

Regulation of chemokine and chemokine receptor expression by PPAR γ in adipocytes and macrophages

Mt Nguyen, Ai Chen, Wendell Lu, Wuqiang Fan, Ping-Ping Li, Dayoung Oh,
David Patsouris

► **To cite this version:**

Mt Nguyen, Ai Chen, Wendell Lu, Wuqiang Fan, Ping-Ping Li, et al.. Regulation of chemokine and chemokine receptor expression by PPAR γ in adipocytes and macrophages. 6th european workshop on immune-mediated inflammatory diseases, Nice, France. BioMed Central, 9 (Suppl 2), pp.P23, 2011. <inserm-00643974>

HAL Id: inserm-00643974

<http://www.hal.inserm.fr/inserm-00643974>

Submitted on 23 Nov 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



POSTER PRESENTATION

Open Access

Regulation of chemokine and chemokine receptor expression by PPAR γ in adipocytes and macrophages

MT Audrey Nguyen^{1†}, Ai Chen^{1†}, Wendell J Lu¹, WuQiang Fan¹, Ping-Ping Li¹, Dayoung Oh¹, David Patsouris^{1,2*}

From 6th European Workshop on Immune-Mediated Inflammatory Diseases
Nice, France. 23-25 November 2011

Background

PPAR γ plays a key role in adipocyte biology, and Rosiglitazone (Rosi), a thiazolidinedione (TZD)/ PPAR γ agonist, is a potent insulin-sensitizing agent [1-3]. Recent evidences demonstrate that adipose tissue inflammation links obesity with insulin resistance and that the insulin-sensitizing effects of TZDs result, in part, from their anti-inflammatory properties [4,5]. However the underlying mechanisms are unclear. Free Fatty Acids (FFAs) are important adipocyte-derived signaling molecules whose plasma levels are elevated in obese and insulin resistant individuals and animal models [6,7]. In this study, we establish a link between free fatty acids (FFAs) and PPAR γ in the context of obesity-associated inflammation.

Methodology and methods

We used 3T3L1 mouse cells as a model of mature adipocytes. Conditioned media were prepared from 3T3L1 mature adipocytes exposed to different conditions and subsequently used for *in vitro* chemotaxis assays with Raw264.7 mouse macrophages cells. 10 weeks old males C57Bl6 mice (littermates) were fed a high fat diet (60% Kcal fat, Research Diet) where rosiglitazone was directly mixed by manufacturer. Normal chow diet consisted of 13.5% kcal fat (Lab Diet).

Results

We show that treatment of adipocytes with FFAs down-regulates PPAR γ protein and mRNA levels. Knockdown of adipocyte PPAR γ resulted in upregulation of MCP1 gene expression and secretion, leading to enhanced macrophage chemotaxis. Rosi inhibited these effects. In a

high fat feeding mouse model, we show that Rosi treatment decreases recruitment of proinflammatory macrophages to epididymal fat. This correlates with decreased chemokine and decreased chemokine receptor expression in adipocytes and macrophages, respectively.

Conclusions

In summary, we describe a novel link between FFAs, PPAR γ , adipocytes, and adipocyte-driven recruitment of macrophages and thus provide an additional potential mechanism for the anti-inflammatory and insulin-sensitizing actions of TZDs.

Author details

¹Dept. of Medicine, University of California, San Diego, La Jolla, USA.

²Laboratoire CarMeN, INSERM U1060, Faculté de médecine Lyon Sud, Oullins, France.

Published: 23 November 2011

References

1. Semple RK, Chatterjee VK, O'Rahilly S: PPAR gamma and human metabolic disease. *J Clin Invest* 2006, **116**:581-589.
2. Kersten S, Desvergne B, Wahli W: Roles of PPARs in health and disease. *Nature* 2000, **405**:421-424.
3. Choi JH, Banks AS, Estall JL, Kajimura S, Bostrom P, Laznik D, Ruas JL, Chalmers MJ, Kamenecka TM, Bluher M, et al: Anti-diabetic drugs inhibit obesity-linked phosphorylation of PPARgamma by Cdk5. *Nature* 466:451-456.
4. Gregoire FM, Zhang F, Clarke HJ, Gustafson TA, Sears DD, Favellyukis S, Lenhard J, Rentzeperis D, Clemens LE, Mu Y, Lavan BE: MBX-102/ JNJ39659100, a novel peroxisome proliferator-activated receptor-ligand with weak transactivation activity retains antidiabetic properties in the absence of weight gain and edema. *Mol Endocrinol* 2009, **23**:975-988.
5. Ruan H, Pownall HJ, Lodish HF: Troglitazone antagonizes tumor necrosis factor-alpha-induced reprogramming of adipocyte gene expression by inhibiting the transcriptional regulatory functions of NF-kappaB. *J Biol Chem* 2003, **278**:28181-28192.
6. Shi H, Kokoeva MV, Inouye K, Tzameli I, Yin H, Flier JS: TLR4 links innate immunity and fatty acid-induced insulin resistance. *J Clin Invest* 2006, **116**:3015-3025.

† Contributed equally

¹Dept. of Medicine, University of California, San Diego, La Jolla, USA
Full list of author information is available at the end of the article

7. Schenk S, Saberi M, Olefsky JM: **Insulin sensitivity: modulation by nutrients and inflammation.** *J Clin Invest* 2008, **118**:2992-3002.

doi:10.1186/1479-5876-9-S2-P23

Cite this article as: Nguyen *et al.*: Regulation of chemokine and chemokine receptor expression by PPARG in adipocytes and macrophages. *Journal of Translational Medicine* 2011 **9**(Suppl 2):P23.

**Submit your next manuscript to BioMed Central
and take full advantage of:**

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit

