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Dental Stem Cells, Dental Pathology & Regeneration

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INTRODUCTION: Dental stem cells play a critical role in tooth homeostasis and repair throughout life. Their fate between self-renewal and differentiation is regulated by both cell intrinsic determinants and signals from a specialized microenvironment. Physical interactions and molecular cross talk with stem cells, as well as the orientation of the cleavage plane during mitosis determine their fate. Molecules of the Notch pathway have been shown to control the balance between symmetric and asymmetric division of stem cells and related cell fate specification outcomes A deregulation in the control of these events could lead to an abnormal tooth formation and a reduced dental tissue repair.

DISCUSSION & CONCLUSIONS: The reparative mechanisms that operate following dental injuries involve a series of highly conserved processes that share genetic programs that occur throughout embryogenesis. Severe injuries are lethal to the odontoblasts and their replacement requires the presence of stem cells that differentiate into a new generation of odontoblasts. In injured teeth, progenitor cells express Notch receptors. Notch signaling re-activation during dental pulp healing might enhance survival of uncommitted precursors, while preserving multi-lineage potential. Notch expression is activated in cells close to the injury site, as well as in cells located at the apex of the roots, suggesting that these sites represent important pools of cells from which different cell types could derive after injury. Bone marrow stem cells express Notch receptors, suggesting that the Notch-positive cells of the pulp possess stem cell properties. Activation of the Notch molecules in endothelial cells after injury may reflect another pool of stem cells. The close association of mesenchymal cells and neovessels in dental diseases and the relation to Notch signaling pathway may be important in the regulation of stem cells to form odontoblasts.

Generation and repair of dental tissues also imply the epithelial compartment of the tooth. Dental epithelial cells are responsible for the formation of enamel, which is the hardest organic tissue of the body. In humans, the most of dental epithelial cells are not present after tooth eruption. This makes our task to generate dental epithelial stem cell lines in vitro difficult. To obtain information about the properties of dental epithelial stem cells we have used continuously growing teeth from other species. Cells responsible for the continual growth of the rodent incisors are located in the cervical loop suggesting that this area is the putative stem cell niche. Cell tracking experiments demonstrated that cells from the cervical loop are maintained in this area, while others migrate towards the anterior part of the incisor where they differentiate into ameloblasts. Cells originated from the cervical loop region exhibit a clonal potential and have the ability to differentiate into cells expressing stem cell markers such as the low affinity neurotrophin receptor P75NTFR. Notch receptors are also expressed in the cells of the cervical loop area, but not in ameloblast precursors. Ameloblast progenitors express the Notch ligands Delta and Jagged. These patterns of expression indicate that the Notch signaling plays a role in the maintenance and determination of the dental stem cell fates. Another molecule involved in this process is Tbx1. Deletion of the Tbx1 locus results in the creation of enamel-free incisors.

In conclusion, the control of dental stem cell fate decisions is a challenge that necessitates a thorough understanding of the cellular and molecular events involved in development, pathology and regeneration of teeth. The identification of dental epithelial and mesenchymal stem cells and the knowledge of molecules involved in their fate determination is a considerable accomplishment. The engineering of tri-dimensional scaffolds with a composition and shape more or less similar to that of the teeth to reconstruct and the addition of signalling molecules might facilitate the transplantation and the differentiation of stem cells towards the desired fate. This scientific knowledge is likely to instruct development of novel therapies in the near future. However, the main challenge in cell therapy is to find a compromise between the benefits to the patients, ethical issues and state regulations.