MASARYKOVA UNIVERZITA

A novel stem cell niche controls skeletal growth

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Lecture Abstract

For children to grow longitudinally, epiphyseal growth plates must continuously supply differentiated chondrocytes throughout the entire period of skeletal growth (i.e., the entire life of rodents and the first 18 years in humans), but how this is achieved remains totally unknown. We hypothesized that during maturation of the plate there is a new stem cell niche is formed, which allows renewal of chondro-progenitors.

Employing clonal genetic tracing, we have shown that upon maturation of the growth plate (i.e., formation of the secondary ossification center, SOC), chondro-progenitors located in close proximity to SOC acquire the capacity for renewal. Furthermore, these cells de novo acquire markers of stem cells. Analysis of the underlying mechanisms revealed that with SOC development a new source of sonic hedgehog (SHH) is formed and hedgehog pathway (HH) maintains cell renewal in the niche. Blocking of HH pathway destroys the niche and causes disappearance of the growth plate. We have also identified another pathway, mechanical target of rapamycin (mTOR), which maintain symmetric stem cell division in the niche.

Altogether, these novel observations change our understanding of the basic mechanisms underlying the sustained longitudinal growth of bones and thereby have profound ramifications for clinical and basic research in this area - from developmental and stem cell biology, to paediatrics and endocrinology.