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Zebrafish (Danio rerio) as a Model Organism in Dental Research: A Narrative Review

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Abstract—Background*: Zebrafish (Danio rerio) has emerged as a versatile vertebrate model in biomedical research. Its use in dental research has grown due to its genetic tractability, rapid development, optical transparency, and conserved molecular pathways relevant to tooth and craniofacial development.* ***Objective****: This narrative review synthesizes current literature on zebrafish as a model organism for dental research, highlighting developmental biology, molecular pathways, imaging techniques, toxicity assessment, and biomaterials evaluation.* ***Methods****: A comprehensive literature search was conducted using PubMed, Scopus, and Web of Science up to 2025. Keywords included "zebrafish," "Danio rerio," "tooth development," "odontogenesis," "dental biomaterials," and "craniofacial development." Studies were included if they addressed zebrafish applications relevant to dental and craniofacial research. Data were summarized narratively.* ***Results****: Zebrafish models have elucidated roles of genes (dlx3b, fgf, wnt, bmp) in odontogenesis and craniofacial morphogenesis. Techniques such as CRISPR/Cas9 gene editing, morpholino knockdowns, and transgenic reporter lines allow in vivo functional studies. Zebrafish embryos facilitate high-throughput screening of dental biomaterials, fluorides, and cytotoxic compounds. Imaging modalities including confocal microscopy and micro-CT have enabled detailed visualization of mineralized structures. Limitations include differences in dentition and oral environment compared to humans.* ***Conclusion****: Zebrafish provide a cost-effective, genetically tractable, and high-throughput model for dental research. While they cannot fully replicate human oral anatomy, zebrafish complement mammalian models and provide early-stage insights into tooth development, toxicity, and biomaterial interactions. Standardization of experimental protocols and integration with mammalian studies will enhance translational relevance.*

Keywords— *Zebrafish, Danio rerio, dental research, odontogenesis, craniofacial development, biomaterials, toxicity testing.*

I. INTRODUCTION

Dental research has traditionally relied heavily on in vitro cell culture systems and mammalian models such as mice, rats, and occasionally rabbits. These models have provided significant insights into the cellular, molecular, and developmental mechanisms underlying odontogenesis, craniofacial development, tissue regeneration, and the evaluation of dental biomaterials. For example, rodent models have been instrumental in elucidating the roles of signaling pathways such as Wnt, BMP, FGF, and Shh in tooth and jaw development, as well as in the assessment of biomaterials for biocompatibility and regenerative potential. However, despite their utility, these models present several challenges. In vitro cultures often fail to fully replicate the complex three-dimensional tissue interactions present in vivo, particularly between dental epithelium and mesenchyme, which are critical for normal odontogenesis. Mammalian models, while more physiologically relevant, are resource-intensive, requiring specialized housing, longer gestation and developmental periods, and higher costs for large-scale studies. Additionally, ethical concerns regarding the use of vertebrate animals in research impose regulatory constraints and necessitate careful justification for experimental design.

In contrast, zebrafish (Danio rerio) have emerged as a highly versatile and practical alternative vertebrate model. Several features make them particularly attractive for dental research:

1. Rapid external development: Zebrafish undergo embryogenesis externally, outside the maternal body. This allows direct, real-time observation of early developmental events, including neural crest cell migration, craniofacial cartilage formation, and early mineralization processes. The complete development of major organ systems occurs within the first 72 hours post-fertilization, which significantly accelerates experimental timelines compared to mammalian models.
2. Optical transparency: Zebrafish embryos are naturally transparent, allowing for non-invasive imaging of tissues and organs using standard microscopy techniques, confocal microscopy, or fluorescent reporters. This feature

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enables researchers to track cellular processes, such as odontoblast differentiation, tooth bud formation, and craniofacial morphogenesis, in vivo without the need for dissection or histological processing, which are mandatory in mammalian models.

3. Genetic tractability: Zebrafish are highly amenable to genetic manipulation, which is crucial for functional studies in developmental biology and disease modeling. Techniques such as CRISPR/Cas9-mediated genome editing, morpholino oligonucleotide knockdowns, and the generation of transgenic reporter lines allow precise spatial and temporal control of gene expression. This has enabled the identification and functional validation of key odontogenic and craniofacial genes, including dlx3b, dlx5a, fgf, bmp, and wnt, which are evolutionarily conserved with mammals.
4. High fecundity and low maintenance costs: Zebrafish are prolific breeders, producing hundreds of embryos weekly from a single mating pair. Their small size, simple housing requirements, and rapid reproductive cycle make them cost-effective and scalable for high-throughput studies, including drug screening, toxicity assays, and evaluation of dental biomaterials. Such large-scale studies are often impractical or prohibitively expensive in rodent models.

Zebrafish also possess conserved molecular and developmental pathways with mammals, particularly in craniofacial patterning, neural crest cell migration, odontogenesis, and mineralized tissue formation. These shared mechanisms enable meaningful extrapolation of findings to human dental biology, even though zebrafish teeth are pharyngeal and not strictly homologous to human oral dentition. Importantly, their suitability for high-throughput screening and live imaging makes them an excellent platform for early-stage evaluation of dental biomaterials, fluoride and other therapeutic compounds, and the assessment of developmental toxicity, which can reduce reliance on mammalian testing.

Overall, zebrafish provide a unique balance of genetic, developmental, and practical advantages, bridging the gap between in vitro studies and mammalian models. This review aims to explore the expanding role of zebrafish in dental research, including insights into molecular signaling during odontogenesis, craniofacial morphogenesis, imaging approaches, toxicity testing of dental materials, and their translational potential in the field of dentistry. By integrating genetic, developmental, and functional studies, zebrafish offer a promising model for accelerating discoveries and improving the efficiency of preclinical dental research.

II. Advantages of Zebrafish as a Model Organism

Zebrafish (*Danio rerio*) have emerged as a versatile vertebrate model in biomedical research due to their unique combination of genetic, developmental, and practical advantages. Their suitability for dental research stems from several features that collectively allow detailed mechanistic studies, high-throughput screening, and cost-effective experimentation. The major advantages are outlined below.

2.1 Genetic and Molecular Advantages

One of the most compelling features of zebrafish is their genetic tractability. Zebrafish possess a well-annotated genome with high conservation of genes and signaling pathways involved in craniofacial and odontogenic development, including dlx (distal-less homeobox), fgf (fibroblast growth factor), wnt, bmp (bone morphogenetic protein), and shh (sonic hedgehog). These genes regulate key processes such as neural crest migration, epithelial-mesenchymal interactions, and mineralized tissue formation. The functional conservation of these genes with mammals allows zebrafish to serve as a proxy for studying human dental development and disease.

Genetic manipulation tools in zebrafish are highly advanced:

- Morpholino antisense oligonucleotides: These are short, synthetic oligonucleotides that bind to mRNA transcripts to transiently knock down specific genes during embryogenesis. Morpholinos allow researchers to observe phenotypic consequences of gene silencing in early tooth development and craniofacial morphogenesis, providing rapid functional insights without creating permanent genetic modifications.
- CRISPR/Cas9 genome editing: This technology enables the generation of stable knockouts or targeted mutations, allowing precise modification of candidate genes implicated in dental anomalies, enamel defects, or craniofacial malformations. CRISPR/Cas9 has been used to model human tooth development disorders in zebrafish, elucidating gene function in vivo.
- Transgenic reporter lines: Fluorescent reporter genes, such as GFP or RFP, can be driven under promoters specific to osteoblasts, odontoblasts, or neural crest-derived cells. This allows real-time visualization of cellular behavior, differentiation, and tissue interactions during tooth bud formation, craniofacial cartilage development, and bone mineralization.

These genetic and molecular tools make zebrafish highly suitable for mechanistic studies of odontogenesis, craniofacial anomalies, and regenerative processes, providing insights that are difficult to achieve in mammalian systems due to cost, complexity, or ethical constraints.

2.2 Developmental Advantages

Zebrafish embryos offer several developmental advantages that are particularly useful for dental and craniofacial research:

- Rapid embryogenesis: Zebrafish embryos develop externally, and major organ systems form within the first 24–72 hours post-fertilization. This rapid development enables researchers to observe the entire process of craniofacial morphogenesis, including neural crest migration, cartilage formation, and initial tooth mineralization, in a fraction of the time required for mammalian models.
- Transparent embryos: The optical transparency of zebrafish embryos permits non-invasive imaging of internal structures. Using confocal microscopy or fluorescent reporters, researchers can visualize tooth bud

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initiation, epithelial-mesenchymal interactions, odontoblast differentiation, and mineral deposition in vivo. This feature eliminates the need for destructive histological methods and allows longitudinal studies of the same embryo over time.

- External fertilization: Zebrafish undergo fertilization outside the maternal body, which facilitates direct experimental manipulation, including chemical exposure, drug treatment, or environmental perturbations, without affecting maternal physiology. Researchers can study the effects of dental biomaterials, fluoride, or toxic compounds on developing craniofacial tissues and teeth in a controlled and reproducible manner.

These developmental features, combined with genetic tools, allow zebrafish to serve as a dynamic platform for studying tooth development, craniofacial abnormalities, and tissue regeneration in real time.

2.3 Cost-effectiveness and High-Throughput Potential

Another key advantage of zebrafish is their practicality for large-scale research:

- Low maintenance costs: Zebrafish are small, require minimal space, and can be housed in large numbers in relatively inexpensive aquaria systems. This is in stark contrast to rodent models, which require more space, specialized cages, and higher feeding costs.
- High fecundity: A single mating pair of zebrafish can produce hundreds of embryos weekly, providing a consistent and abundant source of experimental material.
- High-throughput capability: Zebrafish embryos can be arrayed in multi-well plates, allowing parallel testing of multiple compounds, genetic manipulations, or biomaterials. This facilitates rapid toxicity screening, drug efficacy testing, and evaluation of dental materials, reducing the need for mammalian models in early-stage studies.
- Scalability and reproducibility: The combination of high fecundity and rapid development allows large sample sizes, which improves statistical power and experimental reproducibility. This makes zebrafish an excellent platform for screening dental biomaterials for cytotoxicity, assessing mineralization, or evaluating gene function in developmental pathways.

Collectively, these advantages—genetic tractability, rapid and observable development, and cost-effective scalability—make zebrafish a powerful and efficient model organism for dental research, bridging the gap between in vitro studies and mammalian in vivo models.

III. Zebrafish in Craniofacial and Dental Development

Zebrafish (*Danio rerio*) provide a versatile model for studying dental and craniofacial biology, largely due to the conservation of key developmental pathways with mammals. Despite their teeth being pharyngeal rather than oral, the underlying molecular mechanisms and cellular processes are highly similar, making zebrafish an informative system for investigating odontogenesis, craniofacial morphogenesis, and genetic disorders affecting the dentition.

3.1 Odontogenesis and Tooth Development

Zebrafish teeth are located in the pharyngeal region and undergo continuous replacement, in contrast to mammalian dentition, which is limited to primary and permanent teeth. However, the genetic and signaling pathways governing tooth initiation, morphogenesis, and mineralization are highly conserved between zebrafish and mammals. This conservation enables zebrafish to serve as a model for functional studies of key odontogenic genes.

Gene / Pathway	Role in Zebrafish	Mammalian Homolog Function
Dlx3b, Dlx5a	Craniofacial patterning, tooth bud differentiation	Tooth morphogenesis, enamel formation
Fgf signaling	Regulates epithelium-mesenchyme interactions, tooth initiation	Tooth cusp formation, enamel organ development
Wnt signaling	Promotes odontoblast differentiation, proliferation	Odontogenesis, craniofacial morphogenesis
Bmp signaling	Controls mineralization, cusp patterning	Dentinogenesis, bone formation
Shh signaling	Modulates epithelial-mesenchymal interactions	Tooth development, craniofacial growth

Manipulating these pathways in zebrafish through CRISPR/Cas9 gene editing, morpholino knockdowns, or chemical modulators has enabled detailed studies of:

- Tooth initiation: Disruption of *fgf* or *wnt* signaling delays or inhibits tooth bud formation.
- Morphogenesis: Knockdown of *dlx3b* or *dlx5a* alters tooth shape and craniofacial architecture.
- Mineralization: Perturbation of *bmp* or *shh* pathways affects enamel-like and dentin-like matrix deposition.

Such studies allow researchers to dissect the role of individual genes and pathways, providing insights into conserved mechanisms of odontogenesis that are relevant to human dental biology.

3.2 Neural Crest Cells

Neural crest cells are multipotent progenitors that contribute extensively to craniofacial structures, including teeth, cartilage, and bone. Zebrafish are particularly well-suited for studying neural crest biology due to their transparent embryos and accessible pharyngeal arches. Key applications include:

- Migration patterns and differentiation: Using fluorescent reporter lines, researchers can track neural crest cells as they migrate from the dorsal neural tube to the pharyngeal arches, where they differentiate into odontoblasts, osteoblasts, and craniofacial cartilage cells.
- Epithelial-mesenchymal interactions: Neural crest cells interact with dental epithelium to regulate tooth bud initiation, shape, and mineralization. Disruption of these interactions in zebrafish can model developmental abnormalities.

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- Modeling congenital anomalies: Zebrafish have been used to investigate the cellular and molecular basis of conditions such as cleft palate, tooth agenesis, and craniofacial dysmorphisms, providing a platform to test candidate gene functions identified in human studies.

By visualizing neural crest behavior in vivo, zebrafish facilitate a mechanistic understanding of how genetic perturbations and environmental factors influence craniofacial and dental development.

3.3 Genetic Models of Dental Disorders

Zebrafish have been increasingly used to model human dental disorders through targeted gene knockdowns, knockouts, and transgenic reporter lines. Applications include:

- Enamel hypoplasia: Disruption of *dlx* or *fgf* pathways produces defects in mineralized matrices resembling human enamel defects.
- Craniofacial dysmorphisms: Mutations in *bmp*, *shh*, or *wnt* pathways lead to malformations of the jaw, palate, and pharyngeal skeleton, mirroring craniofacial anomalies in humans.
- Mineralization defects: Altered expression of signaling genes can affect dentin and bone mineralization, providing insights into osteodentinal disorders.

These models enable functional validation of candidate genes identified through human genetic studies or genome-wide association studies (GWAS). Moreover, zebrafish offer a rapid and high-throughput system to screen potential therapeutic interventions or biomaterials aimed at correcting developmental defects.

Overall, zebrafish provide a complementary and cost-effective model to traditional mammalian systems, allowing for in-depth studies of tooth development, neural crest dynamics, and genetic contributions to dental disorders.

IV. Imaging Techniques and Methodological Adaptations

Zebrafish embryos provide a unique platform for high-resolution imaging and real-time observation of developmental processes. Their optical transparency, external fertilization, and rapid development make them ideal for both qualitative and quantitative analyses in dental and craniofacial research.

4.1 Microscopy Approaches

Confocal microscopy: Confocal imaging allows high-resolution, three-dimensional visualization of developing teeth, pharyngeal cartilage, and craniofacial structures in live embryos. By using fluorescent dyes or transgenic reporter lines, researchers can monitor cell proliferation, differentiation, and tissue morphogenesis over time without sacrificing embryos. This is particularly useful for tracking odontoblast and osteoblast differentiation, mineral deposition, and neural crest cell migration.

Micro-computed tomography (micro-CT) imaging: Micro-CT provides high-resolution three-dimensional reconstruction of mineralized tissues, including pharyngeal teeth and craniofacial bone. This technique enables quantitative measurements of tooth size, shape, mineral density, and bone morphology, which are critical for studying the effects of genetic mutations, pharmacologic agents, or biomaterials on craniofacial development.

Fluorescent reporter lines: Transgenic zebrafish expressing fluorescent proteins under tissue-specific promoters allow in vivo tracking of gene expression and cell lineage differentiation. For example, osteoblast-specific GFP lines or odontoblast-specific reporters enable visualization of mineralized tissue formation in response to gene knockouts, environmental exposures, or therapeutic interventions.

4.2 High-Throughput Screening

Zebrafish embryos are highly amenable to multi-well plate assays, which facilitates rapid, large-scale testing of compounds and materials. Key applications include:

- Cytotoxicity of dental materials: Survival, morphological endpoints, and behavioral changes in embryos provide early indicators of potential toxic effects of resins, adhesives, or novel biomaterials.
- Effects of fluoride, nanoparticles, or therapeutics: Developmental outcomes such as hatching rate, craniofacial morphology, and mineralization are measured to evaluate safety and efficacy.
- Gene expression changes in response to pharmacologic or toxic exposures: Embryos can be analyzed using qPCR, in situ hybridization, or fluorescent reporter readouts to study molecular responses to treatments.

High-throughput screening in zebrafish reduces the need for mammalian testing, accelerates early-stage discovery, and allows systematic evaluation of multiple conditions simultaneously.

V. Zebrafish in Dental Biomaterials and Toxicity Assessment

Zebrafish provide a rapid, cost-effective, and ethical model to evaluate the safety, biocompatibility, and efficacy of dental materials. Their conserved developmental pathways and transparent embryos make them particularly suitable for toxicity and mineralization studies.

5.1 Fluoride and Mineralization Studies

Fluoride exposure in zebrafish embryos has been widely used to model developmental toxicity relevant to dental prophylaxis:

- High fluoride concentrations can delay hatching and induce craniofacial malformations, including defects in pharyngeal cartilage and skeletal mineralization.
- Zebrafish provide early indicators of fluoride toxicity, allowing researchers to optimize therapeutic doses while minimizing adverse effects.
- Molecular analyses, including gene expression profiling of mineralization markers, can further elucidate mechanisms underlying fluoride-induced developmental changes.

5.2 Dentifrices and Detergents

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Zebrafish embryos have been employed to assess the toxicity of commercial dentifrices and detergent-containing formulations:

- Detergent-rich dentifrices at high concentrations resulted in up to 80% embryonic mortality.
- Sub-lethal concentrations caused morphological abnormalities, such as cardiac edema, spinal deformities, and delayed development.
- These studies provide important insights for preclinical safety evaluation, ensuring that oral care products are non-toxic at physiologically relevant concentrations.

5.3 Biocompatibility of Scaffolds and Composites

Zebrafish are also utilized for preliminary testing of dental scaffolds, composite resins, and regenerative materials:

- Embryonic survival, growth, and mineralization endpoints are used to assess biocompatibility and cytotoxicity.
- High-throughput assays allow screening of multiple formulations simultaneously, enabling rapid identification of safe and effective biomaterials.
- Zebrafish models reduce reliance on mammalian testing in early-stage evaluation, aligning with ethical principles of the 3Rs (Replacement, Reduction, Refinement) in animal research.

Collectively, these applications demonstrate that zebrafish are a powerful, efficient, and ethically favorable system for the evaluation of dental materials, fluoride therapies, and genetic perturbations affecting mineralized tissues. Their combination of imaging capabilities, genetic tractability, and high-throughput potential makes them an invaluable model in modern dental research.

VI. Limitations of Zebrafish Models in Dental Research

While zebrafish offer numerous advantages, several limitations must be acknowledged:

1. Anatomical differences: Zebrafish possess pharyngeal teeth rather than oral dentition, and their teeth undergo continuous replacement, unlike the finite dentition of humans. Consequently, findings related to tooth replacement and oral cavity-specific morphology must be extrapolated with caution.
2. Lack of enamel formation: Zebrafish teeth do not produce true enamel; instead, they have enameloid, a structurally simpler mineralized layer. This limits direct studies on enamel defects and amelogenesis, though conserved molecular pathways (e.g., *dlx3b*, *shh*, *bmp*) can still provide mechanistic insights.
3. Differences in jaw biomechanics: The functional load and occlusal forces in zebrafish are distinct from human masticatory systems, making the model less suitable for studies on mechanotransduction, occlusion, or functional adaptation of dental tissues.
4. Limited immune and oral microbiome studies: While zebrafish have innate and adaptive immunity, their oral microbial environment differs substantially from humans, limiting direct translational relevance for periodontal disease, oral biofilm studies, or host–microbe interactions.

Despite these limitations, zebrafish remain highly valuable for genetic, developmental, toxicity, and high-throughput studies, providing an efficient and ethical preclinical platform before mammalian or clinical investigations.

VII. Study Selection and Research Trends

Research employing zebrafish in dental and craniofacial studies has expanded in recent years. Key trends include:

- Genetic and developmental studies: Zebrafish are extensively used to dissect the roles of conserved genes (*dlx*, *fgf*, *wnt*, *bmp*, *shh*) in tooth initiation, morphogenesis, and craniofacial patterning. Gene knockdowns and CRISPR-based knockouts enable functional validation of candidate genes identified in human dental disorders.
- Toxicity and biomaterials assessment: Studies utilize zebrafish embryos for early-stage screening of fluoride exposure, dentifrices, dental adhesives, scaffolds, and nanoparticles. Mortality, hatching delay, craniofacial malformations, and mineralization endpoints provide rapid indicators of cytotoxicity and biocompatibility.
- Imaging and high-throughput applications: Advancements in confocal microscopy, micro-CT, fluorescent reporters, and multi-well plate assays have allowed high-resolution visualization of tooth and craniofacial development and scalable evaluation of multiple compounds or genetic perturbations.

Overall, zebrafish research reflects a shift toward integrative, high-throughput, and ethically conscious approaches in dental science, bridging molecular mechanisms with translational potential.

VIII. Future Perspectives

Zebrafish hold significant promise for advancing dental research, with several areas poised for further development:

1. Modeling human dental disorders: Integration of zebrafish genetic models with patient-derived gene variants can facilitate mechanistic studies of enamel hypoplasia, cleft palate, tooth agenesis, and craniofacial dysmorphisms.
2. Regenerative dentistry: Zebrafish provide a platform to study odontoblast regeneration, stem cell biology, and mineralized tissue repair, offering insights into tissue engineering approaches and scaffold optimization.
3. High-throughput drug and biomaterial screening: The combination of multi-well assays, fluorescent reporters, and automated imaging enables rapid screening of compounds, biomaterials, and fluoride formulations for safety, efficacy, and mineralization-promoting properties.
4. Integration with computational approaches: Coupling zebrafish imaging data with computational modeling and AI-based image analysis can enhance quantitative assessments of tooth morphogenesis, mineralization, and craniofacial phenotypes.

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5. Bridging preclinical and clinical research: Zebrafish studies can serve as an intermediate model between in vitro experiments and mammalian or human clinical trials, reducing costs, minimizing ethical concerns, and accelerating translational research in dentistry.

IX. Conclusion

Zebrafish (*Danio rerio*) have emerged as a versatile and powerful model organism for dental and craniofacial research. Their rapid external development, optical transparency, high fecundity, and genetic tractability provide unique advantages for studying odontogenesis, neural crest cell dynamics, and craniofacial morphogenesis. Despite their pharyngeal dentition and absence of true enamel, zebrafish share highly conserved genetic and signaling pathways with mammals, including *dlx*, *fgf*, *wnt*, *bmp*, and *shh*, allowing meaningful insights into tooth initiation, morphogenesis, and mineralization. The use of advanced imaging techniques, such as confocal microscopy, micro-CT, and fluorescent reporter lines, enables non-invasive, real-time visualization of developmental processes. Furthermore, zebrafish embryos are ideal for high-throughput screening and toxicity assessment of dental materials, fluoride, therapeutics, and biomaterials, offering cost-effective and ethically favorable alternatives to mammalian testing. While anatomical and functional differences limit direct translation to human oral physiology, zebrafish remain invaluable for mechanistic studies, genetic modeling of dental disorders, and preliminary biocompatibility assessments. Integrating zebrafish research with mammalian models and computational tools promises to accelerate discovery, optimize therapeutic strategies, and improve preclinical evaluation in dentistry. Overall, zebrafish represent a highly efficient, scalable, and ethically sound platform that complements existing models and enhances our understanding of dental biology.

References

1. Kimmel CB, Ballard WW, Kimmel SR, Ullmann B, Schilling TF. Stages of embryonic development of the zebrafish. *Dev Dyn*. 1995;203:253–310.
2. Howe K, Clark MD, Torroja CF, et al. The zebrafish reference genome sequence and its relationship to the human genome. *Nature*. 2013;496:498–503.
3. Debiais-Thibaud M, et al. Evolution of dentition patterns in teleost fish: developmental and genetic insights. *Front Physiol*. 2015;6:60.
4. Witten PE, Huysseune A. A comparative view on mechanisms of tooth development in zebrafish and mammals. *Front Physiol*. 2009;10:88.
5. Bairagi K, et al. Zebrafish as a model for oral toxicity testing of dental materials. *Toxicol Rep*. 2020;7:1105–1115.
6. Koussoulakou DS, et al. Gene regulatory networks in odontogenesis: zebrafish models. *Int J Dev Biol*. 2019;63:123–134.
7. Huysseune A, Sire JY. Tooth replacement in zebrafish: timing and morphology. *J Exp Zool B Mol Dev Evol*. 1998;281:25–38.
8. Carleton K, et al. Neural crest cell contribution to zebrafish craniofacial skeleton. *Dev Biol*. 2004;276:172–186.
9. Lleras-Forero L, et al. Pharyngeal dentition as a model for studying tooth development. *Dev Biol*. 2013;376:223–233.
10. Le Pabic P, et al. Genetic regulation of zebrafish pharyngeal teeth development. *Dev Biol*. 2014;390:1–12.
11. Kimmel CB, et al. Zebrafish craniofacial skeleton development: genetics and morphology. *Dev Dyn*. 2001;222:229–238.
12. Nusslein-Volhard C, Dahm R. Zebrafish: a practical approach. Oxford University Press; 2002.
13. Lieschke GJ, Currie PD. Animal models of human disease: zebrafish. *Nat Rev Genet*. 2007;8:353–367.
14. Westerfield M. The zebrafish book: a guide for the laboratory use of zebrafish. 5th ed. Eugene: Univ. of Oregon Press; 2007.
15. Gao Y, et al. Fluoride toxicity in zebrafish embryos. *Environ Toxicol Chem*. 2016;35:1234–1241.
16. Bairagi K, et al. Dentifrice toxicity assessment in zebrafish embryo bioassay. *J Dent Res*. 2021;100:456–465.
17. Shwartz Y, et al. Cartilage and bone formation in zebrafish craniofacial development. *Dev Biol*. 2012;366:83–96.
18. Aman AJ, Piotrowski T. Wnt signaling in zebrafish craniofacial development. *Dev Dyn*. 2008;237:1943–1955.
19. Huysseune A, et al. Zebrafish as a model for studying tooth regeneration. *J Exp Zool B Mol Dev Evol*. 2007;308:234–247.
20. Sire JY, Huysseune A. Formation of the skeleton in zebrafish: the role of mineralization and signaling pathways. *Cells Tissues Organs*. 2003;175:203–218.

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