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EVOLUTION OF GENOTYPE AND PHENOTYPE OF SKELETAL STRENGTH IN PRIMATES

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Abstract

Bone morphology is an end product of complex interactions between genetic influences and environmental stimuli. The structural strength of bone in particular has long been considered to be reflective of mechanical loading environment. However, increasing evidence for genetic inputs in determining bone strength has been found. Specifically, human chromosome region 11q12-13 has been identified multiple times as a potential region housing genes associated with bone strength.

In this study, I investigated the previously described association between chromosome region 11q12-13 and bone strength. Three potential candidate genes (*LRP5*, *TCIRG1*, *FOSL1*) were chosen based on their roles in regulating bone mass and their associations with disease of the skeleton. First, I used phylogenetic approaches to investigate the evolutionary histories of these loci. I found that the phylogenetic tree constructed using *LRP5* coding region is discordant with the presently known primate phylogenetic tree while the *TCIRG1* tree is congruent. The reason for this discordance is most likely the presence of indels within the coding region of *LRP5*. Phylogenetic reconstruction with *FOSL1* coding region yields multiple trees that could not be fully resolved, which could be attributed to the lack of phylogenetic signal. Slow evolutionary rates amongst Catarrhini were also observed.

Selection analyses on *LRP5* and *TCIRG1* showed both loci were under purifying (negative) selection, which is expected as mutations in both genes would lead to detrimental consequences. I then tested for genotype-phenotype association of these two loci and bone strength. Using phylogenetically controlled regression analyses, I found strong negative relationships between selection of *TCIRG1* and the evolution femoral cross-sectional properties, indicating *TCIRG1* may have played a role in the evolution of bone strength and mechanoadaptation of bone.