

論文 / 著書情報
Article / Book Information

題目(和文)	四肢動物における生息環境の酸素濃度と指間細胞死の進化的獲得
Title(English)	Environmental oxygen levels and the evolution of interdigital cell death in tetrapods
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出典(和文)	学位:博士(理学), 学位授与機関:東京工業大学, 報告番号:甲第11243号, 授与年月日:2019年9月20日, 学位の種別:課程博士, 審査員:田中 幹子,本郷 裕一,太田 啓之,木村 宏,川上 厚志
Citation(English)	Degree:Doctor (Science), Conferring organization: Tokyo Institute of Technology, Report number:甲第11243号, Conferred date:2019/9/20, Degree Type:Course doctor, Examiner:,,,,
学位種別(和文)	博士論文
Category(English)	Doctoral Thesis
種別(和文)	論文要旨
Type(English)	Summary

(博士課程)
Doctoral Program

論文要旨

THESIS SUMMARY

専攻 : Department of	Biological Sciences	専攻	申請学位 (専攻分野) : 博士 Academic Degree Requested	Doctor of	(Science)
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要旨 (英文 800 語程度)

Thesis Summary (approx.800 English Words)

Amphibians (frogs, salamanders and caecilians) form digits free of webbing through differential growth of the digital and interdigital regions, and are often aquatic for part of their lives. Amniotes (birds, reptiles and mammals) use cell death to remove their interdigital membranes, and develop in an egg or uterus lined with membranes which deliver oxygen in a very efficient way. Here I investigated the role of environmental oxygen in the evolution of interdigital cell death (ICD) in tetrapods. Chickens had extensive interdigital production of reactive oxygen species (ROS), while in African clawed frogs (*Xenopus laevis*) cell death and ROS were restricted to the limb margins. In chicken, low oxygen levels (hypoxia) inhibited ICD, while higher oxygen levels (hyperoxia) increased the number of dying cells. Surprisingly, incubating tadpoles under hyperoxia was sufficient for inducing cell death specifically across their interdigital regions; environmental oxygen levels increased ROS production within the limb, promoting ICD in an amphibian that typically lacks it. Next, the role of blood vessels, which are essential for tissue oxygenation, was investigated by studying transgenic *X. laevis* frogs with an increased limb vasculature (*Prrx1-VegfA-EGFP*). These tadpoles had ectopic cell death as well as ROS production in the interdigital region, revealing that increasing the density of blood vessels - the source of oxygen in the limbs - promoted cell death specifically in the interdigital mesenchyme of *X. laevis*. To add a comparative perspective, the distribution of cell death and ROS was assessed in two other amphibian species. Japanese fire-bellied newts (*Cynops pyrrhogaster*), which have aquatic tadpoles as *X. laevis*, had no ICD or interdigital ROS production. However, a surprising pattern was observed in the coquí frog (*Eleutherodactylus coqui*): dying cells and high ROS production was found in their interdigital regions. There is an important ecological distinction between this species and the previous investigated *X. laevis* and *C. pyrrhogaster*: coquí frogs have direct development, in which fertilized eggs are laid on land and an immature adult animal emerges at the end of the embryonic period without an aquatic larval stage. Thus, *E. coqui* embryos are exposed to the higher atmospheric oxygen levels, comparable to amniotes. This way, high oxygen availability is correlated with the presence of cell death during limb development of tetrapods, although it is not clear if these dying cells are required for shaping the limbs or only a byproduct of increased ROS levels. Then, the local oxygen tension in the limbs was measured using EF5, a hypoxia marker. Chicken limbs had a high oxygen tension in the interdigital region, while *X. laevis* had low oxygen tension in their interdigital regions in all investigated stages. Then, I evaluated experimentally if the oxygen concentration in the tissue was responsive to environmental oxygen levels. Hypoxia reduced tissue oxygen tension in chickens' interdigital mesenchyme. On the other hand, incubating *X. laevis* under hyperoxia - the same condition that previously induced ectopic ICD - increased oxygen tension in the interdigital region. Thus, oxygen tension of the interdigital region, a highly vascularized tissue, is correlated with environmental oxygen levels that surround the embryo or tadpole. In conclusion, the life history strategy regulates oxygen availability in the limbs, and that high oxygen levels were necessary for the appearance of interdigital cell death. It is key to understand why the amphibian interdigital region is already permissive for the induction of cell death. Two features important for patterning the fingers of all tetrapods - Bmp signaling and blood vessel remodeling - are also required for induction of cell death in the interdigital regions. I propose that an independent developmental step, ICD, might have emerged from preexisting traits of digit morphogenesis in the presence of increased environmental oxygen levels.

備考 : 論文要旨は、和文 2000 字と英文 300 語を 1 部ずつ提出するか、もしくは英文 800 語を 1 部提出してください。

Note : Thesis Summary should be submitted in either a copy of 2000 Japanese Characters and 300 Words (English) or 1 copy of 800 Words (English).

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