DIFFERENTIAL REGULATION OF RESISTIN GENE EXPRESSION BY ROSIGLITAZONE IN DIFFERENT CELL LINES

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The resistin, a new adipocyte hormone, has been proposed to link obesity to type 2 diabetes by modulating steps in the insulin-signaling pathway and inducing insulin resistance.
Thiazolidinedione (TZD), a new class of antidiabetic drugs, regulate gene expression by binding to peroxisome proliferator-activated receptor ã, a nuclear hormone receptor found at its highest levels in adipocytes.
Since the expression of resistin is inhibited by thiazolidinedione in 3T3-L1 adipocytes, it has been suggested that peroxisome proliferator-activated receptor ã (PPAR-ã) agonists induce an increase of insulin sensitivity through a decrease of resistin gene expression. Successively, others authors showed a stimulatory effect *in vivo* of TZD on the resistin expression. Therefore, the role of resistin to induce insulin resistance has been called in question.
To clarify the resistin functional role, we have study its expression after rosiglitazone treatment in different cell lines, whether cells from primary cultures or cell lines. In particular, we have used 3T3-L1 cells, white adipocytes isolated enzymaticaly from mice epididimal fat and mouse preadipocytes differentiated in culture. Furthermore, we have verify the resistin expression in mononuclear cells, either in cell lines (RAW 264.7 and U 937) or in mononuclear primary cells of human peripheral blood (HPBMC). Using RT-PCR amplification and Northern Blot analysis, we verify in 3T3-L1 that a rosiglitazone treatment of 18h at 10ìM inhibits by 40% resistin expression. In white adipocytes isolated enzymaticaly and preadipocytes differentiated in culture, the same treatment induces, on the contrary, an increase by 50% of resistin expression. In the mononuclear cells (HPBMC, RAW 264.7 and U937), where the resistin is expressed, this treatment seems to have no effect on the mRNA levels.
Our results suggest, therefore, that resistin is regulated differently by TZD according to the cellular type analysed.
In conclusion, these results may explain in part controversial dates reported so far in the literature but further studies are needed to determine the mode of regulation and biological functions of resistin.

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3T3-L1	- 40%
White adipocytes isolated enzymaticaly	+ 48%
Preadipocytes differentiated in culture	+ 50%
RAW 264.7, U937 and HPBMC	=