Distinct ATOH1 and Neurog3 requirements define tuft cells as a new secretory cell type in the intestinal epithelium

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ABSTRACT

The unique morphology of tuft cells was first revealed by electron microscopy analyses in several endoderm-derived epithelia. Here, we explore the relationship of these cells with the other cell types of the intestinal epithelium and describe the first marker signature allowing their unambiguous identification. We demonstrate that although mature tuft cells express DCLK1, a putative marker of quiescent stem cells, they are post-mitotic, short lived, derive from Lgr5-expressing epithelial stem cells, and are found in mouse and human tumors. We show that whereas the ATOH1/MATH1 transcription factor is essential for their differentiation, Neurog3, SOX9, GFI1, and SPDEF are dispensable, which distinguishes these cells from enteroendocrine, Paneth, and goblet cells, and raises from three to four the number of secretory cell types in the intestinal epithelium. Moreover, we show that tuft cells are the main source of endogenous intestinal opioids and are the only epithelial cells that express cyclooxygenase enzymes, suggesting important roles for these cells in the intestinal epithelium physiopathology.


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