Study of alligator dental regeneration process may lead to tooth regeneration in humans

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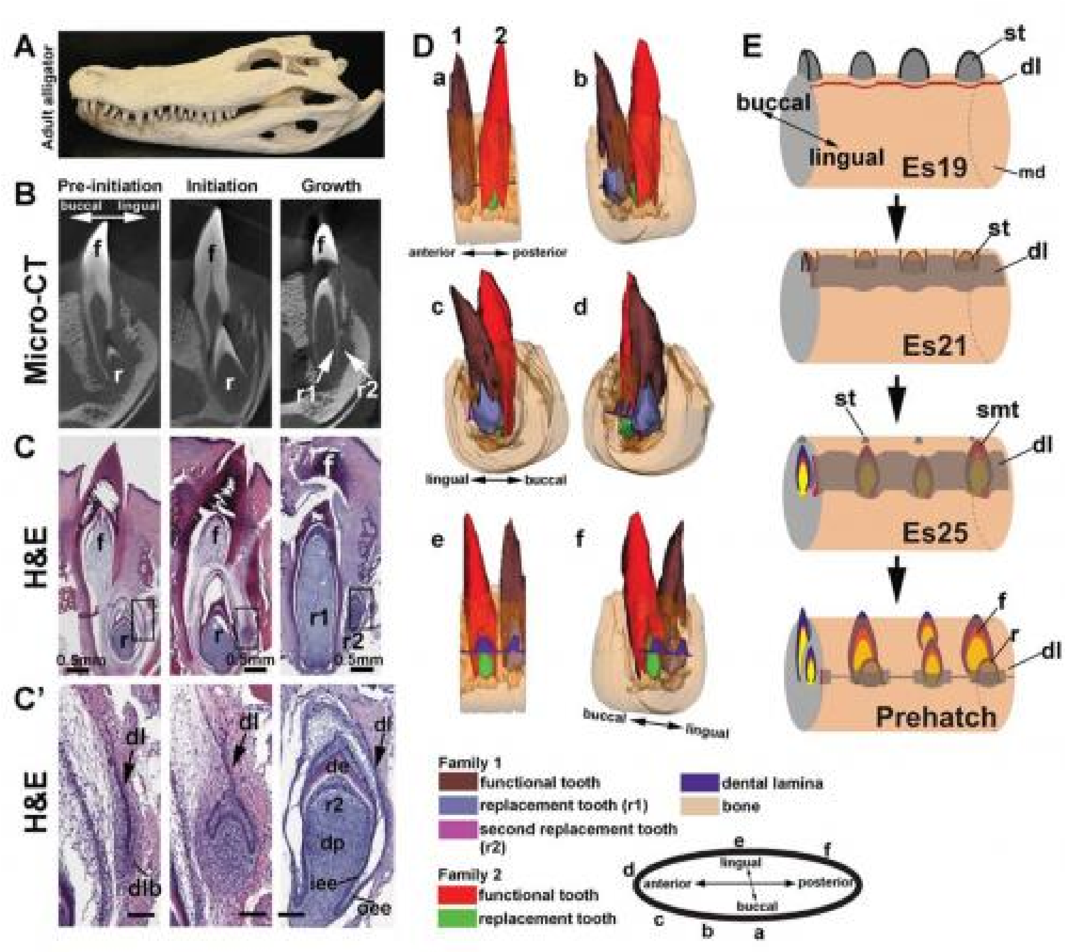

Alligator teeth are arranged in tooth family units with 3 members at each position, enabling repetitive replacement. Credit: PNAS, doi: 10.1073/pnas.1213202110

(Phys.org) —A team of researchers from the U.S., Taiwan and China analyzing tooth regeneration in alligators reports that a similar process might possibly be instigated in humans through artificial means. In their paper published in the *Proceedings of the National Academy of Sciences*, the team describes how they uncovered the tooth regeneration process in alligators and why it might apply to human dentistry.

Scientists have long known that tooth regeneration occurs in alligators, but until now, most believed the process followed a schedule—like snakes shedding their skin or birds molting. This new research indicates that the process is actually an on-demand system—when a tooth is lost, a new tooth re-grows in its place. This is an exciting development because alligator tooth structure is very similar to human tooth structure.

To find out what actually occurs with alligator tooth replacement, the research team used a variety of techniques (x-rays, tissue analysis, etc.) to study the tooth structure of embryonic, hatchling and three year old alligators. They found that the structure was made up of three parts: a mature tooth, an immature replacement tooth-in-waiting and tissue with stem cells in it. By extracting teeth from a juvenile they were able to watch the tooth replacement process in action. They found that upon loss of a tooth, the tooth-in-waiting began to mature and the tissue with stem cells in it formed a bulge that over time caused the development of a new tooth-in-waiting. The process in alligators is so effective, the researchers found, that all of their 80 teeth are replaced an average of 50 times over their lifetime.

The researchers note that because of tooth structure similarity between humans and alligators, it might be possible one day to coax new teeth to grow to replace those that are lost. This is because other studies have shown that humans also have stem cell tissue beneath their teeth. It's responsible for replacing baby teeth with adult teeth and in rare cases for a condition known as supernumerary teeth—where people grow extra teeth. In humans, the stem cells are believed to shut off after doing their job just once. If a way could be found to turn them back on again, the researchers suggest, it might be possible to cause new teeth to grow when old ones are lost.

More information: Specialized stem cell niche enables repetitive renewal of alligator teeth, *PNAS*, Published online before print May 13, 2013, doi: 10.1073/pnas.1213202110

Abstract
Reptiles and fish have robust regenerative powers for tooth renewal. However, extant mammals can either renew their teeth one time (diphyodont dentition) or not at all (monophyodont dentition). Humans replace their milk teeth with permanent teeth and then lose their ability for tooth renewal. Here, we study tooth renewal in a crocodilian model, the American alligator, which has well-organized teeth similar to mammals but can still undergo life-long renewal. Each alligator tooth is a complex family unit composed of the functional tooth, successional tooth, and dental lamina. Using multiple mitotic labeling, we map putative stem cells to the distal enlarged bulge of the dental lamina that contains quiescent odontogenic progenitors that can be activated during physiological exfoliation or artificial extraction. Tooth cycle initiation correlates with β-catenin activation and soluble frizzled-related protein 1 disappearance in the bulge. The dermal niche adjacent to the dermal lamina dynamically expresses neural cell adhesion molecule, tenascin-C, and other molecules. Furthermore, in development, asymmetric β-catenin localization leads to the formation of a heterochronous and complex tooth family unit configuration. Understanding how these signaling molecules interact in tooth development in this model may help us to learn how to stimulate growth of adult teeth in mammals.

Press release