# APP promotes osteoblast survival and bone formation by regulating mitochondrial function and preventing oxidative stress

## Pan et al.

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Amyloid precursor protein (APP) is ubiquitously expressed in various types of cells including bone cells. Mutations in App gene result in early-onset Alzheimer's disease (AD). However, little is known about its physiological function in bone homeostasis. Here, we take advantage of APP gene knockout (APP-/-) mice, Comparing them with WT control littermates. We found that mice that knocked out App gene exhibit osteoporotic-like deficit, including reduced trabecular and cortical bone mass. Such a deficit is likely due in large to the decrease in osteoblast (OB)-mediated bone formation, as little change in bone resorption was detected in the mutant mice. Further mechanical studies of APP-/- OBs showed an impairment in mitochondrial function, accompanied with increased reactive oxygen species (ROS) and apoptosis. Intriguingly, these deficits not only resemble to those in Tg2576 animal model of AD that expresses Swedish mutant APP (APPswe), but also were diminished by treatment with an anti-oxidant NAC (n-acetyl-l-cysteine), uncovering ROS as a critical underlying mechanism. Taken together, these results identify an unrecognized physiological function of APP in promoting OB survival and bone formation, implicate APPswe acting as a dominant negative factor, and reveal a potential clinical value of NAC in treatment of AD-associated osteoporotic deficits.