Response to J.W. Pike by C.M. Girgis, N. Mokbel, K.M. Cha, P.J. Houweling, M. Abboud, D.R. Fraser, R.S. Mason, R.J. Clifton-Bligh, and J.E. Gunton.

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Response to Counterpoint on: "The Vitamin D Receptor (VDR) is Expressed in Murine Skeletal Muscle and Modulates 25-Hydroxyvitamin D (25OHD) Uptake in Myofibers"

Christian M. Girgis, Nancy Mokbel, Kuan Minn Cha, Peter J. Houweling, Myriam Abboud, David R. Fraser, Rebecca S. Mason, Roderick J. Clifton-Bligh,
Jenny E. Gunton

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We thank Professor Bouillon for his comments in the "News and Views" and Professor Pike for his comments above. We agree that clear detection of VDR in skeletal muscle has been controversial due to a number of technical factors including protein extraction methods, variability in different muscle models, past problematic antibodies and of course, the low level of VDR that is present in mature muscle at baseline. Our work shows clear absence of VDR in VDR knockout mice by immunohistochemistry and Western blotting, and perhaps more importantly, conclusive proof of functional presence comes with the demonstration of a novel physiological function, specifically the VDR-mediated uptake of 25-hydroxyvitamin D in muscle fibers (i.e. non-genomic as indicated by inhibition using the chloride-channel blocker DIDS). We agree that the substantially higher levels of VDR in muscle of younger mice and immature muscle cells is intriguing; this suggests the possibility for a pleiotropic role for VDR in muscle and its potential activation following muscle injury from relatively low baseline levels of expression. We hope the findings of our study bring some closure to this controversial field and may assist in future work examining roles of VDR in muscle development, regeneration and 25-OHD uptake, ultimately justifying the generation of a skeletal muscle-specific VDR knockout model.