

頸部神経堤細胞の移動・分化を制御する  
Hoxa3 遺伝子の機能解析

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## はしがき

本研究は、生存に重要な器官形成を司る Hoxa3 遺伝子の機能を詳細に解析したものです。かなりの部分は投稿中で、未発表ですが、発生生物学の教科書に記載されるべきデータを含んでいます。3年間で4回の研究場所の引っ越しなどを強いられる中、本研究費はこのような研究を支えるのにとっても有用でした。ここに深く感謝致します。また、研究の大半を実際に行ってくれた元大学院生の（現カリフォルニア大学バークレー校研究員）五島一渡利夏子さんと北里大学医学部の亀田英子先生にも深く感謝の意を捧げたいと思います。

## 研究組織

研究代表者：千坂 修（京大大学生命科学研究科助教授）

研究分担者：なし

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平成15年度	2,600	0	2,600
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## 研究発表

### (1) 学会誌等

Kameda, Y., Arai, Y., Nishimaki, T., and Chisaka, O.  
The Role of Hoxa3 Gene in Parathyroid Gland Organogenesis of the Mouse. *Journal of Histochemistry and Cytochemistry* 52, 641-651, 2004

Chisaka, O. and Kameda, Y. Hoxa3 Regulates the Proliferation and Differentiation of the Third Pharyngeal Arch Mesenchyme in Mice. *Cell and Tissue Research* 320, 77-89, 2005

### (2) 口頭発表 なし

### (3) 出版物 なし

研究成果による工業所有権の出願・取得状況  
なし

## 「研究成果」

既に発表済みの部分は印刷物を添付した。未発表の部分は原稿を添付した。早急に投稿する予定である。

## The Role of *Hoxa3* Gene in Parathyroid Gland Organogenesis of the Mouse

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**Summary** While only a limited number of the *Hoxa* gene family members of the third branch of the mouse genome are expressed in the third pharyngeal pouch, to address the role of the *Hoxa3* gene in parathyroid organogenesis, we examined the third pharyngeal pouch development by transgenic heterozygosity (*Hox3*) using the regulatory protein SP-1/Myb transcription factor, which regulates the parathyroid fate as initial formation signal. At embryonic day (E) 11.5, the SP-1 chromogram demonstrated the primary rudiment of the parathyroid appeared in the rostral region of the third pharyngeal pouch of wild-type embryos. In *Hox3* null mutants, the third pharyngeal pouch was normally formed but failed to differentiate into the parathyroid rudiment, showing no immunoreactivity for SP-1/Myb transcription factor. Classical using single-cell-clonal cultures have demonstrated that the ectodermally derived neural crest cells are required for proper development of the embryonic crest-derived organs, including the thymus and parathyroid glands. To elucidate the migration and development of neuroepithelial neural crest cells in *Hox3* mutants, the heterozygous wild crossed with *cre-loxP*-*lacZ* transgenic mice in which *β-galactosidase* expression was specific to the neural crest cells. In *Hox3* heterozygotes and in wild types, ectodermally derived neural crest cells heavily populated the pharyngeal pouch, including the third one, via keratinized the third pouch epithelium. These results indicate that lack of the *Hoxa3* gene affects the migratory ability of the third pharyngeal pouch to form the parathyroid rudiment and has no detectable effect on the migration of neural crest cells. *J. Neurochem.* 84:641–651, 2004.

**KEY WORDS**  
*Hoxa3*  
 parathyroid  
 thymus  
 neuroepithelial neural crest cells  
 SP-1/Myb transcription factor  
 single-cell-clonal cultures  
 keratinized

THE PARATHYROID GLAND synthesizes and secretes parathyroid hormone (PTH), which is essential for regulation of serum calcium concentration. The parathyroid and thymic primordia develop from the third pharyngeal pouch in mice (Cowder and Hammar, 1980). However, there is little information regarding parathyroid organogenesis during pharyngeal pouch development because of the lack of a specific marker that defines the rudiments. These developmental requirements in heterozygous *Hoxa3* mutants sessions have been used to examine parathyroid development (Chisaka et al., 2001):

1. Myb transcription factor, the major regulatory protein of adenyl cyclase cells, is a marker of the parathyroid

transcription factor family of a DNA glycoprotein that participates in the origin and secretion of parathyroid hormone and are expressed in many endocrine and exocrine cells, thymic cells (Cowan et al., 1973; Fisher-Collins et al., 1987; Walker and Fisher-Collins, 1992), bone marrow plasma cells (SP-1) derived via parathyroid cells (Cowan et al., 1984). SP-1 and Myb transcription factor are chemically similar DNA binding proteins (Cowan et al., 1987). The present study shows that SP-1 immunoreactivity appears in the parathyroid rudiment of the third pharyngeal pouch from the earliest stage of its organogenesis.

*Hoxa3* belongs to the *Hox* family of transcription factors that play multiple roles in the segmental processes of neuroepithelial patterning (Krumlauf, 1994; Izquierdo and Izquierdo, 2000). In the *Hoxa3* heterozygous wild mutant mouse produced in our laboratory, the thymus and parathyroid glands derived from the

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