

人类与医学遗传学

影响中国女性峰值骨密度的潜在基因间相互作用

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摘要 峰值骨密度是由遗传和环境因素及其相互作用共同决定的复杂性状。维生素D受体基因、雌激素α受体基因、白介素6基因、副甲状腺素基因、I型胶原α2基因、骨钙素基因、α2巯基糖蛋白基因是与骨代谢相关的7个重要的候选基因。本研究旨在检测影响这7个候选基因之间的相互作用对中国女性峰值骨密度的影响。样本为中国上海的361个无关、健康的绝经前女性,均为汉族人,年龄为20~44岁。采用Hologic QDR 2000+双能X射线扫描仪对腰椎与髌部的骨密度进行了检测。采用聚合酶链式反应-限制性片段长度多态分析方法对每个个体的以下8个多态性标记位点进行基因分型:维生素D受体基因的Apa I位点,雌激素α受体基因的Pvu II和Xba I位点,白介素6基因的BsrB I位点,副甲状腺素基因的BstB I位点,I型胶原α2基因的Msp I位点,骨钙素基因的HindIII位点,α2巯基糖蛋白基因的Sac I位点。本研究采用二元方差分析对基因相互作用与骨密度的关系进行研究。结果表明,白介素基因和雌激素α受体基因(Pvu II)的相互作用对髌部(P = 0.019)、转子间区(P = 0.016)和股骨颈(P = 0.019)的骨密度有显著作用。在这3个部位,GGPp基因型携带者比GGpp基因型携带者的骨密度值分别高出18.0%,19.5%和14.8%。另外观察到α2巯基糖蛋白基因与白介素6基因的相互作用对股骨颈骨密度有显著影响(P = 0.046)。GGSS基因型携带者的股骨颈骨密度值比GGSs基因型携带者高出18.8%。该项群体水平的统计分析表明:对于中国女性峰值骨密度的遗传决定,白介素基因和雌激素α受体基因、α2巯基糖蛋白基因的相互作用显著。

关键词 峰值骨密度; 基因; 相互作用; 方差分析

分类号

Potential Effect of Inter-genic Action on Peak Bone Mass (PBM) in Chinese Females

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Abstract

Peak bone mass (PBM) is a complex trait, determined by both genetic and environmental factors and also their interaction. Vitamin D receptor (VDR), estrogen receptor α (ERα), interleukin 6 (IL6), parathyroid hormone (PTH), collagen type I alpha 2 (COL1A2), bone Gla protein (BGP), alpha2-HS glycoprotein (AHSG) are among the important candidate genes of bone metabolism. The study aims to detect significant effect of potential inter-genic action underlying PBM in Chinese females. 361 unrelated healthy premenopausal Chinese females (aged 20–44 years) with Han ethnicity were recruited from the Shanghai city in China. Bone mineral density (BMD) at the hip and the lumbar spine (L1-4) was measured using a Hologic QDR 2000+ dual-energy X-ray absorptiometry (DXA) scanner. Eight polymorphism among the seven genes were genotyped, i.e. Apa I in VDR, PvuII and Xba I in ERα (ERX and ERP, respectively), BsrB I in IL6, BstB I in PTH, Msp I in COL1A2, HindIII in BGP, and Sac I in AHSG, using PCR-RFLP (polymerase chain reaction-restriction fragment length polymorphism) methods. Two-way analysis of variance (ANOVA) showed significant effect of IL6 × ERP interaction on PBM at the total hip (P = 0.019), intertrochanter (P = 0.016), and femoral neck (P = 0.019). The BMD difference between GGPp carriers and GGpp subjects (at these two loci) amounted to 18.0%, 19.5%, and 14.8% at the hip, intertrochanter, and femoral neck, respectively. The potential interaction effect of AHSG × IL6 was observed on femoral neck PBM (P = 0.046). GGSS individuals (at these two loci) have, on average, 18.8% higher

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femoral neck BMD than those subjects with GGSs genotype. The population-level statistical analysis indicates that IL6 × ERP and AHSG × IL6 have significant inter-genic effect on the genetic determination of PBM in Chinese females.

Key words [peak bone mass \(PBM\)](#) [gene](#) [interaction](#)

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