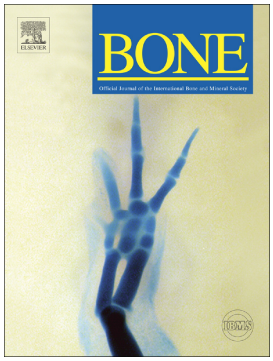

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Heterotopic Ossification: mechanistic insights and clinical challenges

Ruoshi Xu[1, 2], Jiajie Hu[1], Xuedong Zhou[2*], Yingzi Yang[1*]

1. Department of Developmental Biology, Harvard School of Dental Medicine, 188 Longwood Ave. Boston, MA 02215, USA;
2. State Key Laboratory of Oral Diseases, West China Hospital of Stomatology, Sichuan University, No. 14, Section 3, South Renmin Rd., Chengdu, 610041, China.

*Correspondence:

Yingzi Yang, yingzi_yang@hsdm.harvard.edu; Xuedong Zhou, zhouxd@scu.edu.cn.

Abstract
Bone formation is exquisitely controlled both spatially and temporally. Heterotopic ossification (HO) is pathological bone formation in soft tissues that often leads to deleterious outcomes. Inherited genetic forms of HO can be life-threatening and can happen as early as in infancy. However, there is currently no effective treatment for HO as the underlying cellular and molecular mechanisms have not been completely elucidated. Trauma-induced non-genetic forms of HO often occurs as a common complication after surgeries or accidents, and the location of HO occurrence largely determines the symptom and outcome. While it has been difficult to determine the complicated factors causing HO, recent advancement in identifying cellular and molecular mechanism causing the genetic forms of HO may provide important insights in all HO. Here in this review, we summarize recent studies on HO to provide a current status of both clinical options of HO treatments and mechanical understanding of HO.

Key words
FOP, POH, AHO, GNAS, ACVR1, trauma-induced, neurogenic, TGF-β, BCSP, Tie2, Scx, Mx1, osteoblast, XLαs, NESP55, imprint, osseous metaplasia, malignancies, ALK, BMP, RABEP1, Gli, PTHrP, hedgehog, nonsteroidal, radiation, RAR-γ, apyrase, ATO, GANT58

Introduction

Bone forms according to a genetically controlled time course and spatial rules. Under pathological conditions, bone can form at extra-skeletal sites and such abnormal bone formation is called heterotopic ossification (HO). HO was first reported by Guy Patin in 1692 in children who had myositis ossifications progressive[1]. The acquired form of HO was first described by Dejerne and Ceillier, who stated that HO was found frequently in soldiers in war, especially those suffered from spinal cord injuries and gunshots[2].