Activating tooth regeneration in mice

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Most reptiles and fish have multiple sets of teeth during their lifetime. However, most mammals, such as humans, have only one set of replacement teeth and some mammals, like mice, have only a single set with no replacement. This diversity raises both evolutionary questions—how did different tooth replacement strategies evolve?—and developmental ones—which mechanisms prevent replacement teeth in

animals that lost them?

In a new paper in *Development*, Professor Abigail Tucker and Ph.D. student Elena Popa of King's College London tackle these questions with a molecular analysis of mouse tooth development. They have pinpointed why mice don't have replacement teeth by comparing gene expression in the dental lamina, the area that forms the teeth, of the mouse and the minipig, which has two sets of teeth.

Wnt signalling is known to be required for tooth replacement in other vertebrates; the researchers from King's Faculty of Dentistry, Oral & Craniofacial Sciences now show that Wnt activity is absent in a rudimentary form of the dental lamina (RSDL) in mice. This structure forms in the mouse but then disappears, stopping the generation of another set of teeth.

Using sophisticated genetic techniques, the researchers activated Wnt signalling in the mouse RSDL at E15.5 and E16 stages of development, revitalising this structure, and additional teeth were formed as a consequence.

These results demonstrate the potential of the RSDL as a source for replacement teeth in mice, and provide an experimental system suitable for studying the mechanisms behind replacement.

"Why the potential for tooth replacement varies so much across vertebrates is an intriguing question", explains Ph.D. student Elena Popa. "Our results show that, although the mouse normally does not form a second replacement set of teeth, it still has the potential to do so given the right signals."

Finally, they report that culturing the RSDL in isolation stimulated its tooth-forming potential, suggesting that the first generation of teeth

might prevent replacement teeth from developing; the previous set of teeth also influence the development of a next set.

Professor Tucker explains: "This is relevant to human tooth replacement, as structures similar to the RSDL have been identified next to the permanent teeth during development. In normal development of our teeth, therefore, the second set or permanent tooth may inhibit the generation of a third set of teeth."

These results provide a conceptual advancement in the tooth-replacement field, as well as providing new insights into how traits are lost during mammalian evolution and how they might be restored.

More information: Elena M. Popa et al, Revitalising the rudimentary replacement dentition in the mouse, *Development* (2019). DOI: 10.1242/dev.171363

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