

CIRCULATING LEVELS OF IRISIN IN OBESE NON DIABETIC PATIENTS AND IN LMNA-MUTATED PARTIAL LIPODYSTROPHIES

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INTRODUCTION Irisin is a myokine, which displays a day-night rhythm, is correlated with lean body mass, and increases after exercise in healthy young individuals, despite an association with major adverse cardiovascular events and polycystic ovary disease (Mantzoros 2014). Increased skeletal muscle volume has been reported in women with familial partial lipodystrophies (FPLD) (Ji JCEM 2014). **Our aim was to determine whether irisin could be a marker of FPLD, which is characterized by a decreased fat mass and an increased lean mass (Clin.gov2009-AO-1169-48/PHRC 2009_09/094).**

METHODS AND PATIENTS

Circulating irisin levels (EIA Phoenix) were measured in :

- 20 LMNA-related FPLD,
- 19 healthy normal-weighted (H) and
- 13 obese non-diabetic (OND) patients

And correlated with :

- body composition (assessed with DEXA and MRI),
- metabolic parameterd (fasting blood glucose (FBG),
- insulin, A1c, lipid, transaminases, leptin) and
- inflammatory markers (leukocytes CD4, CD8, CRP)

Values were expressed as median IQR and were compared with the non-parametric Kruskal–Wallis test (Statview). Correlations were studied by the non-parametric Spearman correlation test. The Wilcoxon non-parametric test was used to compare biological data between H, FPLD, and OND.

RESULTS Irisin median differed significantly between the 3 groups (p:0.0076), was higher in OND (p: 0.0099) and FPLD (p: 0.047) than in H groups, without any difference between FPLD and OND and was similar between male and female.

Irisin was not correlated with leptin or inflammatory markers. Leptinemia was higher in OND compared to H and FPLD (p<0.0001), without difference between these 2 groups. Irisin/leptin ratio, a biomarker of lean/fat mass, was lower in OND (21(13-32)) than in FPLD (166 (71-214)) or control (164(128-222)) groups (p<0.0001 without difference between FPLD and H.

| | HC ⁽¹⁾ | [Q ₀ , Q ₃] | OND ⁽²⁾ | [Q ₀ , Q ₃] | FPLD ⁽³⁾ | [Q ₀ , Q ₃] | P ₁₊₂₊₃ [†] | P _{1/2} [*] | P _{1/3} [*] | P _{2/3} [*] |
|-----------------------------|-------------------|------------------------------------|--------------------|------------------------------------|---------------------|------------------------------------|---------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Number (n) | 19 | | 13 | | 20 | | | | | |
| Age (years) | 37 | [23-55] | 51 | [21-56] | 45 | [33-58.5] | 0.22 | - | - | - |
| Weight (kg) | 69 | [55-76.8] | 100.4 | [94-104] | 67.3 | [55.6-80.75] | <0.0001 | <0.0001 | 1.000 | <0.0001 |
| BMI (kg/m ²) | 22.3 | [21-24.2] | 39 | [36.8-41] | 25.6 | [21.97-28.5] | <0.0001 | <0.0001 | 0.1 | <0.0001 |
| Fasting blood glucose (g/l) | 0.86 | [0.83-0.94] | 0.92 | [0.83-0.99] | 1.06 | [0.89-1.51] | 0.0084 | 0.87 | 0.009 | 0.19 |
| Fasting blood insulin (g/l) | 4.5 | [3.1-5.8] | 7.3 | [4.5-10.55] | 9.3 | [6.4-18.4] | 0.001 | 0.07 | 0.001 | 0.84 |
| Hemoglobin A1c (%) | 5 | [4.9-5.6] | 5.8 | [5.4-6.2] | 6.15 | [5.6-7] | <0.0001 | 0.0033 | <0.0001 | 0.45 |
| Transaminases (U/L) | | | | | | | | | | |
| SGOT | 22 | [19-25] | 20 | [19-25] | 32 | [23.5-39] | 0.0059 | 1.000 | 0.02 | 0.03 |
| SGPT | 17 | [14-25] | 20 | [19-27] | 29 | [22.5-52] | 0.004 | 0.089 | 0.009 | 0.33 |
| Lipids (g/l) | | | | | | | | | | |
| Total cholesterol | 1.95 | [1.8-2.12] | 1.88 | [1.75-2.13] | 1.76 | [1.59-2.12] | 0.34 | - | - | - |
| Triglycerides | 0.88 | [0.62-1.16] | 1.31 | [1.07-1.59] | 2.14 | [1.08-2.66] | 0.0015 | 0.05 | 0.004 | 0.23 |
| Leptin (ng/ml) | 4.6 | [4.1-10.7] | 49.6 | [31.9-67.6] | 6.8 | [4.15-11.95] | <0.0001 | <0.0001 | 1.000 | <0.0001 |
| Irisin (ng/ml) | 804 | [732-876] | 934 | [872-1046] | 940 | [810-1066] | 0.0076 | 0.006 | | |
| CRP (mg/l) | 0 | 0 | 7 | [3-15] | 3 | [0.0-3.5] | <0.0001 | <0.0001 | 0.0009 | 0.11 |

Tab 1 : Median distribution of metabolic and inflammatory parameters in healthy controls, obese non diabetic and FPLD patients.

| | HC ⁽¹⁾ | [Q ₀ , Q ₃] | OND ⁽²⁾ | [Q ₀ , Q ₃] | FPLD ⁽³⁾ | [Q ₀ , Q ₃] | P ₁₊₂₊₃ [†] | P _{1/2} [*] | P _{1/3} [*] | P _{2/3} [*] |
|--|-------------------|------------------------------------|--------------------|------------------------------------|---------------------|------------------------------------|---------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Fat mass (DEXA) | | | | | | | | | | |
| Total fat mass (%) | 22.7 | [20-30.7] | 45.4 | [43.9-48.9] | 20.75 | [16.75-28.15] | <0.0001 | <0.0001 | 0.99 | <0.0001 |
| Fat mass/height ² (g/m ²) | 0.52 | [0.43-0.87] | 1.78 | [1.64-2.02] | 0.58 | [0.34-0.65] | <0.0001 | <0.0001 | 1.000 | <0.0001 |
| Lean mass (DEXA) | | | | | | | | | | |
| Lean Mass (%) | 73.38 | [66-76.4] | 52.4 | [48.75-54.25] | 75.66 | [68.55-79.88] | <0.0001 | <0.0001 | 0.99 | <0.0001 |
| Lean mass/height ² (g/m ²) | 1.64 | [1.5-1.8] | 2.06 | [1.91-2.2] | 1.8 | [1.7-2.13] | <0.0001 | <0.0001 | 0.08 | 0.07 |
| Total fat mass/ total lean mass | 0.31 | [0.26-0.5] | 0.87 | [0.81-1] | 0.29 | [0.21-0.44] | <0.0001 | <0.0001 | 1.000 | <0.0001 |
| Abdominal fat mass (MRI) | | | | | | | | | | |
| Total abdominal fat mass (cc) | 276 | [166-374] | 833 | [711.5-937.5] | 216.5 | [153.5-310.5] | <0.0001 | <0.0001 | 1.000 | <0.0001 |
| Intra abdominal fat mass (cc) | 50 | [21-92] | 182.5 | [122.5-336] | 124.5 | [65-164.5] | 0.0002 | 0.0006 | 0.03 | 0.13 |
| Intra abdominal fat mass/ Total abdominal fat mass (g/m ²)/ (cc) | 0.2 | [0.11-0.3] | 0.25 | [0.15-0.33] | 0.57 | [0.46-0.7] | 0.0001 | 0.74 | 0.0006 | 0.0075 |
| Lean mass/height ² / intra abdominal fat mass (g/m ²)/ (cc) | 0.03 | [0.02-0.07] | 0.01 | [0.01-0.02] | 0.02 | [0.01-0.02] | 0.0005 | 0.0015 | 0.04 | 0.1 |
| Lean mass/height ² / total abdominal fat mass (g/m ²)/ (cc) | 0.006 | [0.004-0.010] | 0.002 | [0.002-0.003] | 0.009 | [0.006-0.012] | <0.0001 | <0.0001 | 0.36 | <0.0001 |

Tab 2 : Median distribution of anthropometrical parameters in healthy controls, obese non diabetic and FPLD patients.

| | r | p |
|--|---------|----------|
| Weight (kg) | + 0,386 | 0,005 |
| BMI (kg/m ²) | + 0,453 | 0,0008 |
| Fasting blood glucose (g/l) | + 0,330 | 0,017 |
| Fasting blood insulin (g/l) | + 0,421 | 0,002 |
| Hemoglobin A1c (%) | + 0,349 | 0,012 |
| SGPT (U/L) | + 0,333 | 0,016 |
| Total cholesterol (g/l) | + 0,397 | 0,0039 |
| Triglycerides (g/l) | + 0,494 | 0,0002 |
| Lean mass/height ² (g/m ²) - DEXA | + 0,517 | < 0,0001 |
| IA fat mass (cc) - MRI | + 0,349 | 0,017 |
| IA fat mass/TA fat mass - MRI | + 0.39 | 0.0069 |

Tab 3 : Correlation between irisin and metabolic, inflammatory and anthropometrical markers IA = intra-abdominal, TA= total abdominal

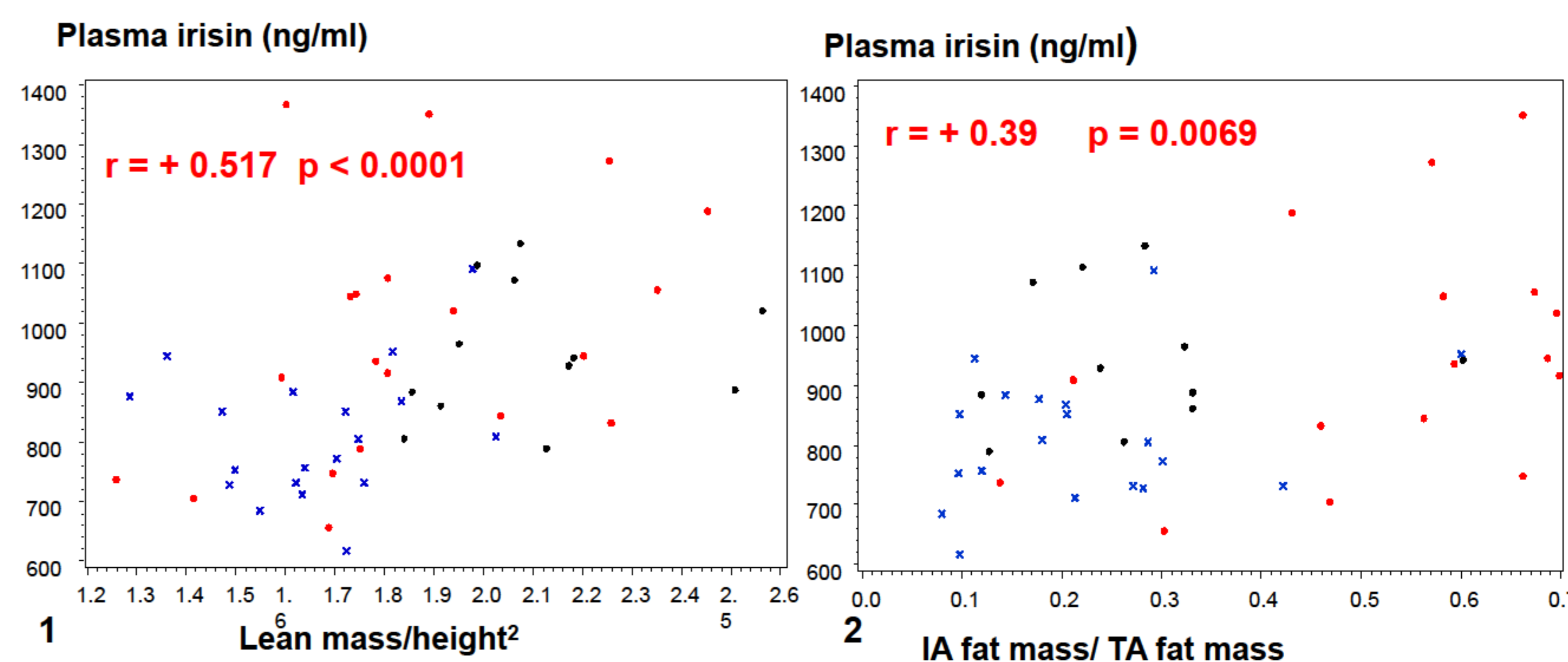


Fig 1 : Correlation of irisin and LEFT lean mass/height² in the whole population and RIGHT IA / TA fat mass, HC, OND, FPLD

CONCLUSION Compared to control, FPLD is characterized by high irisinemia and similar leptinemia, OND by both high leptinemia and irisinemia. Irisin is increased in diseases characterized by higher lean mass whatever the amount of fat mass.

