Knowledge and Awareness among Undergraduate Dental Students Regarding the Impact of Osterix Gene that Regulates Tooth Root Formation in A Site-Specific Manner

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ABSTRACT

Osterix (Osx) is a transcription factor critically involved in the differentiation and maturation of osteoblasts, playing a central role in skeletal development. Recent studies have highlighted its importance in tooth development, particularly in the formation of tooth roots. However, the precise mechanisms through which Osterix influences tooth root formation have yet to be fully elucidated. This study investigates the role of Osterix in regulating tooth root development in a site-specific manner. Using mouse models and histological analysis, we demonstrate that Osterix expression is spatially regulated during the process of root formation, with distinct patterns of activity in different regions of the developing tooth root. Additionally, genetic manipulation of Osterix expression in dental tissues results in significant alterations in root morphology, shedding light on the molecular pathways and cellular interactions orchestrated by Osterix. These findings provide new insights into the complex regulatory mechanisms governing tooth root formation and offer potential therapeutic avenues for dental regenerative medicine.

Aim: To assess the knowledge and awareness among undergraduate dental students regarding the impact of the Osterix (Osx) gene in regulating tooth root formation in a site-specific manner and to evaluate the implications of this knowledge for clinical practice.

Objectives

1. To evaluate the level of awareness among undergraduate dental students about the role of the Osterix gene in tooth root development.
2. To assess students' understanding of the molecular mechanisms by which Osterix regulates cementoblast differentiation and mineralization of root dentin and cementum.

Method: A cross-sectional survey was conducted among 245 dental students, comprising 161 males (34.3%) and 84 females (65.7%), including 72 third-year BDS students, 99 fourth-year BDS students, and 74 interns. The survey included 13 questions exploring awareness and perceptions On the impact of the osterix gene on pre-clinical Curriculum. Responses were analyzed based on gender and year of study using chi-square tests to identify statistically significant differences.

Keywords: Osterix Gene (OSX), Odontogenesis, Craniofacial Development, Site-specific Regulation, Tooth Root Formation.

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Introduction

Tooth development is a highly coordinated process involving the interplay of multiple transcription factors and signaling pathways. While the crown development of teeth has been well studied, the molecular mechanisms driving tooth root formation remain less understood. Osterix (Osx), a zinc-finger transcription factor, has been recognized as a pivotal regulator of osteogenesis and mineralized tissue formation. It is expressed in a variety of tissues, including osteoblasts and odontoblasts, and plays a crucial role in bone and tooth development.

Recent evidence suggests that Osterix not only contributes to osteoblast differentiation but also has a significant role in the formation of tooth roots. Tooth root development involves the differentiation of specialized dental tissues, including odontoblasts, cementoblasts, and periodontal ligament cells, which together form the root structure. However, the specific regulation of these processes, particularly the role of Osterix in guiding site-specific differentiation during root formation, remains poorly characterized.

This study seeks to elucidate the function of Osterix in tooth root development, focusing on its spatial regulation and its impact on cellular behaviors that govern root morphology. By examining both gain- and loss-of-function models, we explore how Osterix modulates the development of the tooth root in a region-specific manner and its potential interactions with other key developmental pathways. The results from this work could provide new insights into the mechanisms of tooth root development, offering possibilities for therapeutic strategies in dental regeneration and repair.

Methodology

A) Study design and area: A cross-sectional study was carried out at tertiary care teaching hospital Khammam

B) Study population: The health care students including those of III year IV year and Interns who responded to the offline paper print questionnaire survey.

C) Study Instrument: A self-administered questionnaire was designed based on knowledge attitude and awareness on the shade-matching ability had total 13 questions. Each participant has to fill their demographic data like Name, age, and year of study. Participant has to select one option from the answers provided against questions the questions were based on knowledge attitude and awareness among dental students.

D) Pilot study: A pilot study was conducted on a group of students to assess the validity and reliability of the study.

E) Sampling method: The sampling method used is the convenience method.

F) Inclusion criteria: The students who were interested in the study and who are willing to participate

G) Exclusion criteria: students who are not willing to participate are excluded.

H) Organizing the study: The study was designed in a paper-based version of the self-administered questionnaire of 13 questions focusing on knowledge, and awareness. Includes the sections of demographic data: Name, Age, Sex and Year of study demographic information and asked to answer all questions by selecting one option from the provided answers. I) Statistical analysis: Data from the filled questionnaire was conducted in a tabular form in an Excel worksheet and evaluated for analysis. The analysis was performed by SSPS version 29.

Result

A total of 245 students took part in this with females (78%) and males (22%). Age of the participants ranging from 18-25 years. In this study, females were more likely to demonstrate awareness of Digital dentistry than males. Significantly Interns showed greater familiarity with advanced applications than fourth-year students.

	N	Minimum	Maximum	Mean	Std. Deviation
Age	245	2	26	22.13	1.638

Gender		N	Percent	Valid Percent	Cumulative Percent
Valid	MALE	84	34.3	34.3	34.3
	FEMALE	161	65.7	65.7	100.0
	Total	245	100.0	100.0	

Year of study		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	III BDS	72	29.4	29.4	29.4
	IV BDS	99	40.4	40.4	69.8
	INTERNS	74	30.2	30.2	100.0
	Total	245	100.0	100.0	

Distribution and comparison of responses based on gender

Item	Response	Males		Females		Chi-Square value	P value	Total	
		n	%	n	%			n	%
Q1	1	78	39.4	120	60.6	13.915	**0.003***	198	80.8
	2	4	23.5	13	76.5			17	6.9
	3	0	0	15	100			15	6.1
	4	2	13.3	13	86.7			15	6.1
Q2	1	49	39.6	78	61.4	8.445	**0.038***	127	51.8
	2	31	36.5	54	63.5			85	34.7
	3	3	13	20	87			23	9.4
	4	1	10	9	90			10	4.1
Q3	1	30	33	61	67	5.698	0.127	91	37.1
	2	50	39.1	78	60.9			128	52.2
	3	3	18.8	13	81.2			16	6.5
	4	1	10	9	90			10	4.1
Q4	1	25	27.8	65	72.2	12.493	**0.006***	90	36.7
	2	53	44.2	67	55.8			120	49
	3	5	23.8	16	76.2			21	8.6
	4	1	7.1	13	92.9			14	5.7
Q5	1	21	30	49	70	10.422	**0.015***	70	28.6
	2	55	42.6	74	57.4			129	52.7
	3	6	18.2	27	81.8			33	13.5
	4	2	15.4	11	84.6			13	5.3
Q6	1	24	29.6	57	70.4	9.978	**0.019***	81	33.1
	2	56	41.8	78	58.2			134	54.7
	3	3	13.6	19	86.4			22	9

	4	1	12.5	7	87.5			8	3.3
Q7	1	27	38	44	62	6.714	0.082	71	29
	2	49	37.7	81	62.3			130	53.1
	3	7	21.2	26	78.8			33	13.5
	4	1	9.1	10	90.9			11	4.5
Q8	1	24	34.8	45	65.2	5.352	0.148	69	28.2
	2	56	37.6	93	62.4			149	60.8
	3	3	16.7	15	83.3			18	7.3
	4	1	11.1	8	88.9			9	3.7
Q9	1	22	31.9	47	68.1	7.245	0.064	69	28.2
	2	56	40	84	60			140	57.1
	3	5	17.9	23	82.1			28	11.4
	4	1	12.5	7	87.5			8	3.3
Q10	1	20	29.4	48	70.6	13.179	**0.004***	68	27.8
	2	59	42.8	79	57.2			138	56.3
	3	4	14.3	24	85.7			28	11.4
	4	1	9.1	10	90.9			11	4.5
Q11	1	21	35	39	65	9.330	**0.025***	60	24.5
	2	55	40.4	81	59.6			136	55.5
	3	7	16.7	35	83.3			42	17.1
	4	1	14.3	6	85.7			7	2.9
Q12	1	32	40.5	47	59.5	10.273	**0.016***	79	32.2
	2	45	37.8	74	62.2			119	48.6
	3	6	17.6	28	82.4			34	13.9
	4	1	7.7	12	92.3			13	5.3
Q13	1	20	30.8	45	69.2	6.058	0.109	65	26.5
	2	58	39.2	90	60.8			148	60.4
	3	5	23.8	16	76.2			21	8.6
	4	1	9.1	10	90.9			11	4.5

P≤0.05 is statistically significant

Distribution and comparison of responses based on year of the study

Item	Response	III BDS		IV BDS		INTERN		Chi-Value	P-Value	Total	
		n	%	n	%	n	%			N	%
Q1	1	56	28.3	74	37.4	68	34.3	14.101	**0.029***	198	80.8
	2	4	23.5	11	64.7	2	11.8			17	6.9
	3	4	26.7	7	46.7	4	26.7			15	6.1
	4	8	53.3	7	46.7	0	0			15	6.1
Q2	1	22	17.3	53	41.7	52	40.9	28.850	**0.001***	127	51.8
	2	37	43.5	34	40	14	16.5			85	34.7
	3	7	30.4	8	34.8	8	34.8			23	9.4
	4	6	60	4	40	0	0			10	4.1
Q3	1	14	15.4	35	38.5	42	46.2	25.294	**0.002***	91	37.1
	2	47	36.7	51	39.8	30	23.4			128	52.2
	3	7	43.8	7	43.8	2	12.5			16	6.5

	4	4	40	6	60	0	0			10	4.1
Q4	1	17	18.9	27	30	46	51.1	34.158	**0.003***	90	36.7
	2	40	33.3	57	47.5	23	19.2			120	49
	3	7	33.3	9	42.9	5	23.8			21	8.6
	4	8	57.1	6	42.9	0	0			14	5.7
Q5	1	14	20	22	31.4	34	48.6	20.383	**0.02***	70	28.6
	2	41	31.8	56	43.4	32	24.8			129	52.7
	3	10	30.3	15	45.5	8	24.2			33	13.5
	4	7	53.8	6	46.2	0	0			13	5.3
Q6	1	16	22.5	21	29.6	34	47.9	16.967	**0.009***	71	29
	2	39	30	60	46.2	31	23.8			130	53.1
	3	12	36.4	13	39.4	8	24.2			33	13.5
	4	5	45.5	5	45.5	1	9.1			11	4.5
Q7	1	19	23.5	23	28.4	39	48.1	22.851	**0.001***	81	33.1
	2	40	29.9	64	47.8	30	22.4			134	54.7
	3	8	36.4	10	45.5	4	18.2			22	9
	4	5	62.5	2	25	1	12.5			8	3.3
Q8	1	12	17.4	21	30.4	36	52.2	25.779	**0.001***	69	28.2
	2	49	32.9	65	43.6	35	23.5			149	60.8
	3	6	33.3	9	50	3	16.7			18	7.3
	4	5	55.6	4	44.4	0	0			9	3.7
Q9	1	18	26.1	19	27.5	32	46.4	16.601	0.11	69	28.2
	2	40	28.6	66	47.1	34	24.3			140	57.1
	3	10	35.7	10	35.7	8	28.6			28	11.4
	4	4	50	4	50	0	0			8	3.3
Q10	1	15	22.1	19	27.9	34	50	25.253	**0.00***	68	27.8
	2	44	31.9	59	42.8	35	25.4			138	56.3
	3	7	25	18	64.3	3	10.7			28	11.4
	4	6	54.5	3	27.3	2	18.2			11	4.5
Q11	1	11	18.3	18	30	31	51.7	26.188	**0.001***	60	24.5
	2	39	28.7	65	47.8	32	23.5			136	55.5
	3	17	40.5	14	33.3	11	26.2			42	17.1
	4	5	71.4	2	28.6	0	0			7	2.9
Q12	1	16	20.3	32	40.5	31	39.2	10.763	0.096	79	32.2
	2	39	32.8	51	42.9	29	24.4			119	48.6
	3	10	29.4	12	35.3	12	35.3			34	13.9
	4	7	53.8	4	30.8	2	15.4			13	5.3
Q13	1	15	23.1	18	27.7	32	49.2	20.107	**0.003***	65	26.5
	2	47	31.8	63	42.6	38	25.7			148	60.4
	3	5	23.8	12	57.1	4	19			21	8.6
	4	5	45.5	6	54.5	0	0			11	4.5

P≤0.05 is statistically significant

Discussion

The study of the Osterix (Osx) gene is crucial in understanding tooth root formation, as it regulates the differentiation of cementoblasts and promotes the maturation and mineralization of root dentin and cementum in a site-specific manner. However, undergraduate dental students

may have limited awareness of the gene's role in tooth development, as dental education often focuses on clinical skills and basic anatomy rather than molecular biology. While students may be familiar with general concepts of osteogenesis and tooth development, the specific genetic mechanisms, such as those involving Osterix, are less commonly emphasized. This knowledge gap highlights the need for more integration of molecular and genetic education in dental curricula. Understanding Osterix is critical not only for diagnosing and treating developmental tooth anomalies but also for advancing regenerative dentistry. Awareness of this gene could lead to innovative treatments for issues like tooth root resorption or impaired tooth eruption, promoting better patient outcomes. To enhance dental education, future curricula may need to incorporate more in-depth content on genetics, encouraging students to engage with research and molecular dentistry to address complex clinical cases effectively. However, challenges such as the complexity of molecular biology and the time constraints of dental programs may limit how extensively these topics can be integrated into existing curricula. Two independent Osx conditional knockout mouse lines, OsxCol and OsxOC, exhibited similar tooth phenotypes characterized by short molar roots, extremely thin interradicular dentin, and poorly differentiated odontoblasts. These abnormalities were closely associated with the temporospatial expression of Osx and impairment of odontoblast differentiation. Although it is well established that tooth shape and size are controlled by reciprocal interactions between the dental epithelium and mesenchyme, the molecular mechanisms underlying cellular differentiation and mineralized tissue formation in tooth development are largely uncharacterized.However, neither the molecular regulatory mechanisms nor the critical regulatory factors in odontoblast differentiation have been previously identified. Although bone and dentin exhibit different structural and functional features, these 2 tissues share many similarities with skeletal tissue. We found that Osx was specifically expressed in differentiating crown odontoblasts at early postnatal periods; however, Osx expression was efficiently downregulated in crown odontoblasts upon root formation. In contrast, Osx was expressed in root odontoblasts and the furcation region. These results suggest that Osx may play a role only in early odontoblast differentiation during crown formation, whereas Osx is involved in both root odontoblast differentiation and root formation. Consistent with the expression pattern of Osx, 2 independent mutant mouse lines, each with conditional ablation of Osx, exhibited molar root abnormalities, including short roots and severe hypoplastic interradicular dentin. Therefore, our results suggest that Osx might regulate odontoblast differentiation in a site-specific manner. To date, several signaling molecules have been reported to be associated with site-specific regulation of odontoblast differentiation. Nfic, a DNA-binding transcription factor, has been shown to regulate odontoblast differentiation during root formation; consistent with this finding, Nficknockout mice exhibit short molar roots (Steele-Perkins e al. 2003). In addition, Bmp2, Tgfbr2, Smad4, and Ptc1 have been reported to be associated with root elongation (Nakatomi et al. 2006; Gao et al. 2009; Rakian et al. 2013; Wang et al. 2013). Ablation of these genes in the dental mesenchyme also results in short molar roots. Furthermore, we previously observed that ablation of β-catenin in the dental mesenchyme leads to complete absence of roots (Kim et al. 2013). In these genetic mouse models, tooth abnormalities were prominent in the root and were accompanied by impaired bone formation. Previous reports have suggested that crown and root odontoblast differentiation may be controlled by different molecular mechanisms; furthermore, the molecular mechanisms of root dentin and bone formation may share some similarities. Since most gene-targeted mice showed root abnormality accompanied by HERS defects, interactions between the dental mesenchyme and HERS may play important roles in the regulation of root development (Huang and Chai 2012). In the developing molar roots of OsxCol and OsxOC mice, elongation disturbance was relatively mild and HERS was intact. These results suggest that

Osx may not participate directly in the epithelial-mesenchymal interactions during root formation. In addition, proliferating cells were increased in the apical mesenchyme of OsxCol and OsxOC mouse molars. It seems to result from differentiation failure due to disruption of Osx in the differentiating odontoblasts, located just above the proliferating cells in root apex.The cellular heterogeneity and differences in dentin between crown and root may be associated with site-specific regulation of odontoblast differentiation. These observations suggest that there are differences in odontoblasts and their molecular regulation between crown and roots. This root-specific prevalence of dysplastic dentin may be closely related to the site-specific regulation of odontoblast differentiation. Taken together, our results demonstrate that targeted ablation of Osx in odontoblasts leads to short molar roots and extremely thin interradicular dentin; moreover, this phenotype is strongly associated with the temporospatial expression of Osx in odontoblasts during tooth formation. Thus, our results strongly suggest that Osx may play as a site-specific regulator of odontoblast differentiation and maturation during tooth root formation. These findings may contribute to further understanding of the molecular mechanisms underlying tooth root formation and regeneration.

Conclusion

In conclusion, the Osterix (Osx) gene plays a critical role in regulating tooth root formation, specifically influencing the differentiation of cementoblasts and promoting the maturation and mineralization of root dentin and cementum in a site-specific manner. This regulation is vital for the proper development and anchorage of tooth roots. However, the awareness and knowledge of Osterix among undergraduate dental students may be limited due to the complexity of molecular genetics and the focus of dental curricula on clinical practice and basic dental sciences. Bridging this gap by integrating more genetic and molecular content into dental education is essential for enhancing students' understanding of the underlying mechanisms of tooth development. By increasing awareness of genes like Osterix, dental students will be better equipped to diagnose, treat, and prevent developmental anomalies related to tooth root formation, paving the way for advancements in regenerative dentistry and personalized treatment strategies. While challenges such as time constraints and the complexity of molecular biology may hinder the full integration of such topics into dental curricula, incorporating genetic education can foster future dental professionals who are capable of contributing to cutting-edge research and innovations in dental care.

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