**Mutations in Frizzled Class Receptor 4 associated with congenital cavus foot deformity**

Wenjin Yan\*1, Haijun Mao\*2, Xingquan Xu\*1, Liming Zheng1, Yannick Yang1, Pengjun Yu1, Jin Dai1, Guangyue Xu2#, Qing Jiang1#

1State Key Laboratory of Pharmaceutical Biotechnology, Department of Sports Medicine and Adult Reconstructive Surgery, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, 321 Zhongshan Road, Nanjing 210008, Jiangsu, China.

# 2State Key Laboratory of Pharmaceutical Biotechnology, Orthopedics Department, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, 321 Zhongshan Road, Nanjing 210008, Jiangsu, China.

\*These authors contributed equally to this work.

Correspondence: Qing Jiang (qingj@nju.edu.cn); Guangyue Xu (15366066188@163.com)

Table 1. FZD4 mutation carried by Congenital Cavus Foot Deformity Patients.

Supplementary Figure 1. The whole exome sequencing (WES) screenshots of coverage at position of gene Frizzled Class Receptor 4 (FZD4) in 3 patients and 2 healthy controls in the Chinese family. The 20× coverage for the RefSeq coding region was 98.23%.

Supplementary Figure 2. Micro CT scanning of the bone fragment of the proband and healthy controls. There’s no significant difference in bone volume fraction (BV/TV), trabecular number (Tb.N), trabecular thickness (Tb.Th), trabecular separation (Tb.SP) and bone mineral density (BMD).

Supplementary Figure 3. Datas from Protein-Protein Interaction (PPI) Database. The gene encoding Wnt receptor FZD4 can positively regulate Wnt/β-catenin signaling pathway either by directly activating via co-expression of FZD4 and LRP5 receptors. Wnt signaling pathway was mediated by these receptors.