APOPTOSIS IN ODONTOGENESIS - A BRIEF REVIEW

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Abstract

Tooth formation is an excellent example of epithelial mesenchymal interaction As the developing tooth passes through the various morphologic stages it is observed that apoptosis occurs selectively in certain locations. Here a review is done to throw light into the role of apoptosis and the factors governing the same during odontogenesis .

Key words – Apoptosis, Tooth formation

Introduction

Apoptosis is an active process of cellular self- destruction and the importance of this process is increasingly recognized both in physiologic regulation and in pathologic conditions. Apoptosis is usually manifested as the death of an individual cell or cells in a given population.The process of tooth development is an example of epithelial mesenchymal interactions and this results in the various stages which exhibits different morphologic patterns. Several studies have proved that apoptosis in epithelial and mesenchymal cells during embryonic tooth development exists in rodent animals .This process exhibits certain distinct morphologic and molecular features such as cell shrinkage,chromatin condensation ,internucleosomal DNA fragmentation and activation or inactivation of specific gene functions[1]. Apoptosis is essential to balance mitosis [2].In other words it is a physiologic mechanism of cellularity control regulating the size of tissues in an inverse situation of mitosis [3] .

MECHANISM OF APOPTOSIS

By understanding the spatially and temporally restricted distribution patterns of apoptotic cells, the multiple roles for apoptosis in dental development can be assessed. In early bud stage apoptotic cells are found in the budding epithelium in particular in the cells facing the oral cavity in rodent studies [4] . When the tooth germ prolongs its central axis at the late bud stage apoptotic cells become concentrated at the tip of the tooth bud. At the bud stage no apoptotic cells are seen in the mesenchyme .In the cap stage this cluster of apoptotic cells are localized within the enamel knot. As development continues the enamel knot does not show any evidence of loss of cell mass suggesting a rapid replacement by proliferating cells surrounding the enamel knot. With disappearance of the primary knot, apoptosis is no longer observed in this area but is detected in the gubernaculum(epithelium joining the enamel organ to the buccal epithelium). At the cap stage a few apoptotic cells are detectable in the condensed mesenchyme but these show no restricted pattern. During bell stage apoptosis is evident in secondary enamel knots, stratum intermedium cells adjacent to the enamel knots and adjacent mesenchyme . All teeth pass through the same developmental stages and consist of the same tissues [4,5]

SIGNALING CENTRE- ENAMEL KNOT

Enamel knot is considered to act as the signaling centre for tooth morphogenesis [6] .The signals of the primary enamel knot is believed to instruct the formation of the secondary enamel knots on the future tips. It is also suggested that there may even be a cellular continuity between the primary and secondary enamel knot due to the migration and division of surviving cells from the former to the latter .The epithelial mesenchymal interactions are largely mediated by exchange of cell signaling proteins and downstream activation of gene transcription. The instructive signals for tooth formation comes from the oral ectoderm and include members of the FGF, BMP ,Wnt ,and Shh families [7]. These proteins bind to receptors on mesenchymal cells which respond by sending signals back to the dental ectoderm . Within the oral ectoderm and mesenchyme planar signaling is also evident .A passive functional role of apoptosis in enamel knots is believed to be the mechanism whereby the function of enamel knots is terminated

APOPTOSIS RELATED MOLECULES

During embryonic programmed cell death different groups of apoptosis regulators have been identified [8].

Cell death signals are communicated through two main types of biochemical pathways in mammalian cells .The intrinsic apoptotic machinery is switched on mainly as a response to DNA damage whereas the extrinsic pathways play a role in developmental apoptosis evoked by extracellular signaling .The intrinsic apoptotic signals originate largely from the mitochondria whereas the extrinsic pathways are triggered by the activation of death receptors belonging to the TNF receptor super family (eg. CD 95,TNFR 1, DR1 , DR2) . These death receptors are found in the plasma membrane of many cells and when triggered by binding of the corresponding cell ligands the receptors initiate the rapid activation of a class of capsases inducing apoptosis execution.

Capsases are key effector components of apoptosis .The 15 mammalian capsases identified so far are produced as inactive zymogens (procapsases). Capsases are divided into two functional subfamilies; Initiator capsases which are involved in upstream regulatory events, and Effector capsases which are directly responsible for cell disassembly events . Till date there is little evidence concerning the molecules involved in the death-receptor mediated signaling during tooth development. The distribution pattern of capsase – 3 positive cells in the odontogenic epithelial tissues of the developing tooth is restricted in the same areas as apoptotic cells [4].

The role of P53 tumor suppressor gene apoptosis is questionable. The general expression pattern suggests that p53 which is strongly expressed in all murine embryonic tissues including tooth germs, may play a role in cell cycle and transcripton regulation rather than in apoptosis in developing teeth [9].

Role of apoptosis in dental development [4]

Multiple roles for apoptosis in odontogenesis have been suggested . Apoptosis may a) play a role in the disruption of dental lamina b) occur in the central cells of the invaginating epithelium during the early and middle bud stage , which may support proliferation of underlying basal, mucosal cells. c) play a role in deciding the final position and size of the tooth in the jaws . d) prevent tooth appositions in edentulous areas by preventing epithelial overgrowth between the teeth. e) play a role in deciding the final number of teeth . f) be an important morphogenic mechanism in shaping the final crown tooth morphogenesis.

Conclusion

The formation of tooth buds of appropriate size and shape at the correct position(odontogenesis) involves regulated cell division and cell death. Apoptosis plays both passive and active roles in bud formation ,morphogenesis, in reduction of the dental lamina and silencing of the enamel knot signaling centres .Apoptosis also has roles in dental diseases and dismorphology but whether these are from primary defects in apoptotic pathways or due to secondary consequence is not yet known .An understanding of the same could provide new modalities of treatment for genetic diseases like hypodontia and agenesis

References

1.Yeldandi AV, Kaufman DG, Reddy JK. Cell injury and cellular adaptations. In Damjanov I, Linder J. eds. Anderson`s pathology 10ed 1996. Mosby Inc.p357-386.

2.Sasaki T. Differentiation and function of osteoclasts and odontoclasts in mineralized tissue resorption. Mic Res Tech 2003;61:483-495.

3. Nishikawa S, Sasaki F. Apoptosis of dental pulp cells and their elimination by macrophages and MHC class II expressing dentritic cells. J His Cyto 1999;47:303-311.4.Lesot H, Vonesch JL, Peterka M, Tureckova J, Peterkova R , Ruch JV .Mouse molar morphogenesis revisited by three dimensional reconstruction .II. Spatial distribution of mitoses and apoptosis in cap to bell staged first and second upper molar teeth. Int J Dev Biol 1996;40:1017-1031.

4. Matalova E, Tucker AS, Sharpe PT. Death in the life of a tooth. J Dent Res 2004;83(1):11-16.

5. Stock DW, Weiss KM, Zhao Z. Patterning of the mammalian dentition in development and evolution . Bioessays1997;19:481-490.

6. Kumar GS .Development and growth of teeth . In: Orbans oral histology and embryology.12th ed.Elsevier 2008.p 22- 44.

7. Thesleff I, Sharpe P.signalling networks regulating dental development. Mech Dev1997; 67:111-123.

8. Meier P ,Finch A ,Evan G .Apoptosis in development .Nature 2000; 407 :796-801

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