Journal of Oral Biosciences ■ (■■■■) ■■■–■■■

Contents lists available at ScienceDirect

Journal of Oral Biosciences

journal homepage: www.elsevier.com/locate/job

Editorial

Oral Biosciences: The annual review 2016

ARTICLE INFO

Keywords:
Physiology
Carcinogenesis
Tooth
Dentin
Microbiome

ABSTRACT

Background: The *Journal of Oral Biosciences* is devoted to the advancement and dissemination of fundamental knowledge concerning every aspect of oral biosciences.
Highlight: This review article features the following topics presented in symposia that were held during the annual meeting of the Japanese Association for Oral Biology: "Frontiers of oral physiology," "Genetic and epigenetic changes to determine development, differentiation, and carcinogenesis," "Analytical methods and interpretation of variation in tooth morphology," "Regulatory mechanisms of vertebrate developmental body plan revealed by live-imaging and mathematical analyses," "Studies on dentin sialophosphoprotein (DSPP) through morphological and functional perspectives," and "Oral biofilm and microbiome research".
Conclusion: These published reviews in the *Journal of Oral Biosciences* have inspired the readers of the Journal to broaden their knowledge regarding the various aspects of Oral Biosciences. The current editorial review introduces these exciting review articles.

1. Introduction

In addition to original articles, the *Journal of Oral Biosciences* publishes review articles by prize-winners of the "Lion Dental Research Award" and the "Rising Members Award," which are presented by the Japanese Association for Oral Biology. The Journal also publishes review articles featuring recent information presented in symposia held during the annual meeting of the Association. In 2016, the Journal published special issues featuring the following reviews: "Frontiers of oral physiology," "Genetic and epigenetic changes to determine development, differentiation, and carcinogenesis," "Analytical methods and interpretation of variation in tooth morphology," "Regulatory mechanisms of vertebrate developmental body plan revealed by live-imaging and mathematical analyses," "Studies on dentin sialophosphoprotein (DSPP) through morphological and functional perspectives," and "Oral biofilm and microbiome research." These reviews in the *Journal of Oral Biosciences* have inspired the readers of the Journal to broaden their knowledge on different aspects of Oral Biosciences. The current editorial review introduces these exciting review articles.

2. Frontiers of oral physiology

Sweet, bitter, salty, sour, and umami are recognized as the five basic taste qualities. These different taste qualities are detected by taste cells (TCs) in taste buds located on the tongue and the palate. Recent studies in rodents have demonstrated that subsets of TCs express gut peptides that are important in energy metabolism, such as glucagon-like peptide-1 (GLP-1) [1], neuropeptide Y [2], glucagon [3], ghrelin [4], vasoactive intestinal peptide [5], and cholecystokinin [6]. The expression patterns of these peptides are correlated with specific markers for TCs. These findings raised the possibility that GLP-1 in TCs may contribute to signal transmission from TCs to gustatory nerve fibers. In their review article, Ninomiya and colleagues discussed the function of GLP-1 expressed in TCs [7]. GLP-1 signaling may contribute to oral sweet and lipid sensing in mice [8–10]. *Glucagon-like peptide-1 receptor* (*GLP-1R*) null mice had diminished behavioral responses to sugars and artificial sweeteners, and exhibited higher thresholds for long chain fatty acid detection compared to those found in wild-type mice. GLP-1 is released from a subset of sweet-sensitive TCs immediately after sweet stimulation. GLP-1 injected in the femoral vein directly activates a subset of sweet-sensitive nerve fibers, and these responses are blocked by pre-treatment with a GLP-1R antagonist. Therefore, GLP-1 released from TCs may be involved in the transmission of sweet and lipid signals, and thereby affecting animal feeding behavior in response to these important nutrient factors.

Flavor is an integrative sensation comprised of taste, odor, and mouthfeel. The interaction between olfactory cues and taste is particularly important for flavor formation [11]. However, it is not entirely understood how and where in the brain that odor information is processed for the formation of flavor. One candidate region is the insular cortex (IC), which integrates chemical senses. Mizoguchi and colleagues discussed the IC as a potential region for the integration of disparate types of chemosignals in animals and humans in their review article [12]. They introduced their own research for the possible role of the IC, which included morphological evidence of bidirectional connections between the piriform

http://dx.doi.org/10.1016/j.job.2016.12.001
1349-0079/

cortex (PC) and the IC [13–15]. In addition, functional data [16] support the notion that odor information is integrated with taste information in the agranular IC (AI) to form flavors. Thus, the AI may be involved in the formation and/or discrimination of food flavors. While the formation or integration of flavors performed in the AI may involve functions of the prefrontal cortex (PFC), it is possible that other brain areas including the endopiriform nucleus, the claustrum, and others also participate in flavor formation. Nevertheless, the role of the IC in the formation of flavor is supported by several findings that the IC and/or surrounding brain areas have important roles in the convergence of odor and taste information.

3. Genetic and epigenetic changes to determine development, differentiation, and carcinogenesis

Cancer remains the leading cause of death throughout the world. The major challenges encountered in cancer therapy are side effects because of chemotherapy, metastasis, and the recurrence of drug-resistant cancers. Tumor formation is a multi-step process from initiation to promotion and progression. Tumor progression is largely dependent on the overexpression of tumor-promoting genes (oncogenes and stimulators) and the dysfunction of tumor-suppressing genes (suppressors) striking a balance between the cell-generating effects of mitosis and apoptotic cell death [17]. Therefore, increasing the amount or activity of a tumor suppressor may be a viable alternative strategy to avoid or mitigate side effects. Hata and colleagues described their strategy to identify CXC chemokine ligand 14 (CXCL14) and the characteristics of *CXCL14* transgenic (Tg) mice in their review article [18]. CXCL14, which is also known as breast and kidney expressed chemokine, was significantly downregulated in cultured HSC-3 cells, which are derived from a head and neck squamous cell carcinoma (HNSCC) cell line cultured under serum-free conditions and treated with epidermal growth factor. Interestingly, the expression of CXCL14 was reduced in tissues from patients with HNSCC [19]. This review is based on their previous study using Tg mice overexpressing *CXCL14*, which found that this chemokine is an extracellular multistep tumor suppressor [20]. These Tg mice had a suppressed rate of carcinogenesis, decreased transplanted tumor volumes, and reduced pulmonary metastasis in addition to an increased survival rate following tumor cell injection compared to that found in wild type mice. In addition, *CXCL14*-overexpressing Tg mice had no apparent abnormality up to 2 years old, a finding that corresponds to a report on a normal human individual without any apparent abnormalities who had a 10-fold higher blood level of CXCL14 than average. These findings indicate that CXCL14 expressed at high levels do not cause severe side effects and therefore, demonstrates that CXCL14 may be a promising molecular target for cancer suppression or prevention.

The coordinated regulation of epigenetic modifications is essential for the establishment of cell identity, and its disruption leads to phenotypic alterations that underlie human cancer and other pathologies [21]. It has been reported that oncogenic reprogramming of gene expression patterns caused by epigenetic alterations result in aggressive behavior of cancer cells, such as the epithelial–mesenchymal transition (EMT), which is characterized by the loss of epithelial markers and the induction of mesenchymal markers [22,23]. Yamazaki and colleagues reviewed the molecular mechanisms by which the *keratin 13 (KRT13)* gene is epigenetically silenced in oral squamous cell carcinoma (OSCC) cells [24]. KRT13, which is an epithelial cytoskeletal protein, is epigenetically repressed through aberrant H3K27me3 expression that is mediated by polycomb repressive complex 2 (PRC2) in poorly differentiated OSCC cells. In addition, H3K27me3 expression is mediated by the potent PRC2 inhibitor, 3-deazaneplanocin A (DZNep), which effectively activates transcription of *KRT13* and other epithelial markers, while suppressing mRNA expression of genes that mediate the aggressive behavior of tumor cells [25,26]. The authors discussed their findings of the effects of epigenetic alterations of *KRT13* and the suppressive effects of PRC2 depletion by the pharmacological inhibitor, DZNep, on the aggressive characteristics of OSCC cells. The identification of epigenetic alterations that underlie OSCC will be useful for the development of epigenetic biomarkers for the diagnosis, prognosis, and discovery of novel therapeutic targets for OSCC.

4. Analytical methods and interpretation of variation in tooth morphology

Tooth form is affected by genetic, environmental, and epigenetic factors [27,28]. In the field of paleoanthropology, tooth form has significantly contributed to the elucidation of evolution from fossil hominids to modern humans based on comparisons of the teeth of fossil remains and extant species. From an anthropological perspective, the analysis of tooth morphological data can aid reconstruction of life history from archeological human remains. In their review article, Kondo and Manabe reviewed the outcomes of numerous studies based on tooth morphology to analyze the following two issues [29]: (1) How has tooth structure been represented in publications to date? That is, how has tooth form been measured or observed? In addition, how have morphological variations of teeth been described? (2) What are the issues that can be clarified with further development of the analytical methods used for tooth morphology? The current analytical methods of tooth structure have provided results on the description of sexual dimorphism, the discussion of population history, the analysis of hereditary, environmental, and epigenetic factors, the discussion of the phylogenetic significance of dental traits, the analysis of teeth asymmetry, and secular trends of tooth size. Recent advances in molecular biology have demonstrated that the odontogenetic homeobox code model of dental patterning proposes candidate genes have specific roles in directing mesenchymal cells to follow a molar or an incisor pathway [30]. The enamel knot is a signaling center of the tooth germ and has a significant morphological role during developmental stages [31]. Recently, tooth evolution has been discussed in association with the developmental process [32], and over the past few decades, the morphological data of teeth have been discussed from both morphological and anthropological perspectives. Kondo and Manabe emphasized that morphologists should intensify their exchanges with molecular biologists to integrate tooth morphogenesis and the genetic basis of tooth structure.

Because of the inherent hardness of tooth enamel and dentin, dental remains are often well preserved in geological deposits and archeological sites, and constitute a major part of fossil and archeological human skeletal collections. The basement membrane between the inner enamel epithelium and the dental mesenchyme in the tooth germ is preserved in a fully formed tooth crown as the enamel–dentin junction (EDJ), whereas the outer enamel surface (OES) is a culmination of enamel deposition above this basement membrane. EDJ and OES morphologies have been intensively studied as important sources of information from both taxonomic and phylogenetic perspectives [33–35]. Recently developed micro-computed tomography (μCT) techniques have facilitated observation of the inner morphological structures of teeth. Three-dimensional (3D) models can be reconstructed from μCT images to enable a more detailed assessment of their morphology. In his review article, Morita introduced μCT-based comparative studies of the EDJ and OES from four perspectives: size and shape