# THE FLEXIBLE MODULATION OF EPITHELIAL DIFFERENTIATION IN THE CERVICAL LOOP SHEDS NEW LIGHT ON THE RELATIONSHIP BETWEEN ROOT FORMATION AND CONTINUOUS GROWTH.

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**INTRODUCTION:** In the classic literature the first sign of root formation is a structural change in the apical epithelium at the tip of the root, the cervical loop. The central epithelial stellate reticulum and stratum intermedium of the cervical loop disappears leaving a double layer of basal epithelium known as Hertwig's epithelial root sheath (HERS) at the tip of the root. The root extends from the crown and the HERS epithelium fragments. This gives rise to another typical epithelial root structure: the epithelial cell rests of Malassez which consists of small islands of epithelial cells above the HERS. It is also sometimes thought that the maintenance of the cervical loop prevents root formation.

Molar tooth germs of the bell stage of development were grown for up to six weeks in a Trowell-type *in vitro* tissue culture system. The tooth germ developed a root on a macroscopic level. On a microscopic level there were interesting peculiarities. The epithelium making contact with the filter on which the tooth germ was cultured resembled cuboidal root epithelium of the Hertwig's epithelial root sheath without producing epithelial cell rests of Malassez. On the opposing side the tissue was exposed to the air and no epithelium formed. However, the epithelium on the lateral sides maintained all the characteristics of the cervical loop of a continuously growing tooth. The *in vitro* molar culture resulted in a tooth composed of elements of continuously growing and non-continuously growing teeth, showing the potential for the molar to acquire the continuously growing fate under the influence of changes in environmental cues.

This flexibility in the modulation of the epithelium is exemplified by the existence of continuously growing roots, such as the sloth molar. This molar lacks a Hertwig's epithelial root sheath despite producing a root phenotype and at the same time has maintained its cervical loop structure, the epithelial stem cell niche of the tooth. This phenotype can be reconstructed in transgenic models such as the incisor of the k14-eda transgenic mouse. The fate of the labial side has changed from crown analogue to root analogue changing the entire incisor into a continuously growing root. And also here the cervical loop is maintained, indicating that the transition from crown to root epithelium is not directly linked to the fate of the epithelial stem cell compartment into HERS and that the cervical loop acts as a stem cell niche in the entire circumference of the tooth instead of one localization.