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Letter to the Editor

Response from Chapkin to Letter from Boucher

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Among the different nuclear receptors, there is some evidence that PPAR and vitamin D receptors (VDR) are targets for fatty acids. However, these nuclear receptors bind *n*-3 and *n*-6 PUFA with equal affinity and appear to lack fatty acid class specificity[1]. Therefore, the unique protective effects of *n*-3 PUFA are probably not directly mediated by PPAR or VDR. Interestingly, we have demonstrated that retinoid X receptors (RXR), an obligatory component of various nuclear receptors (including VDR), preferentially bind *n*-3 PUFA in colonocytes, and that the nuclear receptor targets for PUFA in the colon are modulated by dietary lipid exposure[2]. This raises the possibility that selected *n*-3 PUFA (e.g. DHA) mediate growth inhibitory/anti-inflammatory effects in the colon through the RXR subunit of nuclear receptor heterodimers. Additional studies are required in order to identify the genes that are immediate responders to this class of activated receptors.

Regarding the potential for curcumin to bind VDR, although curcumin can compete with 1,25-dihydroxy vitamin D binding to VDR and transactivate 1,25-dihydroxy vitamin D target genes in a colonic cell line[3], to date, *in vivo* validation of this hypothesis is lacking. The effects of curcumin could be examined in tissue-specific VDR knockout mice in order to definitively assess the role of VDR in mediating colon-cancer chemoprevention.

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References

1. Haussler MR, Haussler CA, Bartik L, *et al.* (2009) Vitamin D receptor: molecular signalling and actions of nutritional ligands in disease prevention. *Nutr Rev* **66**, S98–S112.
2. Fan YY, Spencer T, Wang N, *et al.* (2003) Chemopreventive *n*-3 fatty acids activate RXRα in colonocytes. *Carcinogenesis* **24**, 1541–1548.
3. Bartik L, Whitfield GK, Kaczmarska M, *et al.* (2010) Curcumin: a novel nutritionally derived ligand of the vitamin D receptor with implications for colon cancer chemoprevention. *J Nutr Biochem* **21**, 1153–1161.

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