/ml, normal follicular range 1–6 mIU/ml), a normal FSH concentration, and elevated total serum testosterone levels (>0.8 ng/ml, normal range 0.06–0.86 ng/ml). The ultrasound criteria were enlarged ovaries with an increased stroma and >10 subcapsular follicles of 3–8 mm diameter, arranged peripherally around a dense core of stroma, as described by Adams et al. (1986).

Serum prolactin and thyroid hormone levels were checked in all patients and were within the normal limits. Cushing’s syndrome and congenital adrenal hyperplasia were excluded by an overnight dexamethasone test (1 mg) and a morning serum 17-hydroxyprogesterone level of >1500 ng/dl.

Ten healthy, lean, age-matched women served as controls. None was hirsute, and all had a normal regular cycling menstrual period. None was taking oral contraceptives. All had a normal appearance of the ovaries on ultrasound and normal LH and FSH levels, and none had elevated androgen levels.

Reagents

Human monoclonal antibodies against human insulin receptor β-subunit or PI3-kinase were purchased from Upstate Biotechnology Inc. Polyclonal rabbit anti-GLUT4 antibody was obtained from Biogenesis Inc. Human anti-β-actin antibody was from Chemicon Inc. The resistin enzyme immunoassay (EIA) kit was purchased from Phoenix Pharmaceuticals Inc. (USA).

Oral glucose tolerance test and homeostasis model insulin resistance index

A 2 h oral glucose tolerance test (OGTT) with 75 g of glucose load was performed after an overnight fast during the early follicular phase (days 3–7) on all women. Four blood samples were collected at 0, 30, 60 and 120 min and the plasma stored at −20°C until assayed for glucose and insulin. The homeostasis model (HOMA) insulin resistance index was calculated using the formula: fasting glucose (mmol/l) × fasting insulin (μIU/ml)/22.5 (Matthews et al., 1985).

Hormonal profile

The hormonal profile (FSH, LH, E₂ and testosterone) was measured in a blood sample collected on the same day as the OGTT. For the patients with amenorrhea, 75 mg progesterone was given i.m. to induce withdrawal bleeding and their blood samples were also collected in the follicular phase.

Blood collection for resistin

Blood samples (7 ml) were collected in Lavender Vacutainer tubes containing EDTA. The blood was then transferred to a centrifuging tube containing aprotinin (0.6 TIU/ml of blood) and rocked several times to inhibit protease activity, then the sample was centrifuged at 1600 g for 15 min at 4°C and the plasma stored at −70°C until assayed for resistin. The plasma sample was diluted 2-fold with EIA buffer to perform the EIA.

Resistin assay

Resistin was measured in a fasting blood sample, collected on the same day as the OGTT, using an EIA kit with a lower limit of sensitivity of 1.21 ng/ml (range: 0–500 ng/ml) and intra- and inter-assay coefficients of variation (CV) of <5 and <14% respectively.

Adipocyte cell isolation

Adipose tissue (5–6 g) was obtained by laparoscopic surgery from the omental fat tissue of five controls undergoing gynaecological surgery and five PCOS patients undergoing ovarian drilling therapy. The adipose tissue was transported to the laboratory in Krebs–Ringer bicarbonate (KRB) buffer (in mmol/l: NaCl 118, MgSO₄ 1.2, CaCl₂ 1.3, NaHCO₃ 2.5, pH adjusted to 7.4 at 37°C) within 30 min and adipocytes isolated following the procedure described by Rodbell (1964) with minor modifications. The adipocyte tissue was finely minced, then disintegrated into cells by gentle shaking for 60 min at 37°C in KRB buffer containing 1 mmol/l pyruvate, 1% bovine serum albumin (BSA), and 0.1% collagenase (10 ml per g of tissue).
The cell suspension was then filtered through a nylon mesh (400 μm) and centrifuged at 100 g for 1 min at room temperature. The supernatant was harvested and washed three times with 50 ml of KRB buffer containing 1 mmol/l pyruvate and 1% BSA. To count the cells and measure their size, an aliquot of diluted cell suspension was fixed overnight in collidine buffer containing 2% osmium tetroxide prior to microscopic photography. The mean cell volume and surface area were calculated from the known lipocrit of the cell suspension. Half of the adipocytes were used immediately for western blots and the rest stored at −70°C for mRNA extraction.

### RNA extraction

Total RNA was extracted from the adipocytes isolated from each patient using a Tri Reagent kit (Molecular Research Center, Inc., USA). The integrity of the total RNA was examined by 1% agarose gel electrophoresis, and the RNA concentration was determined by UV absorbance at 260 nm (Genequant RNA/DNA calculator; Pharmacia, LKB Biotech, UK).

### Quantification of resistin mRNA

Levels of resistin and β-actin mRNA in adipocytes were assessed by RT–PCR based on the known cDNA sequences for resistin and β-actin; we designed the two pairs of primer listed in Table I. For RT, 5 μg of RNA template was incubated for 30 min at 37°C with 1 μl of RNase-free deoxyribonuclease (DNase) and 7 μl of H2O, followed by incubation for 10 min at 70°C with 1 μl of 25 mmol/l EDTA to inactivate the DNase, then 2 μl of 100 ng/μl of oligo(dT) primer (Promega, USA) and 7.1 μl of H2O were added and the sample incubated for 10 min at 70°C. RT was then carried out for 50 min at 42°C in a total volume of 50 μl containing 1×RT buffer, 10 mmol/l dithiothreitol, 0.5 mmol/l dNTP (HT Biotechnology Ltd), 16 IU of human placental ribonuclease inhibitor (HT Biotechnology Ltd), and 1 IU of Super RT reverse transcriptase (HT Biotechnology Ltd, UK). The RT mixtures were then heated for 3 min at 95°C to inactivate the reverse transcriptase. The resistin cDNA was amplified by touch-down PCR using a DNA Thermal Cycler (PCT-100; MJ Research, USA). The total volume of 25 μl contained 2 μl of the cDNA template, 500 mmol/l each of the sense and antisense primers, 0.625 IU of FailSafe Enzyme, and a final concentration of 1×FailSafe buffer D (both from Epicentech Technologies, USA). In a preliminary run, we found that a minimum of 30 PCR cycles was required to produce an optimal amount of nucleic acids for measuring on an agarose gel.

As a reference for the quantitative gene expression, the housekeeping gene β-actin was simultaneously amplified under conditions identical to those for resistin PCR. For example, to determine the relative quantities of resistin mRNA, 5 μl each of resistin and β-actin PCR products amplified from the same RT template solution were combined and electrophoresed on a 2% agarose gel in 0.04 mol/l Tris–acetate/0.001 mol/l EDTA buffer for 40 min. After staining the gel with ethidium bromide (0.5 μg/ml) for 15 min, the resistin and β-actin cDNA bands were measured by densitometry, using Image Master VDS and Image Quant Analysis Software (Amersham Pharmacia Biotech, Hong Kong).

### Western blots

Homogenates of isolated adipocytes were centrifuged at 6000 g for 10 min at −4°C, then the proteins (50 μg) in the supernatant were separated by 7.5 or 10% sodium dodecylsulphate polyacrylamide gel electrophoresis (SDS–PAGE), and transferred to a polyvinylidene fluoride membrane. The membrane was blocked with 5% skimmed milk in phosphate-buffered saline, for 1 h at room temperature, then reacted with antibodies against the insulin receptor β-subunit, PI3-kinase, or GLUT4, followed by secondary antibody (Jackson Immunoresearch), and enhanced chemiluminescence (ECL) reagent. Chemiluminescence were quantified using a Personal Densitometer (Molecular Dynamics, USA) with a range of 0.01–4.0 OD units.

### Statistics

All results are expressed as the mean ± SD. Differences between the PCOS and control groups were compared by Student’s t-test for independent samples. Correlations between variables were evaluated by Pearson’s correlation coefficient and regression analysis. P < 0.05 was considered significant.

### Results

As shown in Table II, the ages of the patients with PCOS ranged from 22 to 37 years (28.9 ± 5.10, mean ± SD) and those of the control group from 19 to 32 years (mean 25.4 ± 4.33; no significant difference). The body mass index values for the PCOS and control groups were 26.7 ± 4.6 and 19.5 ± 1.27 kg/m² respectively (P < 0.0001).

### Insulin resistance in PCOS

Table II shows that, although fasting insulin levels were higher in our PCOS patients than in the controls, the difference was not statistically significant. In addition, there was no difference in fasting glucose levels. Nevertheless, after a 75 g oral glucose challenge, the 2 h insulin levels increased from 6.1 ± 3.94 to 24.3 ± 12.15 mIU/ml in the PCOS patients, a highly significant difference compared to the normal controls. Forty-seven per cent of the PCOS patients fulfilled World Health Organization (1985) criteria for impaired glucose tolerance on the basis of serum glucose levels at 2 h after a 75 g glucose load. In addition, 52.9% of the PCOS women showed insulin resistance (HOMA >2.7), which was confirmed by western blot analysis showing that adipocyte levels of insulin receptor, PI3-kinase...

<table>
<thead>
<tr>
<th>Table I. List of primers used for semiquantitative RT-PCR</th>
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<tbody>
<tr>
<td><strong>mRNA</strong></td>
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<tr>
<td>Resistin</td>
</tr>
<tr>
<td>Sense</td>
</tr>
<tr>
<td>Anti-sense</td>
</tr>
<tr>
<td>β-Actin</td>
</tr>
<tr>
<td>Sense</td>
</tr>
<tr>
<td>Anti-sense</td>
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Table II. Clinical and endocrine characteristics of women with polycystic ovary syndrome (PCOS) and controls

<table>
<thead>
<tr>
<th></th>
<th>Lean controls (n = 10)</th>
<th>PCOS (n = 17)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.4 ± 0.33</td>
<td>28.9 ± 0.10</td>
<td>0.083</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160.4 ± 5.44</td>
<td>160.6 ± 5.62</td>
<td>0.933</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>50.2 ± 0.47</td>
<td>68.7 ± 14.04</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>66.9 ± 3.30</td>
<td>79.1 ± 10.69</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hip (cm)</td>
<td>89.5 ± 3.52</td>
<td>99.3 ± 7.51</td>
<td>0.001</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>19.5 ± 1.27</td>
<td>26.7 ± 4.60</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.75 ± 0.29</td>
<td>0.79 ± 0.06</td>
<td>0.014</td>
</tr>
<tr>
<td>FSH (mIU/ml)</td>
<td>6.52 ± 3.11</td>
<td>5.34 ± 1.78</td>
<td>0.218</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td>3.42 ± 1.76</td>
<td>12.7 ± 4.58</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LH/FSH</td>
<td>0.61 ± 0.41</td>
<td>2.42 ± 0.43</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Estradiol (pg/ml)</td>
<td>35.3 ± 10.72</td>
<td>63.7 ± 35.68</td>
<td>0.006</td>
</tr>
<tr>
<td>Testosterone (ng/ml)</td>
<td>0.41 ± 0.18</td>
<td>0.80 ± 0.39</td>
<td>0.007</td>
</tr>
<tr>
<td>Prolactin (ng/ml)</td>
<td>11.6 ± 3.92</td>
<td>10.2 ± 4.20</td>
<td>0.392</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl)</td>
<td>84.7 ± 4.52</td>
<td>85.5 ± 12.1</td>
<td>0.849</td>
</tr>
<tr>
<td>2 h glucose (mg/dl)</td>
<td>82.3 ± 15.1</td>
<td>129.7 ± 20.85</td>
<td>0.001</td>
</tr>
<tr>
<td>Fasting insulin (µIU/ml)</td>
<td>4.35 ± 2.57</td>
<td>6.1 ± 3.94</td>
<td>0.225</td>
</tr>
<tr>
<td>2 h insulin (µIU/ml)</td>
<td>10.4 ± 5.43</td>
<td>24.3 ± 12.15</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HOMA</td>
<td>0.91 ± 0.56</td>
<td>2.57 ± 1.44</td>
<td>0.082</td>
</tr>
<tr>
<td>Resistin</td>
<td>12.17 ± 0.25</td>
<td>12.13 ± 0.13</td>
<td>0.601</td>
</tr>
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</table>

Values are mean ± SD.  
P < 0.05 is considered significant.  
HOMA = homeostasis model insulin resistance index.

and GLUT4 were decreased by 56, 39.4 and 55.4% respectively in the PCOS patients compared with the controls (Figure 1).

Gonadotrophins and sex steroids in PCOS

The basal serum hormone levels in women with PCOS and the control group are shown in Table II. Mean plasma LH levels, testosterone levels, and estradiol levels were all significantly higher in the PCOS group.

Correlations between variables

Both fasting insulin and glucose levels were significantly negatively correlated with the FSH or LH levels. Correlations were found between estradiol levels and fasting insulin levels, 2 h glucose levels, or 2 h insulin levels (P < 0.05). No correlations were found between testosterone levels and fasting glucose levels, fasting insulin levels, 2 h glucose levels, or 2 h insulin levels. No correlation was found between serum resistin levels and BMI (R = 0.184, P = 0.479), testosterone levels (R = 0.022, P = 0.934), fasting insulin levels (R = 0.153, P = 0.557), or 2 h insulin levels (R = 0.324, P = 0.204).

Serum resistin levels and resistin gene expression in adipocyte

No difference was found between serum resistin levels in the two groups (P = 0.601). However, resistin mRNA levels were 2-fold higher in adipocytes from PCOS patients than in those from normal controls (Resistin/β-actin: control 0.3; PCOS: 0.6; Figure 2).

Discussion

In the present study, we found that adipocytes from women with PCOS had a lower content of insulin receptor, PI3-kinase, and GLUT4 glucose transporter. This suggests that insulin resistance in PCOS represents post-binding defects in signal transduction and that there are multiple defects in insulin action in PCOS that affect metabolism (Stuart et al., 1986; Freidenberg et al., 1988; Rosenbaum et al., 1993; Marsden et al., 1994; Ciaraldi et al., 1997). These results differ from those of Book (1999) who reported a defect in metabolic, but not mitogenic, signalling pathways in PCOS fibroblasts, with no difference in insulin receptor or PI3K activity between fibroblasts from PCOS patients and controls. However, the number of PCOS patients in which the cellular aspects were examined in the present study was small and a further study is required.

The combined results of the clinical diagnosis methods (OGTT and HOMA index) and the western blotting experiments showed that the PCOS patients were insulin-resistant. Although fasting insulin levels were higher in the PCOS group, the difference was not statistically significant. After challenge with 75 g of oral glucose, both the 2 h insulin and 2 h glucose levels were significantly higher in the PCOS group than in the controls, showing that the PCOS women were hyper-insulinemic with glucose intolerance. Taking into account the additional evidence of the HOMA insulin resistance index and the signal transduction pathway defects in adipocytes from PCOS patients, we conclude that our patients were insulin-resistant. In fact, western blotting analysis may be the most accurate test for identifying insulin-resistant PCOS patients for targeted treatment with insulin-sensitizing agents.

Resistin has been described as a potential link between obesity and insulin resistance (Steppan et al., 2001) and resistin mRNA levels have been shown to be increased in 3T3-L1 cells and to be down-regulated by antidiabetic thiazolidinediones (TZD) drugs, which bind to peroxisome proliferator activated receptor-γ (PPAR-γ) in fat cells (Steppan et al., 2001). Resistin might therefore be expected to play a role in PCOS, and serum levels in these patients might be expected to be elevated. However, we found that serum resistin levels in PCOS did not differ from those in normal cycling women of a similar age and with a similar BMI. It should be noted that none of the 17 PCOS women studied displayed hyper-resistinaemia. Furthermore, serum resistin levels did not correlate with either fasting insulin or 2 h insulin levels in the PCOS group. These results may indicate that serum resistin levels did not affect insulin sensitivity in PCOS. However, a difference was seen in resistin mRNA levels in adipocytes, these being twice as high in PCOS patients as in controls, suggesting that resistin may have a local paracrine action in the regulation of insulin resistance in obesity and PCOS.

The poor correlation found between serum resistin levels and BMI in this study conflicts with the report by Steppan (2001) of increased levels of serum resistin in ob/ob and db/db mice. Steppan’s observation is inconsistent with the aforementioned expectation that insulin resistance should correlate positively with increased serum resistin levels. Furthermore, adipocyte resistin mRNA levels were increased in our women with PCOS, who had high testosterone levels. This agrees with the results of Ling et al. (2001) who showed that resistin mRNA levels are increased 2.6-fold in control male mice with...
elevated testosterone levels. Testosterone administration to obese males can improve insulin sensitivity (Marin et al., 1992), but may produce hyperinsulinaemia in women (Nestler et al., 1988; Mortola and Yen, 1990).

Women with PCOS had significantly higher estradiol levels than normal controls. This result fits with the hypothesis proposed by Fox et al. (1991) that estrogenization is a key feature of PCOS. Furthermore, there was a strong association between estradiol levels and fasting insulin levels or 2 h insulin levels. This association is of special interest because the estradiol levels could be a surrogate marker for hyperinsulinemic insulin resistance in PCOS. The increased estradiol levels are thought to be due to the combined secretion of estradiol and estrone by numerous follicles, resulting in substantial release (Wajchenberg et al., 1988) and the peripheral aromatization of circulating androgens in adipose tissue (Marsden et al., 1999).

The modest hyperandrogenism characteristic of PCOS has been proposed to be associated with insulin resistance (Dunaif et al., 1991; Rittmaster et al., 1993). However, androgen administration to healthy females does not produce insulin resistance of the same magnitude as that seen in PCOS (Polderman et al., 1994). In our study group, we did not find any correlation between testosterone levels and fasting or 2 h insulin levels. These results demonstrate that testosterone

Figure 1. Western blot analysis of adipocytes from women with polycystic ovary syndrome and controls. Blots were probed with antibody against human insulin receptor β-subunit (a), phosphatidylinositol-3 kinase (b), or glucose transporter 4 (c). Left: western blot; right quantitative data. The experiment was performed twice with similar results.

Figure 2. (a) RNA extracted from the omental adipose tissue of women with polycystic ovary syndrome and normal controls; 28S and 18S RNA are shown. (b) Adipocyte resistin gene expression (412 bp) in the two groups. (c) Human β-actin (528 bp) gene expression in the two groups.
levels are of limited use in predicting insulin resistance in
PCOS.
In conclusion, we have shown that insulin resistance in
PCOS women involves both receptor and post-receptor defects,
including defects in PI3-kinase and the GLUT4 glucose
transporter. Serum resistin levels in PCOS women were similar
to those in the control group. Nevertheless, the increased levels
of resistin mRNA in PCOS adipocytes suggest that resistin may
be a determinant factor in the local pathogenesis of PCOS. Estradiol,
serum levels of which were significantly elevated in the
PCOS group, could be a surrogate marker for hyper-
insulinaemic insulin resistance in PCOS.

Acknowledgements
This study was supported by grants from the Shin Kong Wu Ho-Su
Memorial Hospital (No. 8302-92-2477) and the Taipei Veteran
General Hospital (No. VGH 92-C329).

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