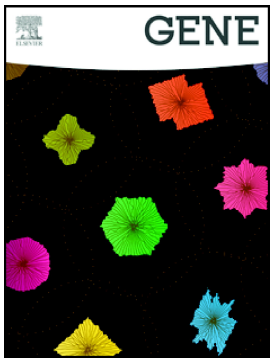

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A Novel Duplication Downstream of BMP2 in a Chinese family with Brachydactyly Type A2 (BDA2)

Wen-bo Wang*, Ya-chao Jia*, Zeng Zhang, Jia Xu, Rong-tai Zuo, Qing-lin Kang#

*: Co First Author

#: Corresponding Author

Affiliation: Department of Orthopedic Surgery, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China

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Abstract

Background

Brachydactyly type A2 (BDA2) is an autosomal dominant disease characterized by the deformation of the middle phalanx of the second fingers and toes. It has been reported to be associated with three genes regulating the osteogenesis, including *BMPR1B*, *GDF5* and *BMP2*.

Materials and Methods

10 BDA2 patients and 7 unaffected individuals in a Chinese family was identified through clinical signs and radiographs. The mutation analyses of *BMPR1B*, *GDF5* and *BMP2* gene was performed in all the available family members and 100 control subjects. The duplication analysis for the downstream of *BMP2* was also performed in all the samples.

Results

A novel 4,671 bp duplication downstream the *BMP2* gene was identified in all the patients undergoing molecular analysis but not in the unaffected individuals and healthy controls, with a 28 bp microhomology flanking it. There was no mutation in all the exons of *BMPR1B*, *GDF5* and *BMP2* in all the tested family members.

Conclusion

The novel duplication has different breakpoints compared with the previous ones but highly overlapped with them. The duplication narrows the range of the potential cis-regulatory sequence, and further supports the association between BDA2 and the duplication downstream *BMP2*.

Keywords: *BMP2*; brachydactyly; molecular genetics; duplication; microhomology

Introduction

Brachydactyly (BD) is a group of diseases with heterogeneous clinical features and relative genes. The distinctive characteristic of BD is the shortening of digits caused by abnormal development of the phalanges and/or the metacarpals[1]. In the embryonic development of hands, related gene expressions are usually regulated by each other with the function overlapping, which makes syndactyly, polydactyly, reduction defects and symphalangism also the universal accompanying manifestations of BD[2-5].

The most common classification of brachydactyly was first introduced by Bell[6] and improved by Temtamy and McKusick, which generally divided brachydactyly into 5 types (type A, B, C, D, E) and several subgroups[7]. All the types share certain clinical features such as hypoplasia of phalanges or interdigital joint malformation, which indicates the relative molecular