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In a targeted RNA interference screen of the human kinome, VEGFR1/Flt1 was identified as a positive regulator of Wnt/β-catenin signaling and found to be synthetic lethal in the context of aberrant Wnt activation, such as that found in colon cancer. Even in the presence of siRNA targeting VEGFR1, immunofluorescence analysis showed nuclear translocation of β-catenin upon stimulation with Wnt. Thus, VEGFR1 likely regulates Wnt signaling at the level of posttranslational modification of β-catenin and represents a potential therapeutic target for treatment of Wnt/β-catenin—addicted cancers. For further details, please see Naik and colleagues on page 7529 in this issue.