ALLERGY, VITAMINS

TOLEROGENIC EFFECTS OF VITAMIN D?

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A new allergy study published last month

hypothesized that prenatal vitamin D supplementation could induce tolerogenic DC at birth. To evaluate this hypothesis in an epidemiological setting, we quantiï¬ed the gene expression levels of ILT3 and ILT4 in cord blood (CB) samples of a population-based birth cohort of farm and reference children. ed the gene expression levels of ILT3 and ILT4 in cord blood (CB) samples of a population-based birth cohort of farm and reference children.

ILT3/IL4 as a marker of tolerogenic DCs may be justified by data published by Chang but not by newer data published by Adorini who

found that incubation of monocyte-derived human DCs, either immature or during maturation, with 1,25(OH)2D3 leads to a selective upregulation of ILT3 (three- to six-fold increase in MFI), but not of ILT1 or ILT4 (…), nor ILT2 or ILT5.

ILT3 and ILT4 is expressed on the surface of monocytes, macrophages, and dendritic cells acting as an inhibitory receptor through recruitment of SHP-1/2 on HLA-A, -B. So these are not very specific for DCs although such marker would have been available

Human DCs were generated from peripheral blood monocytes in the presence of 1alpha,25-dihydroxyvitamin D(3) (VD3), which gave rise to a phenotype that resembles immature DCs, with the exception of high CD14 and reduced CD1a on the cell surface. These VD3-treated DCs exert a long-lasting inefficient T cell stimulation and induce T cell hyporesponsiveness with regulatory potential. Importantly, such VD3-treated DCs were readily distinguishable from untreated DCs by low levels of interleukin-23 secretion and low expression of miR-155.

Results of the allergy study above are therefore difficult to interpret in particular as results are only borderline significant for ILT4. Furthermore any putative D3 effect on DCs would not come isolated with the main effector being the T cell

> We observed that stimulation of CD4(+)CD25(-) T cells in the presence of 1,25(OH)(2)D(3) inhibited production of proinflammatory cytokines including IFN- gamma, IL-17, and IL-21.

which is allergenic and not tolerogenic at all. We may close the circle here with a study ~~intenionally~~ not mentioned in the discussion – on maternal vitamin D status during pregnancy and child outcomes

> Children whose mothers had a 25(OH)-vitamin D concentration in pregnancy >75 nmol/l had an increased risk of eczema on examination at 9 months (OR 3.26, 95% CI 1.15â€“9.29, P=0.025) and asthma at age 9 years (OR 5.40, 95% CI, 1.09â€“26.65, P=0.038) compared to children whose mothers had a concentration of <30 nmol/l.

– more or less the opposite of what the new allergy study wants to show. To summarize

- although an overall tolerogenic effect of vitamin D on dendritic cells is plausible from in vitro experiments, there is poor evidence that this may be the case in vivo.
- it is unclear how any tolerogenic DCs relate to common allergens.
- the study above fails to show any major ILT3 upregulation, however, this may be not the best marker of vitamin D exposed DCs.
- the weak effects on ILT4 mRNA do not tell if this will lead to any Th1 or Th2 bias in the newborn

which leads finally to the conclusion that this paper does not contain any relevant information, yea, yea.