Many lower vertebrate animals are able to renew their teeth repeatedly throughout their lifetime. However, extant mammals can either renew their teeth only one time (i.e., diphyodont dentition) or not at all (i.e., monophyodont dentition). Humans, for example, replace their milk teeth with permanent teeth, and then, they lose their ability to renew.

To gain insight into why mammals do not continue to renew their teeth, we examined the molecular and cellular mechanisms underlying this process. The dental lamina plays a pivotal role in this process by providing odontogenic stem cells for tooth renewal (1, 2). Mammals, such as young postnatal ferrets, regenerate permanent teeth from the dental lamina, which is connected to the lingual side of the deciduous tooth (1). Geckos, which can renew their teeth multiple times, localize their putative stem cells to the lingual portion of the dental lamina (3).

We searched for a living lower vertebrate animal that would be a good model in which to study tooth renewal. Of these animals, crocodilians are closest to mammals from the perspectives of phylogeny, tooth structure, tooth embedding, and palate structure. Additionally, crocodilian teeth can undergo life-long renewal (4). Here, we integrate our knowledge of ectodermal organ epithelial–mesenchymal interactions to study the molecular and cellular basis of alligator tooth renewal. Each adult American alligator tooth becomes a complex tooth family (Fig. P1D), which includes a functional tooth, a replacement tooth, and a dental lamina at each tooth position.

In summary, alligators have a putative stem cell niche in the distal dental lamina that resides in a socket, which structurally resembling mammals. Thus, we showed that the alligator dental lamina has a higher level of regional organization than squamata reptiles (3). In alligators, functional states may be maintained by complex adjacent dermal niches that change dynamically during the tooth renewal cycle. Our data suggest that ectodermal organs can undergo episodic remodeling for tooth replacement throughout the cycle.


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renewal repetitively using different strategies. This study on alligator tooth renewal may inspire future bioengineering applications for human tooth replacement.