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Sections from control animals (A–E) and animals treated with TCDD for 7 days (F–I). In control animals, cells stained positive only with anti-PCB CAB033742 (A,D). Following treatment with TCDD, bone marrow stromal cells were positive with anti-PCB HPA043922 (B,E). With the IHC, both anti-PCB stained bone marrow tissue from both control (F) and TCDD-treated animals (G,H) [pone.0177242.g001][pone.0177242.g001] Discussion [psec009] ===== A number of studies have been conducted on the potential toxic effects of TCDD on bone marrow cells. Here, the effect of TCDD was examined on the expression of genes involved in the osteogenic pathway and the effects on bone cell lineage differentiation using an animal model. We showed that TCDD exposure for 7 days affected the expression of a number of genes associated with bone formation, including increased \*RUNX2\*, decreased \*BMP2\* and \*BMP4\*, and decreased \*ALP\* and \*BGLAP\* (osteocalcin) and \*COL1a1\*. These results were in agreement with previous studies [pone.0177242.ref025], which showed that TCDD caused a reduction in the number of osteoblasts and their activity. TCDD may alter the activity of osteoblasts by blocking the Wnt signaling pathway. Rief \*et al\*. [pone.0177242.ref026] showed that Wnt signaling is required for osteoblastogenesis. TCDD blocked the Wnt signaling pathway by inhibiting the expression of Wnt receptors, Fzd2, and Wnt-activated Lrp5 and Lrp6. In addition, TCDD disrupted the interaction of Lrp6 with Wnt ligands and the transport of Wnt to the cell membrane. Treatment of MC3T3-E1 cells with TCDD and  $\beta$ -glycerophosphate, a key factor for bone mineralization, resulted in a reduction in \*BMP2\* expression [pone.0177242.ref027]. These results suggest that TCDD suppressed Wnt signaling to reduce bone formation by blocking the differentiation of osteoblasts 82157476af

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