Los Trabajos Fin de Grado académicamente dirigidos

Trabajos experimentales:
capítulos de que consta y forma
de presentación de los resultados

Estructura

Estos proyectos deben incluir siempre la siguiente estructura (conviene incluirlos como índice):

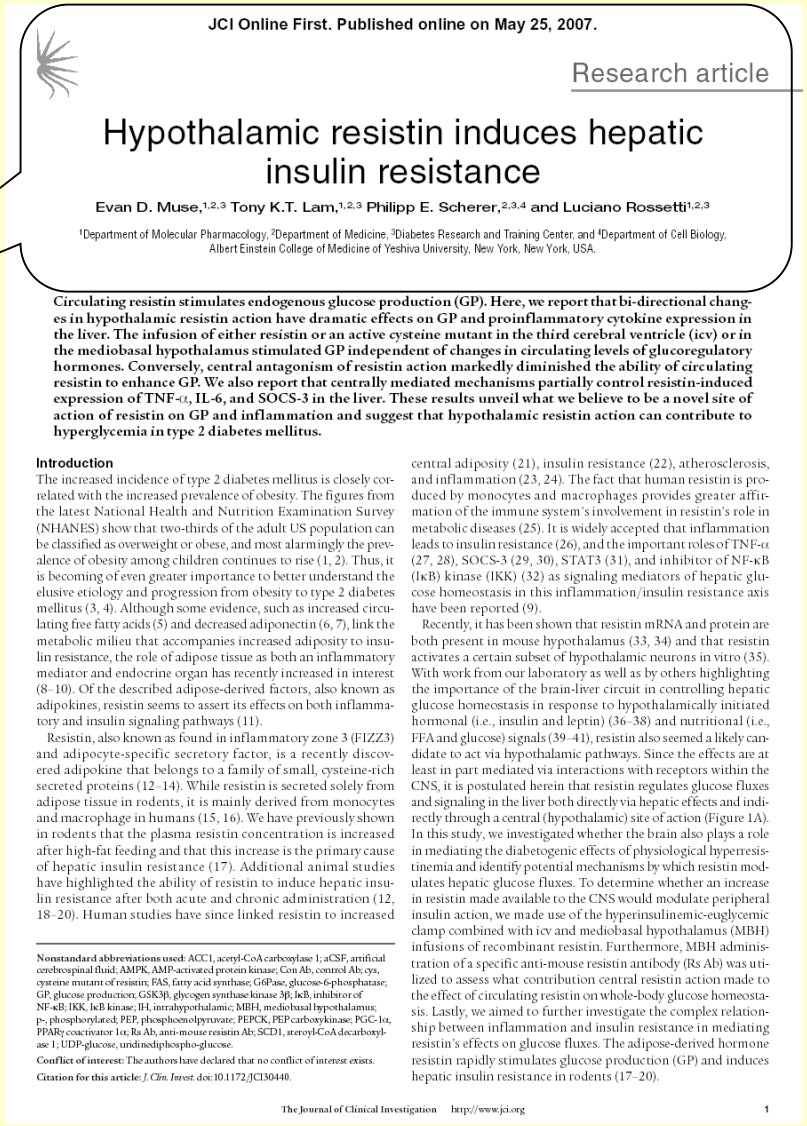
- **Título**
- **Resumen**
- **Introducción**
- **Materiales y Métodos**
- **Resultados**
- **Discusión**
- **Bibliografía**

TITULO: debe ser suficientemente explicativo del contenido del trabajo

El título contiene en realidad tres partes:

1. **El título propiamente dicho**
2. **Los autores**
3. **La institución en la que se ha realizado el trabajo**

Para el caso del TFG, y tal como se sugiere en las instrucciones, debe omitirse el laboratorio en el que se ha realizado, y aparecer un único autor.



JCI Online First. Published online on May 25, 2007.

Research article

Hypothalamic resistin induces hepatic insulin resistance

Evan D. Muse,[1,2,3] Tony K.T. Lam,[1,2,3] Philipp E. Scherer,[2,3,4] and Luciano Rossetti[1,2,3]

[1]Department of Molecular Pharmacology, [2]Department of Medicine, [3]Diabetes Research and Training Center, and [4]Department of Cell Biology, Albert Einstein College of Medicine of Yeshiva University, New York, New York, USA.

Circulating resistin stimulates endogenous glucose production (GP). Here, we report that bi-directional changes in hypothalamic resistin action have dramatic effects on GP and proinflammatory cytokine expression in the liver. The infusion of either resistin or an active cysteine mutant in the third cerebral ventricle (icv) or in the mediobasal hypothalamus stimulated GP independent of changes in circulating levels of glucoregulatory hormones. Conversely, central antagonism of resistin action markedly diminished the ability of circulating resistin to enhance GP. We also report that centrally mediated mechanisms partially control resistin-induced expression of TNF-α, IL-6, and SOCS-3 in the liver. These results unveil what we believe to be a novel site of action of resistin on GP and inflammation and suggest that hypothalamic resistin action can contribute to hyperglycemia in type 2 diabetes mellitus.

Introduction

The increased incidence of type 2 diabetes mellitus is closely correlated with the increased prevalence of obesity. The figures from the latest National Health and Nutrition Examination Survey (NHANES) show that two-thirds of the adult US population can be classified as overweight or obese, and most alarmingly the prevalence of obesity among children continues to rise (1, 2). Thus, it is becoming of even greater importance to better understand the elusive etiology and progression from obesity to type 2 diabetes mellitus (3, 4). Although some evidence, such as increased circulating free fatty acids (5) and decreased adiponectin (6, 7), link the metabolic milieu that accompanies increased adiposity to insulin resistance, the role of adipose tissue as both an inflammatory mediator and endocrine organ has recently increased in interest (8–10). Of the described adipose-derived factors, also known as adipokines, resistin seems to assert its effects on both inflammatory and insulin signaling pathways (11).

Resistin, also known as found in inflammatory zone 3 (FIZZ3) and adipocyte-specific secretory factor, is a recently discovered adipokine that belongs to a family of small, cysteine-rich secreted proteins (12–14). While resistin is secreted solely from adipose tissue in rodents, it is mainly derived from monocytes and macrophage in humans (15, 16). We have previously shown in rodents that the plasma resistin concentration is increased after high-fat feeding and that this increase is the primary cause of hepatic insulin resistance (17). Additional animal studies have highlighted the ability of resistin to induce hepatic insulin resistance after both acute and chronic administration (12, 18–20). Human studies have since linked resistin to increased central adiposity (21), insulin resistance (22), atherosclerosis, and inflammation (23, 24). The fact that human resistin is produced by monocytes and macrophages provides greater affirmation of the immune system's involvement in resistin's role in metabolic diseases (25). It is widely accepted that inflammation leads to insulin resistance (26), and the important roles of TNF-α (27, 28), SOCS-3 (29, 30), STAT3 (31), and inhibitor of NF-κB (IκB) kinase (IKK) (32) as signaling mediators of hepatic glucose homeostasis in this inflammation/insulin resistance axis have been reported (9).

Recently, it has been shown that resistin mRNA and protein are both present in mouse hypothalamus (33, 34) and that resistin activates a certain subset of hypothalamic neurons in vitro (35). With work from our laboratory as well as by others highlighting the importance of the brain-liver circuit in controlling hepatic glucose homeostasis in response to hypothalamically initiated hormonal (i.e., insulin and leptin) (36–38) and nutritional (i.e., FFA and glucose) signals (39–41), resistin also seemed a likely candidate to act via hypothalamic pathways. Since the effects are at least in part mediated via interactions with receptors within the CNS, it is postulated herein that resistin regulates glucose fluxes and signaling in the liver both directly via hepatic effects and indirectly through a central (hypothalamic) site of action (Figure 1A). In this study, we investigated whether the brain also plays a role in mediating the diabetogenic effects of physiological hyperresistinemia and identify potential mechanisms by which resistin modulates hepatic glucose fluxes. To determine whether an increase in resistin made available to the CNS would modulate peripheral insulin action, we made use of the hyperinsulinemic-euglycemic clamp combined with icv and mediobasal hypothalamus (MBH) infusions of recombinant resistin. Furthermore, MBH administration of a specific anti-mouse resistin antibody (Rs Ab) was utilized to assess what contribution central resistin action made to the effect of circulating resistin on whole-body glucose homeostasis. Lastly, we aimed to further investigate the complex relationship between inflammation and insulin resistance in mediating resistin's effects on glucose fluxes. The adipose-derived hormone resistin rapidly stimulates glucose production (GP) and induces hepatic insulin resistance in rodents (17–20).

Nonstandard abbreviations used: ACC1, acetyl-CoA carboxylase 1; aCSF, artificial cerebrospinal fluid; AMPK, AMP-activated protein kinase; Con Ab, control Ab; cys, cysteine mutant of resistin; FAS, fatty acid synthase; G6Pase, glucose-6-phosphatase; GP, glucose production; GSK3β, glycogen synthase kinase 3β; IκB, inhibitor of NF-κB; IKK, IκB kinase; IH, intrahypothalamic; MBH, mediobasal hypothalamus; p-, phosphorylated; PEP, phosphoenolpyruvate; PEPCK, PEP carboxykinase; PGC-1α, PPARγ coactivator 1α; Rs Ab, anti-mouse resistin Ab; SCD1, steroyl-CoA decarboxylase 1; UDP-glucose, uridinediphospho-glucose.

Conflict of interest: The authors have declared that no conflict of interest exists.

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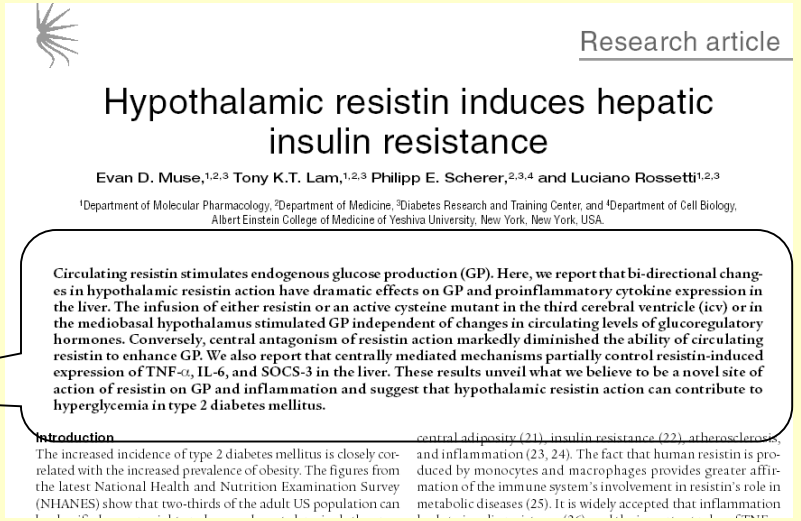
RESUMEN

Se trata de una descripción breve del objeto del trabajo, los métodos empleados y los principales resultados y conclusiones alcanzados. (Conviene consultar artículos para hacerse una idea de lo que es un resumen)



Research article

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Suelen ser 8 o 10 frases con un máximo de 300 palabras.

INTRODUCCION

Debe incluir:

1.- ¿Qué se va a estudiar?

2.- ¿Qué se sabe y qué no se sabe

3.- Abundante bibliografía que documente lo que se afirme sobre el tema

4.- Es muy importante resaltar los objetivos del estudio, incluso en una sección específica

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En esta primera página vemos que aparecen las abreviaturas empleadas. En el TFG deberían incluirse al principio, antes incluso del resumen o abstract.

MATERIALES Y METODOS

Aquí deben describirse:

1. **Si se han empleado modelos animales, vegetales o celulares, han de describirse al principio de este apartado**
2. **Si se han realizados estudios en campo, la descripción del área y de los muestreos**
3. **Las técnicas empleadas**
4. **Los reactivos y aparatos utilizados indicando el proveedor (recomendado)**
5. **Los métodos han de describirse con detalle a excepción de técnicas muy conocidas. Es importante aportar referencias bibliográficas en las que se haga la descripción original o adaptada de una determinada técnica**
6. **No olvidar el mencionar los métodos estadísticos empleados**

RESULTADOS

En este apartado se describen todos los datos obtenidos durante el desarrollo del proyecto.

No es preciso introducir muchas referencias bibliográficas en esta sección puesto que es una simple descripción de resultados.

Los datos se presentan por lo general en forma de Tablas y Figuras. Tanto unas como otras deben ir acompañadas de un pie de Tabla o pie de Figura, que debe ser explicativo en sí mismo, es decir, los datos deben poder entenderse observando la figura y leyendo el pie de figura.

En el texto debe hacerse mención a todas las figuras y tablas.

FORMAS DE REPRESENTAR DATOS

TABLA

Contiene un título e información sobre el análisis estadístico empleado

Table 1 Characteristics of the rats. Data are the mean±S.E.M. of 10–20 separate determinations

	3 months	8 months	8 months-FR	24 months	24 months-FR
Body weight (g)	383±8	511±6[a]	431±4[c]	700±12[b]	603±15[c]
Fasting plasma glucosa (mmol/l)	4·5±0·2	4·5±0·1	4·6±0·2	5·0±0·1	4·5±0·2
Fasting plasma insulin (nmol/l)	0·19±0·02	0·19±0·04	0·09±0·01[c]	0·26±0·02	0·23±0·04
Fasting plasma adiponectin (µg/ml)	3·1±0·2	2·5±0·2	4·1±0·3[c]	3·0±0·2	2·9±0·2
Fasting plasma leptin (ng/ml)	4·6±0·5	7·5±0·9[a]	2·0±0·1[c]	27·6±4·0[b]	7·1±1·2[c]
Fasting plasma resistin (ng/ml)	18·0±2·5	32·2±2·1[a]	17·3±1·0[c]	23·2±1·7[d]	24·7±1·6

One-way ANOVA indicates a significant effect of age on body weight ($P=0·001$), plasma leptin ($P=0·001$) and resistin ($P=0·0002$), and no significant effect on plasma adiponectin, glucose and insulin levels ($P>0·05$). [a]$P<0·05$ versus 3-month-old rats; [b]$P<0·05$ versus 3- and 8-month-old rats; [c]$P<0·05$ versus same age fed *ad libitum*; [d]$P<0·05$ versus 8-month-old rats. FR, food restricted.

DIAGRAMAS DE CORRELACIÓN DE VARIABLES

Se presentan en forma de nube de puntos los valores correspondientes a dos variables para una población. Se incluye la estadística referente al coeficiente de correlación, la significatividad de la misma, etc..

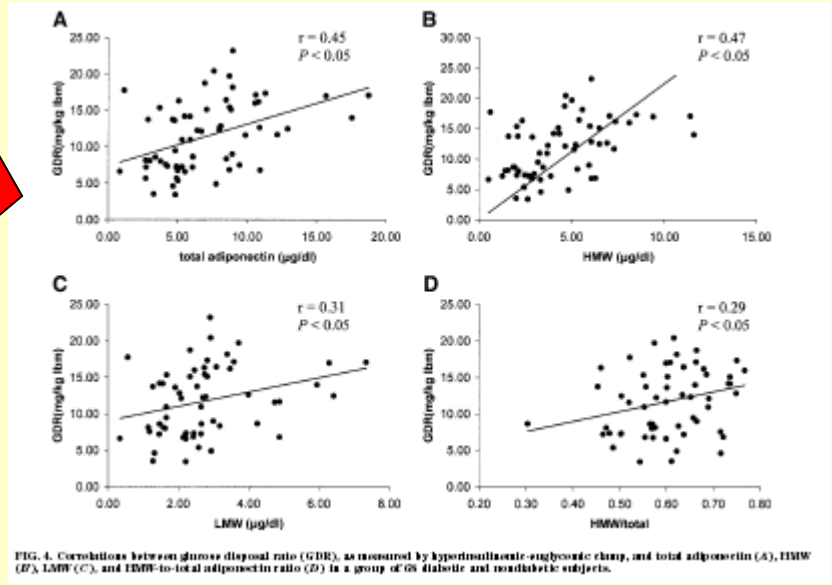


FIG. 4. Correlations between glucose disposal rate (GDR), as measured by hyperinsulinemic-euglycemic clamp, and total adiponectin (*A*), HMW (*B*), LMW (*C*), and HMW-to-total adiponectin ratio (*D*) in a group of 68 diabetic and nondiabetic subjects.

FORMAS DE REPRESENTAR DATOS (II)

HISTOGRAMAS

Incluye un pie de figura con información estadística relativa al error de cada variable y a la significatividad de las diferencias entre dos ó más valores

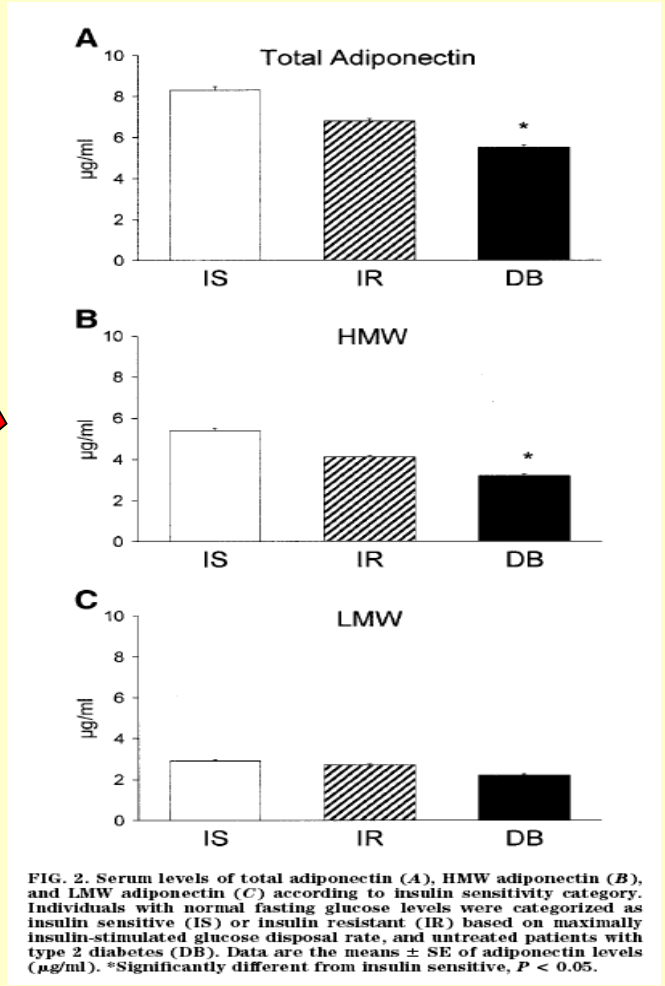
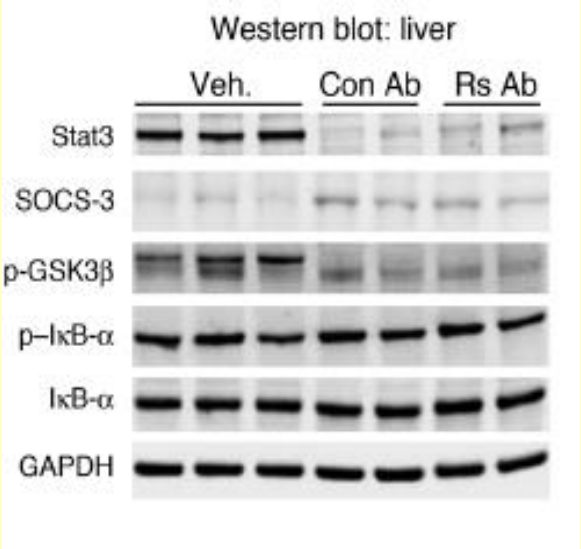


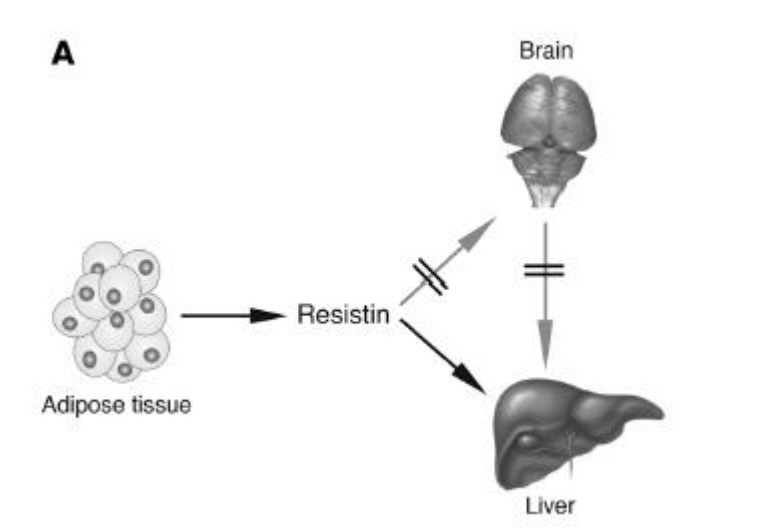
FIG. 2. Serum levels of total adiponectin (*A*), HMW adiponectin (*B*), and LMW adiponectin (*C*) according to insulin sensitivity category. Individuals with normal fasting glucose levels were categorized as insulin sensitive (IS) or insulin resistant (IR) based on maximally insulin-stimulated glucose disposal rate, and untreated patients with type 2 diabetes (DB). Data are the means ± SE of adiponectin levels (µg/ml). *Significantly different from insulin sensitive, $P < 0.05$.

FORMAS DE REPRESENTAR DATOS (III)

GELES

Debe especificarse claramente qué se muestra en cada fila o columna





ESQUEMAS, FOTOGRAFÍAS

Conviene utilizar flechas o asteriscos para destacar lo que se quiere mostrar

DISCUSION

Este apartado debe incluir:

1. **La interpretación que damos de nuestros resultados**
2. **Dicha interpretación se hace siempre en un marco de referencia que es el conocimiento y los datos preexistentes**
3. **Hay que hacer énfasis en el avance que los nuevos datos suponen para el conocimiento en ese campo**
4. **La discusión debe llevar, por tanto, abundante bibliografía**
5. **Al final de la misma debe hacerse un pequeño resumen de conclusiones o un apartado de conclusiones**

BIBLIOGRAFIA

En este apartado se recogen todas las citas bibliográficas mencionadas a lo largo de la memoria.

Básicamente existen dos métodos de presentar la bibliografía:

• **Método numérico**: a cada cita se le asigna un número y dicho número se incluye en el texto cuando se menciona esa cita

[1] D. Porte Jr., R.J. Seeley, S.C. Woods, D.G. Baskin, D.P. Figlewicz, M.W. Schwartz, Obesity, diabetes and the central nervous system, Diabetologia 41 (1998) 863–881

• **Método alfabético**: las citas se introducen en el texto mencionando al autor y el año (dos autores en su caso, o un autor y col. si hay más de dos autores) y luego se ordenan en la sección bibliografía por orden alfabético.

*Baskin DG, Seeley RJ, Kuijper JL, Lok S, Weigle DS, Erickson JC, Palmiter RD & Schwartz MW 1998 Increased expression of mRNA for the long form of the leptin receptor in the hypothalamus is associated with leptin hypersensitivity and fasting. Diabetes **47** 538–543*

Esta cita en el texto se incluiría como “Baskin y col. (1998)”