

# Serum IRAP: a novel biomarker for the diagnosis of insulin-resistance

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## Introduction

- Insulin resistance (IR) affects more than half of the adult population ( $> 250 \times 10^6$ ) worldwide.
- IR when not treated evolves to Type 2 diabetes
- Type 2 diabetes (T2D) affects  $> 425$  million people
- T2D represents  $> 10\%$  of the health budget in industrialized countries and approximately  $750 \times 10^9$  \$ worldwide.
- 30% - 75% of T2D cases ( $> 250 \times 10^6$ ) are undiagnosed**

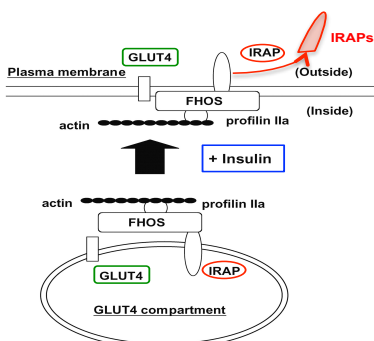
A preventive public health policy is urgently needed in order to stop this constantly progressing epidemic. Indeed, early management of IR does not only strongly reduce its evolution towards T2D but also strongly reduces the appearance of cardiovascular comorbidity as well as that of associated cancers.

**Currently there is however no simple and reliable test available for the diagnosis or screening of IR nor T2D**

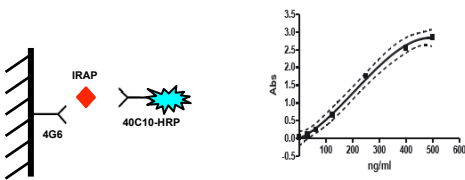
- We developed a highly sensitive and specific ELISA for the quantitative determination of a novel circulating biomarker of IR: **IRAP**
- IRAP is associated with and translocated with GLUT4 to the plasma membrane in response to insulin in skeletal muscle and adipose tissue.
- Its extracellular domain (IRAPs) is subsequently cleaved and secreted in the blood stream.
- In T2D IRAP translocation in response to insulin is strongly decreased.**

**Serum IRAP may therefore be a direct marker of insulin sensitivity and its determination may thus allow large-scale screening of populations at risk for IR and T2D**

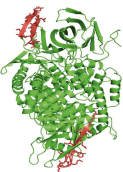
## Principle & Methods



Upon stimulation by insulin, IRAP is translocated to the plasma membrane along with GLUT4, cleaved and secreted in the bloodstream

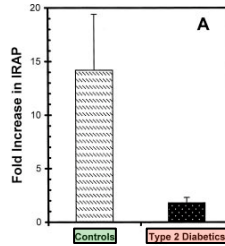


IRAP ELISA: principle and standard curve. Anal. sensitivity: 10 ng/ml  
Reference values (young healthy indiv.):  $101.4 \pm 15.9$   $\mu\text{g/ml}$



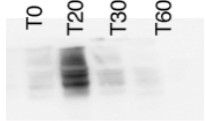
Structure of the extracellular domain of IRAP targeted epitopes in red

## Results

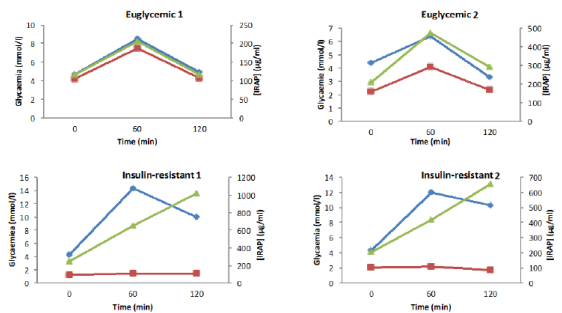


**In T2D adipocytes, IRAP translocation in response to insulin is reduced 7-fold**

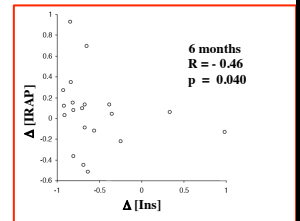
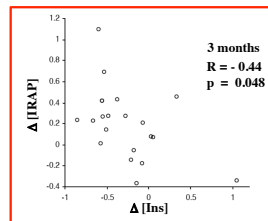
Maianu L et al.: J Clin Endocrinol Metab 2001



**Serum IRAP kinetics in response to insulin in an euglycemic patient**



**Glycemia, insulinemia and serum IRAP during an OGTT in euglycemic and insulin-resistant patients**



**Changes (x 100) in [IRAP] vs. changes in insulinemia after bariatric surgery:**  
 $\Delta[\text{IRAP}] \approx \text{insulin sensitivity}$

## Conclusions

### Advantages of IRAP ELISA

- Simple and robust assay
- Cheap
- Highly specific and sensitive ( $10,000 \times \text{Vref}$ )
- Low dispersion of Vref ( $101.4 \pm 15.9$ ) as compared to insulinemia
- (21 – 181 pM) and C-peptide (0.4 – 1.7 nM)
- Very stable
- Low sample (serum or plasma) volume: 20  $\mu\text{l}$
- First direct biomarker of insulin sensitivity**
- Easy to interpretate**

### Potential indications

- Screening, diagnosis and follow-up of:
  - IR/prediabetes
  - Metabolic syndrome
  - T2D
  - Gestational diabetes