2026 年 7 月 15 日（水）

Fgf18 marks reserve skeletal progenitors in the fibrous periosteum contributing to bone fracture repair

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Cell Reports, Vol. 45, 117525

線維性骨膜に存在し骨折修復に寄与する予備的骨格前駆細胞を Fgf18 が標識する

The periosteum supports both normal bone growth and fracture repair. However, the identity and location of periosteal progenitor cells that mainly respond to injury remain unclear. In this study, the authors used single-cell RNA sequencing, RNAscope, inducible lineage tracing, immunostaining, and a mouse femoral fracture model to identify and examine repair-related cells in the periosteum.Single-cell analysis identified multiple periosteal cell populations, including two potential skeletal progenitor groups, SP1 and SP2. Fgf18, Chad, and Comp were enriched in these populations, especially in SP1. Spatial analysis showed that the potential progenitor cells were mainly located in the outer fibrous periosteum. $Fgf18^+$ cells were positioned outside the OSX^+ inner cambium layer and partially overlapped with $PDGFR\alpha^+$ periosteal progenitors. Their co-expression with CD34 differed depending on the long-bone location.During normal growth, Fgf18-lineage cells remained mainly in the outer periosteum and contributed very little to cortical osteoblasts or osteocytes.

In contrast, after fracture, these cells expanded, proliferated, and generated chondrocytes, osteoblasts, and osteocytes in the callus. Genetic removal of $Fgf18^+$ cells reduced early callus size and bone formation and resulted in thinner cortical bone with more gaps after healing. The authors therefore propose that $Fgf18^+$ cells act as reserve skeletal progenitors that remain relatively quiet during homeostasis but become activated after injury.

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