

Figure Legends for Supporting Information Figures S1 and S2 (JBC-D-21-00705R2)

**Molecular determinants for the chemical activation of the warmth-sensitive TRPV3 channel by the natural monoterpene carvacrol**

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**Supplementary Figure 1.** (A-E) Amino acid interaction energy contribution for binding pocket 1-5.

**Supplementary Figure 2.** (A) Molecular docking predicts that carvacrol isopropyl arms show  $\pi$ -alkyl interaction with F524 residue. (B) Representative whole-cell current recordings of TRPV3-F524A in response to different concentrations (0.3-3.0 mM) of carvacrol, 50  $\mu$ M 2-APB or 10 mM camphor (n = 5).