Alendronate inhibits adipocyte differentiation in 3T3-L1 through a Vitamin D3 mediated effect

ALN displayed a marked anti-adipogenic effect as shown by a significant reduction in number and size of differentiation foci in 3T3-L1 preadipocytes. Such effect was not dose-dependent. For this reason we kept using 10^-8 M of ALN as also currently used in literature. On the other hand VD3 showed a clear dose-dependent effect in the inhibition of adipocyte differentiation. Interestingly co-incubation of 10^-8 M of ALN and 10^-9 M of VD3 did not show synergic effect in the inhibition of adipogenesis.

To confirm this hypothesis, we explored the effects of ALN and VD3 in a different pre-adipocyte murine model (3T3-F44). These cells are in a more advanced differentiation stage in adipogenesis, compared to 3T3-L1. Of relevance, the expression of VDR mRNA is much lower than in 3T3-L1 cells. For this reason 3T3-F44 cells represent a suitable model to validate the role of VDR in mediating effects of ALN.

Interestingly adipocyte differentiation in this cell was not affected by ALN nor VD3 differently to what was observed in 3T3-L1 cells. This represents an indirect evidence of the important role of VDR in mediating the anti-adipogenic effect of ALN.

We analyzed through RT-PCR the effect of 7 days treatment with ALN and VD3 upon mRNA expression of main molecular markers of adipocyte differentiation, PPARγ and C/EBPα and VD3 Receptor (VDR). As expected PPARγ mRNA expression was significantly reduced by ALN and VD3, whereas co-incubation with ALN (10^-8 M) and VD3 (10^-9 M) did not display a significant effect. Differently mRNA expression of C/EBPα was reduced only by the highest doses of VD3, and not by ALN. Interestingly we observed a concomitant parallel increase in VDR mRNA expression in the presence of ALN and VD3, suggesting that VDR may represent the molecular target of the anti-adipogenic effect of ALN.