

Signalling molecules regulate the development, morphogenesis and homeostasis of tissues and organs. These molecules are re-activated in pathological and regenerating tissues upon injury. However, we still have only an incomplete understanding of their involvement in the generation and organisation of new cell lines within regenerating tissues. Notch signalling is involved in cell fate specification at developmental stages and during pathology and tissue regeneration. To address the role of Notch signalling in dental pathology and regeneration we used *Notch1*<sup>CreER</sup>;*R26*<sup>mT/mG</sup> transgenic mice. Immunohistochemistry and confocal imaging analysis demonstrated that Notch1-expressing cells and their progeny participate in tissue remodelling within pathological and injured dental tissues. Injection of the Notch  $\gamma$ -secretase inhibitor DAPT in *Notch1*<sup>CreER</sup>;*R26*<sup>mT/mG</sup> transgenic mice dramatically reduced the healing process. The same results were reproduced in “organs-on-chip” and spheroids of human organs. These findings uncover the significant role of Notch signalling in pathological and injured organs by promoting expansion and reorganisation of cell populations that are important for tissue recovery and functionality.