Nature Reviews Rheumatology | Published online 30 Nov 2017; doi:10.1038/nrrheum.2017.199

BONE

DJ-1 orchestrates osteoclastogenesis

> Interestingly, only male mice showed statistically significant levels of bone loss

The antioxidant protein/nucleic acid deglycase DJ-1 (encoded by *PARK7*), a reactive oxygen species (ROS) scavenger, has been linked to the development of cancer and early onset Parkinson disease.

Music-Images/Alamy Stock Photo

Despite ROS having a known role in osteoclastogenesis, the potential role of DJ-1 in this process had not been explored. Now, a new study has revealed the pivotal role of DJ-1 in regulating bone homeostasis.

"Our results indicate that DJ-1 is critical for normal physiological bone homeostasis," states corresponding author Wahn Soo Choi. "Its deficiency or dysfunction leads to overproduction of osteoclasts and eventually causes bone-associated diseases."

Choi and colleagues characterized the bone pathology of *Park7*$^{-/-}$ mice, which are deficient in DJ-1. Interestingly, only male mice showed statistically significant levels of bone loss by μCT imaging. These mice also had increased numbers of tartrate-resistant acid phosphatase type 5-positive osteoclasts (a marker of terminal osteoclast differentiation) compared with male wild-type mice.

In vitro, suppression of DJ-1 production using small interfering RNAs increased the differentiation of human CD14^{+} monocytes or murine bone marrow macrophages into osteoclasts. In comparison with bone marrow macrophages from wild-type mice, the same cells from *Park7*$^{-/-}$ mice produced an increased number of osteoclasts.

The researchers noticed high levels of signalling molecules and transcription factors usually associated with the receptor activator of nuclear factor-κB ligand (RANKL) signalling pathway in *Park7*$^{-/-}$ bone marrow macrophages. Treating these cells with a ROS scavenger reduced the levels of RANKL-activated signalling molecules to levels similar to those seen in wild-type bone marrow macrophages, suggesting that DJ-1 exerts its inhibitory effect on osteoclastogenesis by regulating levels of ROS.

Translating these findings into a disease setting, Choi and colleagues investigated the role of DJ-1 in collagen-induced arthritis (CIA), a model in which bone damage is caused by osteoclasts. Induction of CIA in *Park7*$^{-/-}$ mice produced higher levels of serum ROS than are found in wild-type mice with CIA. *Park7*$^{-/-}$ mice also had more severe disease, including increased synovial inflammation and bone erosion, than wild-type mice.

"On the basis of these results, we will conduct research to develop therapeutic methods to treat bone-associated diseases by controlling the function of DJ-1," concludes Choi.

Joanna Collison

ORIGINAL ARTICLE Kim, H. S. *et al.* DJ-1 controls bone homeostasis through the regulation of osteoclast differentiation. *Nat. Commun.* **8**, 1519 (2017)