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   2022G023

2. Title
   Analysis of Dysregulated Bone Healing Mechanisms via Aryl Hydrocarbon Receptor by Smoking and Its Regulation

3. Period
   2022-2024

4. Summary
   The aryl hydrocarbon receptor (AhR), which acts as a transcriptionfactor when bound by a ligand, regulates a variety of physiological processes, most notably cellular activities related to immune responsivity. Observations of disrupted bone tissue healing and slowedendochondral ossification in AhR $^{-/-}$ mice indicate strongly that AhR also modulates skeletal remodeling, though the signaling mechanism through which AhR affects osteoclastogenesis remains to be resolved. Recent studies have shown that receptor activator of nuclear factor kappa-B ligand (RANKL) causes rapid upregulation of AhR expressionin bone marrow-derived osteoclasts. Ligand activated AhR by the smoke toxin B[a]P and Kynurenine increased osteoclast differentiation in a receptor AhR-dependent manner. On the other hand, endocrine AhR ligand FICZ represses the osteoclast differentiation via RANKL/Cyp1a1 signaling. Mitochondrial biogenesis in osteoclasts is subject to regulation by AhR. AhR involvement in osteoclastogenesis makes AhR a potential therapeutic target for the treatment of inflammatory and metabolic bone diseases. This research highlights the recently uncovered critical role that RANKL–AhR–c-Fos signaling plays in osteoclastogenesis and bone fracture healing through the various AhR ligands.