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A molecular model of the interaction between vitamin D binding protein-derived macrophage activating factor and vitamin D receptor

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We previously demonstrated that the response of human monocytes to vitamin D binding protein-derived macrophage activating factor (DBP-MAF) is dependent on vitamin D receptor (VDR) polymorphisms [1]. Therefore, in order to verify the type of molecular interaction between DBP-MAF and VDR, we compared the amino acid sequences at their respective vitamin D binding sites. There are 23 hydrophobic amino acids (aa) near the amino terminus of DBP-MAF, and 23 aa near the carboxyl terminus of VDR. When these two sequence are aligned, it is possible to observe not only that in both proteins there is a long stretch (13-14) of hydrophobic aa, but that 4 hydrophobic aa are identical and 11 aa have similar functional valence. According to this model, the last 23 hydrophobic aa of VDR, located at the inner part of the plasma membrane, interact with the first 23 hydrophobic aa of the DBP-MAF located at the external part of the plasma membrane, with vitamin D sandwiched in between the two vitamin D-binding proteins. Oleic acid, taken as an example of an unsaturated fatty acid bound to DBP-MAF, could stabilize the complex at the level of the plasma membrane. Therefore, it can be hypothesized that DBP-MAF and VDR have multiple sites of interaction at the level of the plasma membrane. Further studies will elucidate whether this interaction occurs only in the presence of vitamin D or whether the hydrophobic profile of the two proteins allows direct interaction without the need for vitamin D.

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References

[1] Pacini et al. (2012) Effect of paricalcitol and GcMAF on angiogenesis and human peripheral blood mononuclear cell proliferation and signaling. J Nephrol 25: 577-81.

Key words
Vitamin D, macrophages, vitamin D receptor, vitamin D binding protein-derived macrophage activating factor.