

# **Magnesium implantation or supplementation ameliorates bone disorder in CFTR-mutant mice through an ATF4-dependent Wnt/β-catenin signaling**

Jiankun XU<sup>1,6</sup>, Peijie HU<sup>2,6</sup>, Xiaotian ZHANG<sup>2</sup>, Junjiang CHEN<sup>2,3</sup>, Jiali WANG<sup>1,4</sup>, Jieting ZHANG<sup>3</sup>, Ziyi CHEN<sup>1,3</sup>, Mei Kuen YU<sup>2,3</sup>, Yiu Wa CHUNG<sup>3</sup>, Yan WANG<sup>3</sup>, Xiaohu ZHANG<sup>3</sup>, Yifeng ZHANG<sup>1,5</sup>, Nianye ZHENG<sup>1</sup>, Hao YAO<sup>1</sup>, Jiang YUE<sup>1</sup>, Hsiao Chang CHAN<sup>3</sup>, Ling QIN<sup>1,\*</sup>, Ye Chun RUAN<sup>2,\*</sup>

<sup>1</sup>*Musculoskeletal Research Laboratory, Department of Orthopedics & Traumatology, The Chinese University of Hong Kong, Hong Kong, China.*

<sup>2</sup>*Department of Biomedical Engineering, Faculty of Engineering, the Hong Kong Polytechnic University, Hong Kong, China.*

<sup>3</sup>*Epithelial Cell Biology Research Centre, School of Biomedical Sciences, Faculty of Medicine, the Chinese University of Hong Kong, Hong Kong, China.*

<sup>4</sup>*School of Biomedical Engineering, Sun Yat-sen University, Guangzhou, China*

<sup>5</sup>*School of Life Science and Technology, ShanghaiTech University, Shanghai, China.* <sup>6</sup>*These authors contributed equally.*

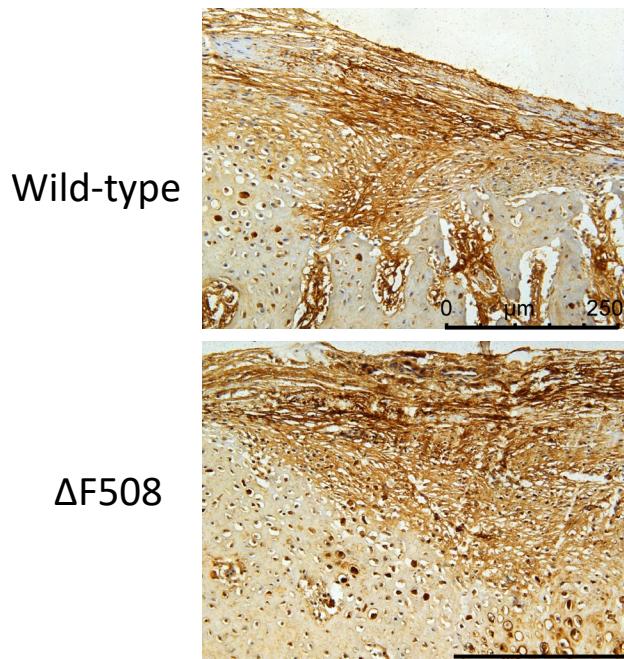
\*Correspondence should be sent to: sharon.yc.ruan@polyu.edu.hk (YCR) and lingqin@cuhk.edu.hk (LQ)

## Supplementary Information

**Supplementary Table. Primer sequences**

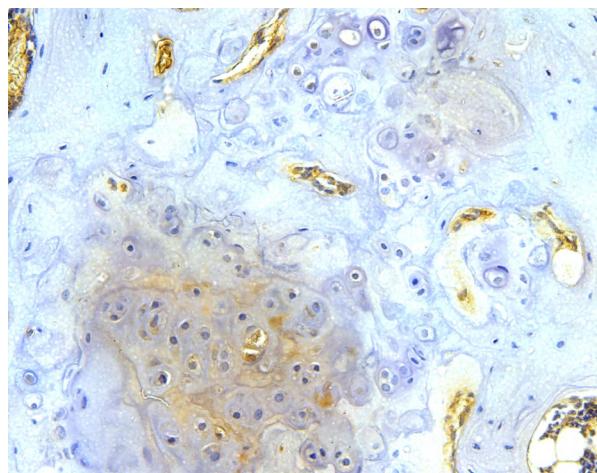
Gene name	Forward (5' - 3')	Reverse (5' - 3')
<i>Cldn16</i>	GAGACCAATAGCAACAGAGG	GTGGAGAATATGCCAAGAA
<i>Cnnm1</i>	GGCCAGTAAGTGATGATGAG	GCAGAGGGTGGAGTTAAC
<i>Cnnm2</i>	GGAGATAGGCACGGTCTATAA	CCGGTTATCATGAAGCAGTC
<i>Cnnm3</i>	GAGCCCTGTACCCTTATC	GTCCAGCGGGTAGTATT
<i>Cnnm4</i>	TCGGAGATTATGGAGAGTGG	GGTTGTAGAACGAGTGATG
<i>Magt1</i>	GCCTTCAGCTCACATTCA	GTGCCTGCTACCATTCTT
<i>Nipa2</i>	GTGTGAAGGGTTGGGTATC	AGAGCCCAGTTAGGTAA
<i>Slc1a1</i>	CTACACTTCTGCCCTCATCCT	CGGTTACCTCCTGCTATCT
<i>Slc41a1</i>	TGCTTCAACTCCTCGTAATC	GGGTCACTACCACTCATT
<i>Slc41a2</i>	GGCTGTTCTACCCATTAG	AGACTACAGTCAGAGAGGT
<i>Trpm6</i>	CACCAATACCTGGAAGAAC	AACACCATCCCTCTGATTG
<i>Trpm7</i>	CGGATTGGTTACGAGATAGAC	GTACAGGAACGAAGGAAATAC
<i>Trpv2</i>	CTGGCTAACCTGCTTAT	CTTACTAGGGCTACAGCAAAG
<i>Trpv4</i>	TGAGATGCTGGCTGTAGA	CCTCCAGTGGCTGATAGTA

## Supplementary Fig 1



**Supplementary Figure 1. Immuno-staining for CGRP in bone tissues from wild-type and age-matched ΔF508 mice.** Scale bars, 250  $\mu\text{m}$ .

## Supplementary Fig 2



**Supplementary Figure 2. Involvement of Wnt signaling in magnesium's effect on ΔF508 mice.** Immunohistochemical staining for active  $\beta$ -catenin in trabecular bones from wild-type mice at 2 weeks post Mg implantation. Active  $\beta$ -catenin was expressed in both osteoblasts and osteocytes. Scale bar, 100  $\mu\text{m}$ .