

1 **Multi-targeting DKK1 and LRP6 Prevents Bone Loss and Improves Fracture Resistance in Multiple**
2 **Myeloma**

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5 Marija K. Simic^{1,2}, Sindhu T. Mohanty¹, Ya Xiao¹, Tegan L. Cheng³, Victoria E. Taylor¹, Olga Charlat⁴, Michael
6 Daley⁴, Peter I. Croucher^{1,2}, Michelle M. McDonald^{1,2,5}

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- 9 1. Skeletal Diseases Program, Garvan Institute of Medical Research, Darlinghurst, NSW Australia
10 2. St Vincent's Clinical Campus, School of Clinical Medicine, University of New South Wales, Kensington
11 NSW Australia
12 3. Centre for Children's Bone and Musculoskeletal Health, The Children's Hospital at Westmead,
13 Westmead NSW Australia
14 4. Novartis Institutes for Biomedical Research, Cambridge MA, USA
15 5. School of Medical Science, Faculty of Medicine and Health, The University of Sydney, NSW Australia

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18 Corresponding author:
19 Michelle M. McDonald, Ph.D
20 Skeletal Diseases Program
21 Garvan Institute of Medical Research
22 384 Victoria Street
23 Darlinghurst NSW 2010
24 Tel: +612 9295 8247
25 Email: m.mcdonald@garvan.org.au

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31 **SUPPLEMENTARY FIGURE LEGENDS**

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33 **Supplementary figure 1. Circulating levels of OPG and RANKL in response to anti-LRP6 antibody**
34 **treatment in naïve mice.** Systemic expression of **(A)** OPG, **(B)** RANKL and **(C)** RANKL/OPG in naïve mice
35 treated with anti-LRP6 Ab or isotype for 7 and 14 days. Results plotted as mean \pm SD.

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37 **Supplementary figure 2. Anti-LRP6 antibody prevented trabecular bone loss in a separate cohort of**
38 **5TGM1-bearing mice.** MicroCT-derived (i) trabecular bone volume fraction (BV/TV, %), (ii) trabecular
39 thickness (Tb.Th, mm), and (iii) trabecular number (Tb.N, N/mm) in the distal femoral metaphysis **(A)** and
40 L4 lumbar vertebrae **(B)** in all respective groups in repeated 5TGM1-bearing mice treated with anti-LRP6
41 AB alone or isotype for 21 days. Results plotted as mean \pm SD.

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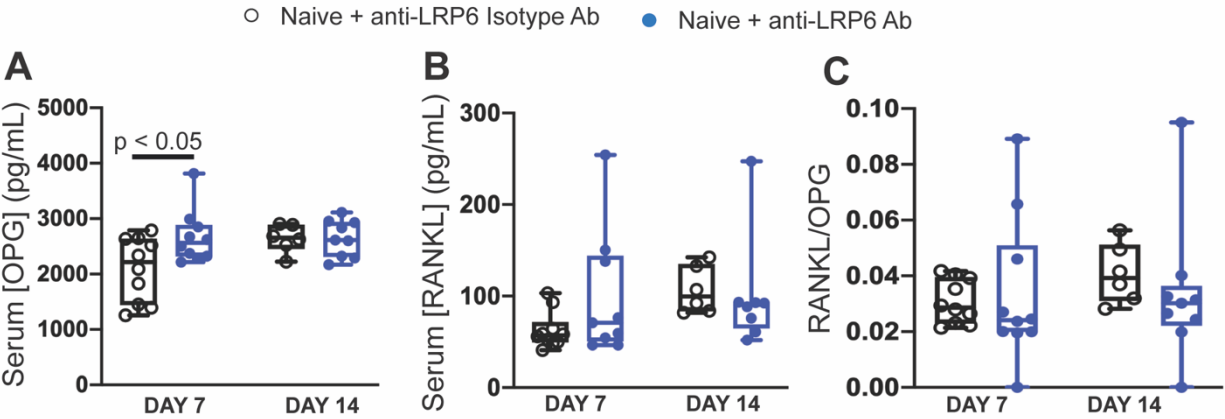
43 **Supplementary figure 3. Anti-DKK1 antibody prevented trabecular bone loss in 5TGM1-bearing mice.**
44 MicroCT-derived (i) trabecular bone volume fraction (BV/TV, %), (ii) trabecular thickness (Tb.Th, mm), (iii),
45 trabecular number (Tb.N, N/mm), (iv) cortical bone volume (Ct.BV, mm³) and (v) cortical thickness (Ct.Th,
46 mm) in the distal femoral metaphysis **(A)** and L4 lumbar vertebrae **(B)** of naïve and 5TGM1-bearing mice
47 treated with anti-DKK1 Ab alone or isotype for 21 days. Results plotted as mean \pm SD.

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49 **Supplementary figure 4. Anti-LRP6/DKK1 combination strategy led to significant elevations in bone**
50 **volume in naïve mice. (A)** MicroCT-derived (i) trabecular bone volume fraction (BV/TV, %), (ii) trabecular
51 thickness (Tb.Th, mm), (iii) trabecular number (Tb.N, N/mm), (iv) cortical bone volume (Ct.BV, mm³) and
52 (v) cortical thickness (Ct.Th, mm) in the distal femoral metaphysis. (i) Mineral apposition rate (MAR,
53 $\mu\text{m}/\text{day}$), mineralising surface (MS/BS, %) and (iii) bone formation rate (BFR, $\mu\text{m}^3/\mu\text{m}^2/\text{day}$) measured on
54 trabecular **(B)** and endocortical bone **(C)** surfaces within femora of naïve mice treated with anti-
55 LRP6/DKK1 Ab combination or isotype for 21 days. Results plotted as mean \pm SD.

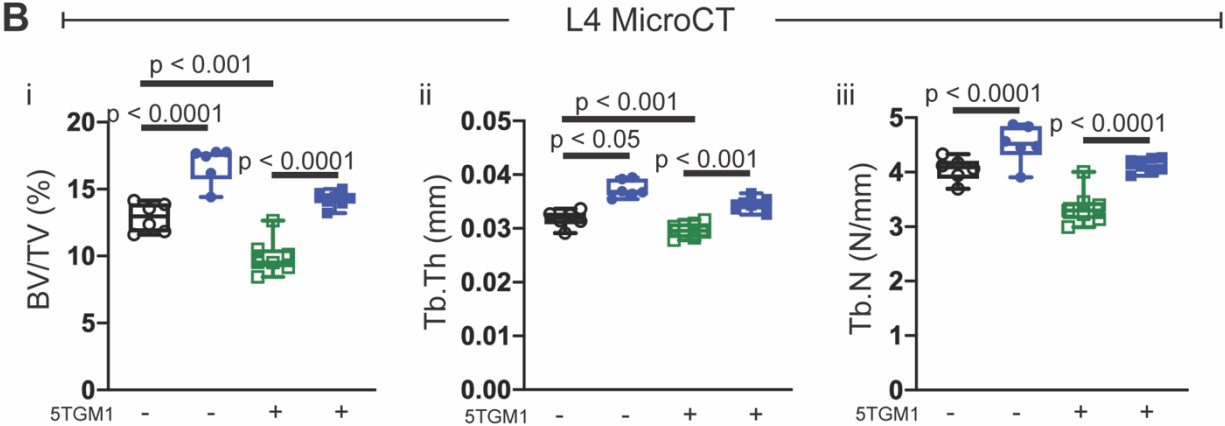
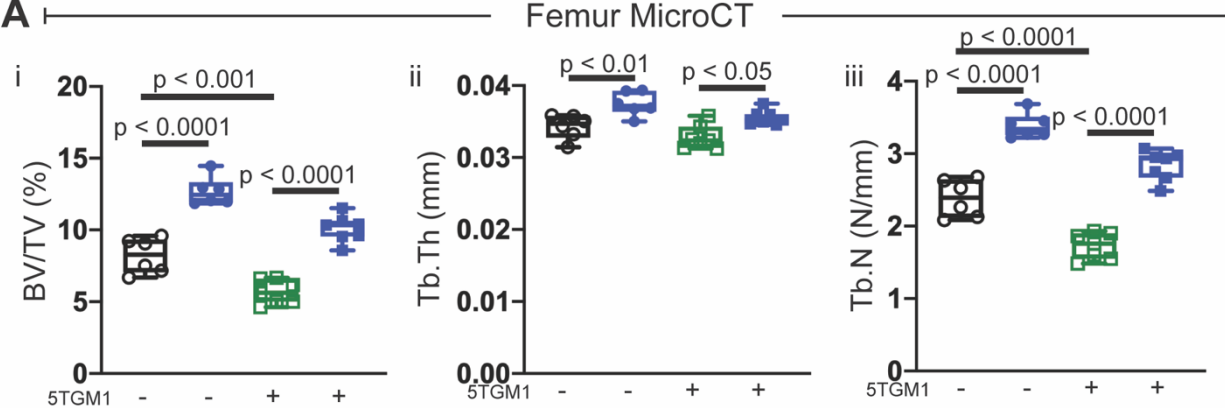
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Supplementary figure 1.



Supplementary figure 2.

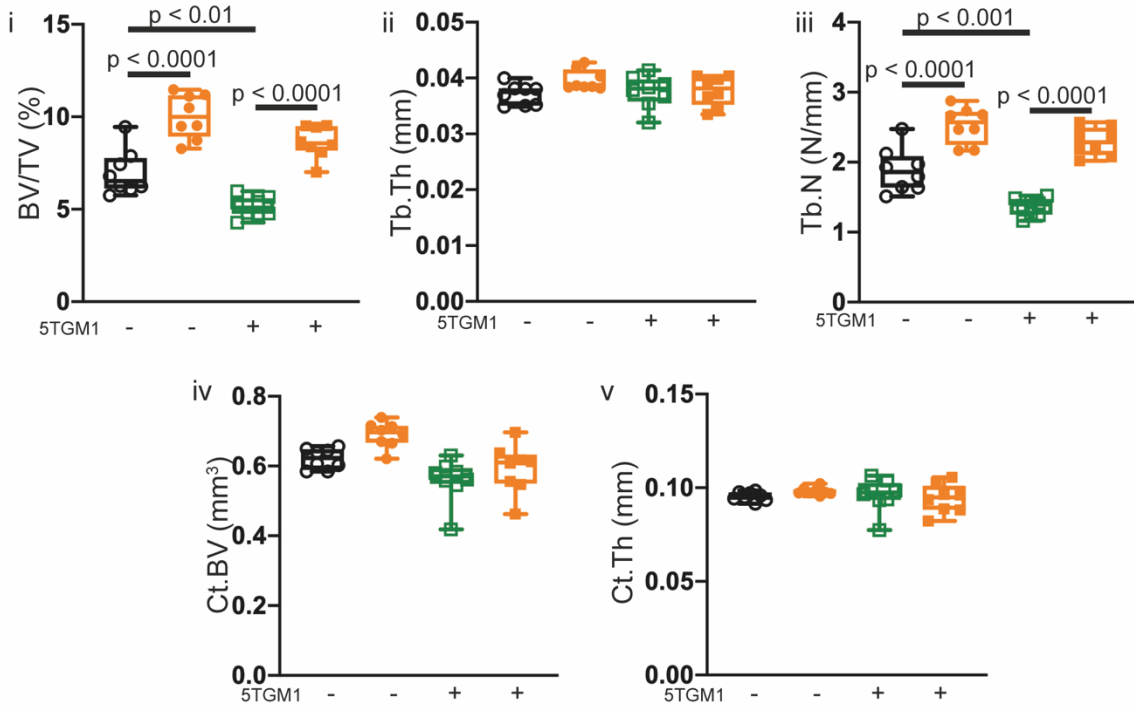
○ Naive + anti-LRP6 Isotype □ 5TGM1 + anti-LRP6 Isotype
 ● Naive + anti-LRP6 Ab ■ 5TGM1 + anti-LRP6 Ab



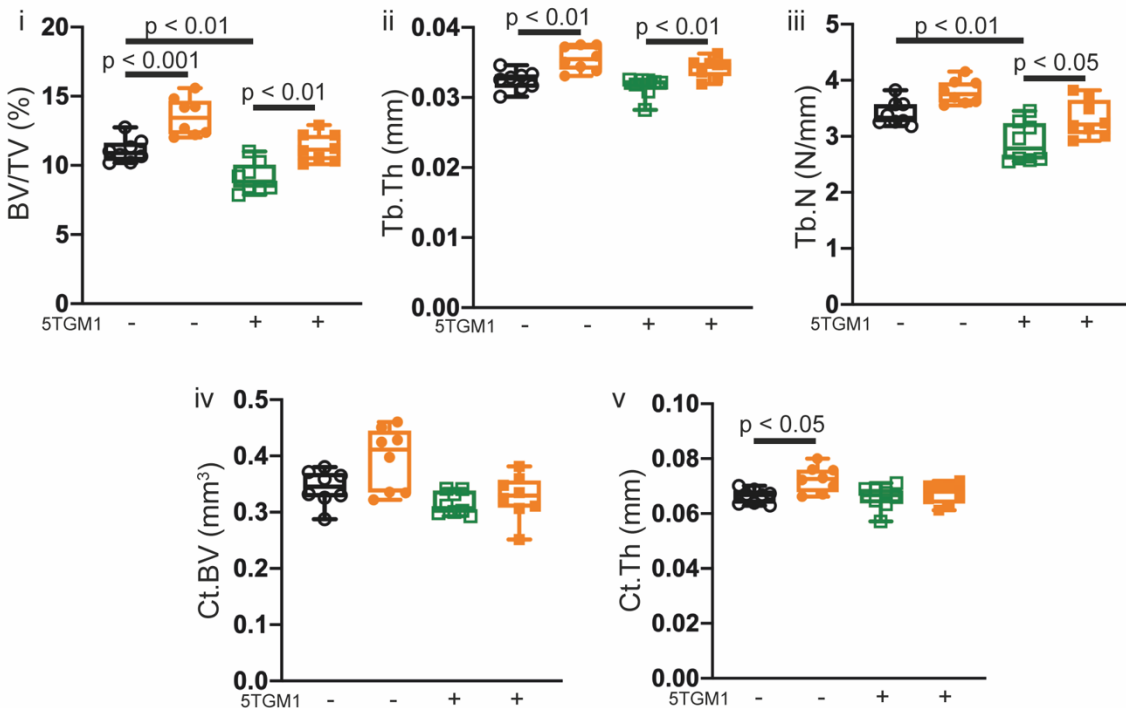
Supplementary figure 3.



A Femur MicroCT



B L4 MicroCT



Supplementary figure 4

○ Naive + anti-LRP6/DKK1 Isotype ● Naive + anti-LRP6/DKK1 Ab

