

**Supplemental Data**

**Mutations in the Gene Encoding the Calcium-Permeable  
Ion Channel TRPV4 Produce Spondylometaphyseal  
Dysplasia, Kozlowski Type and Metatropic Dysplasia**

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Figure S1. TRPV4 mutations in SMDK and metatropic dysplasia.

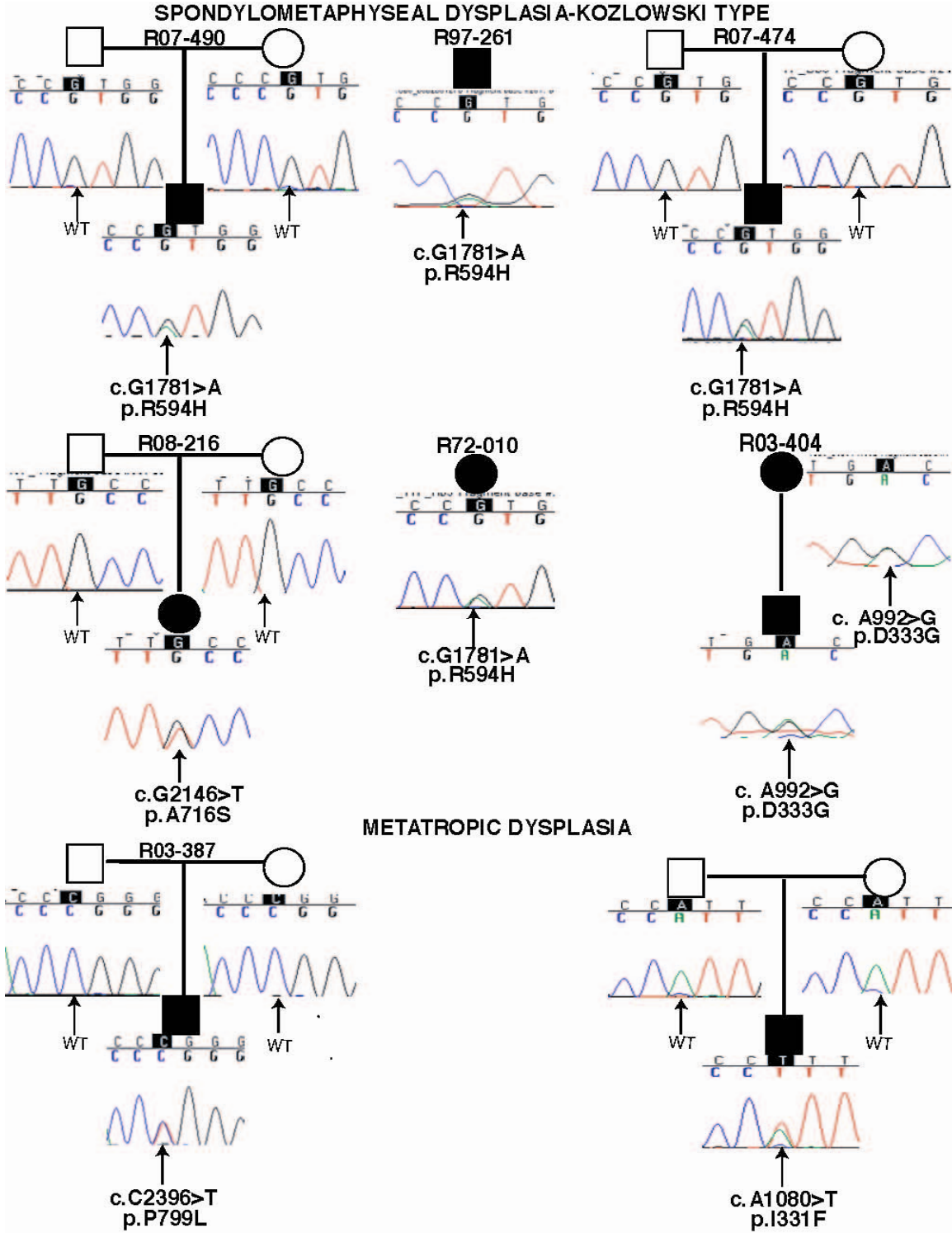


Figure S2. Activation of wild type and mutant TRPV4 by 4 $\alpha$ -PDD (A), hypotonic stimulation (HTS) (B) and arachidonic acid (AA) (C). Current-voltage relations obtained before (black) and after (red) stimulation with indicated stimulus. (D), maximal increases in in- and outward current at -150 and +150 mV on stimulation with 2 $\mu$ M 4 $\alpha$ PDD, hypotonic stimulation (E) and arachidonic acid (F). For every condition,  $n > 5$ . \*, significant differences when compared with cells expressing wild type TRPV4.

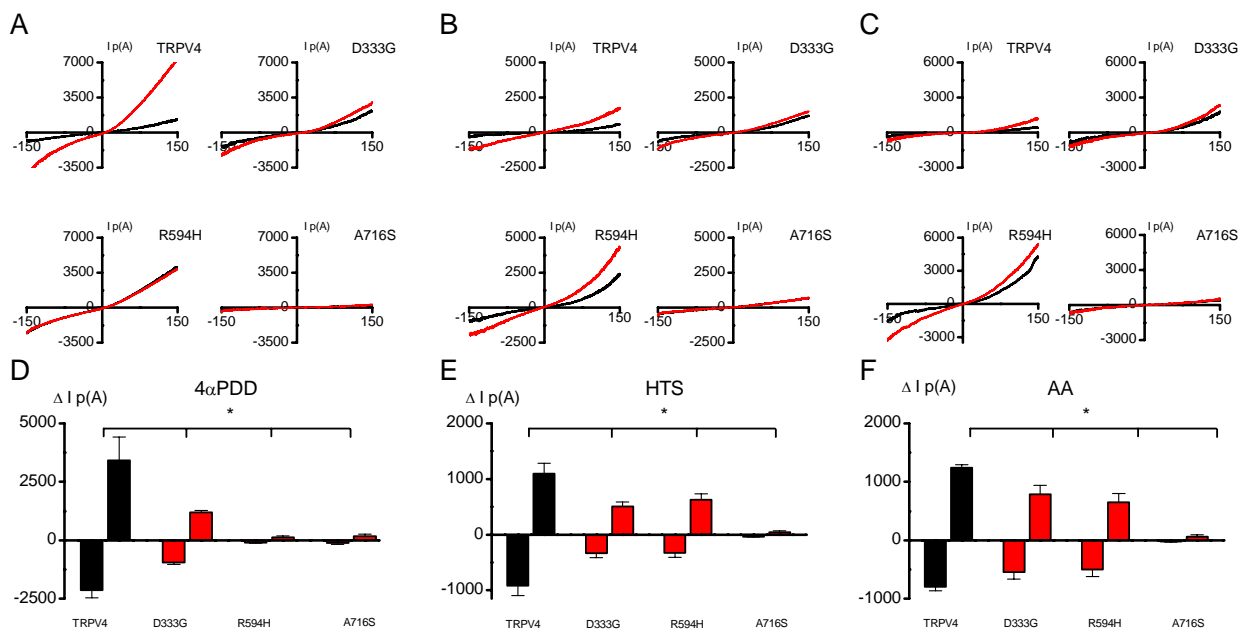


Figure S3. Influence of point mutations on TRPV4 activation by cell swelling and arachidonic acid. (A-D) effect of stimulation with a hypotonic solution on internal fluorescence ratio in wild type TRPV4 (A), D333G (B), R594H (C) and A716S (D) transfected HEK cells. (E-F), effect of stimulation with 10  $\mu$ M arachidonic acid on internal fluorescence ratio in wild type TRPV4 (E), D333G (F), R594H (G) and A716S (H) transfected HEK cells.  $n > 27$  in at least three independent recordings.

