

## CORRESPONDENCE



## Wnt Signaling and Dupuytren's Disease

**TO THE EDITOR:** Dolmans et al. (July 28 issue)<sup>1</sup> report significant associations between susceptibility to Dupuytren's disease and genetic markers implicating *WNT2*, *WNT4*, and *WNT7B*. It seems feasible that variant Wnt signaling critically enhances risk by altering immunologic processes that have critical cell-fate decisions in Dupuytren's disease. For example, *WNT4* can activate a non-canonical calcium–WNT pathway that differentially modulates hematopoietic stem cells and progenitor T cells.<sup>2</sup> *WNT4* also induces thymopoiesis by expanding FMS-like tyrosine kinase 3–positive lymphoid-primed multipotent progenitors in bone marrow. Studies have implicated Wnt proteins as regulatory molecules in various immunologic processes such as B-cell and T-cell development, maturation, and activation.<sup>3</sup> In fact, the activation of T cells, B cells, and innate cells is a common feature of Dupuytren's disease.<sup>4,5</sup> We propose that the presence of “susceptibility” WNT variants confers a risk of disease through enhanced T-cell and B-cell activation, rather than through the WNT canonical pathway.

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No potential conflict of interest relevant to this letter was reported.

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**THE AUTHORS REPLY:** Balaji et al. hypothesize that variant Wnt signaling contributes to Dupuytren's disease through its involvement in innate and adaptive immunity, rather than through the canonical pathway. They correctly point out that our data support functional studies that do not focus solely on the canonical pathways. However, we were unable to detect gene-expression levels of most of the implicated “WNT-relevant” genes in whole blood (data not shown); this could be interpreted as preliminary evidence against an immunologic cause of Dupuytren's disease. Our genetic findings have spurred new hypotheses such as that described by Balaji et al., the testing of which we hope will lead to a better understanding of the disease.

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Since publication of their article, the authors report no further potential conflict of interest.

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