

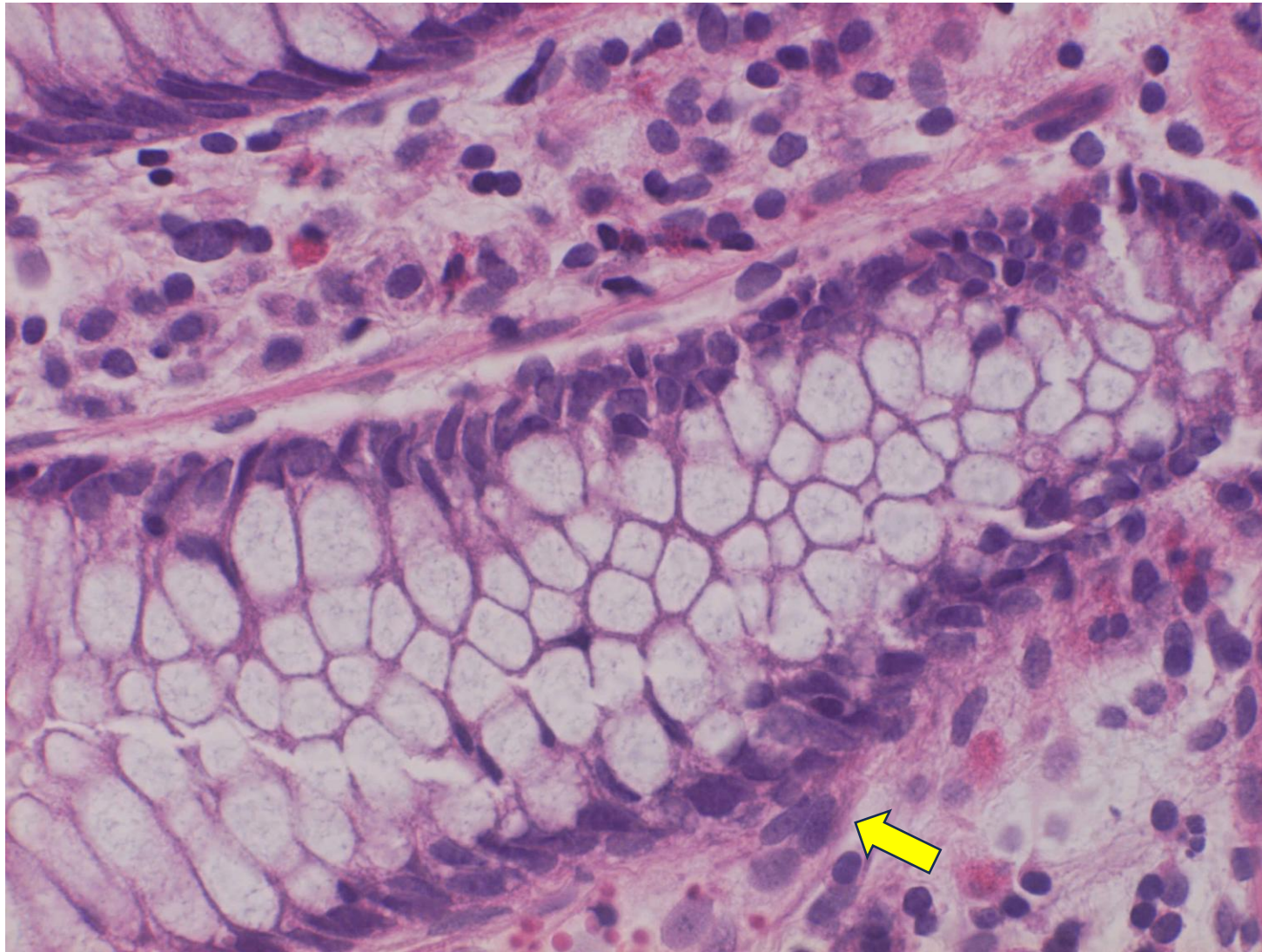
Pericryptic subepithelial myofibroblasts in the colonic mucosa

The self-renewal, proliferation and differentiation of the intestinal stem cells are prompted by molecular signals from nearby cells called “niche cells”. In the human colon, different levels of stem cell compartments exist. First, the crypt epithelial stem cells have a role in the normal crypt epithelial cell dynamics and in colorectal carcinogenesis. Close to the crypts, the second layer of stem cells can be found. The local subepithelial stem cell niche, the pericryptic subepithelial myofibroblasts, regulate the epithelial cell differentiation and have a crucial role in cancer progression and chronic inflammation-related fibrosis. As the third level of stem cell compartment, the immigrating bone-marrow-derived stem cells have an important role in wound healing after severe mucosal inflammation, but are also involved in cancer invasion.

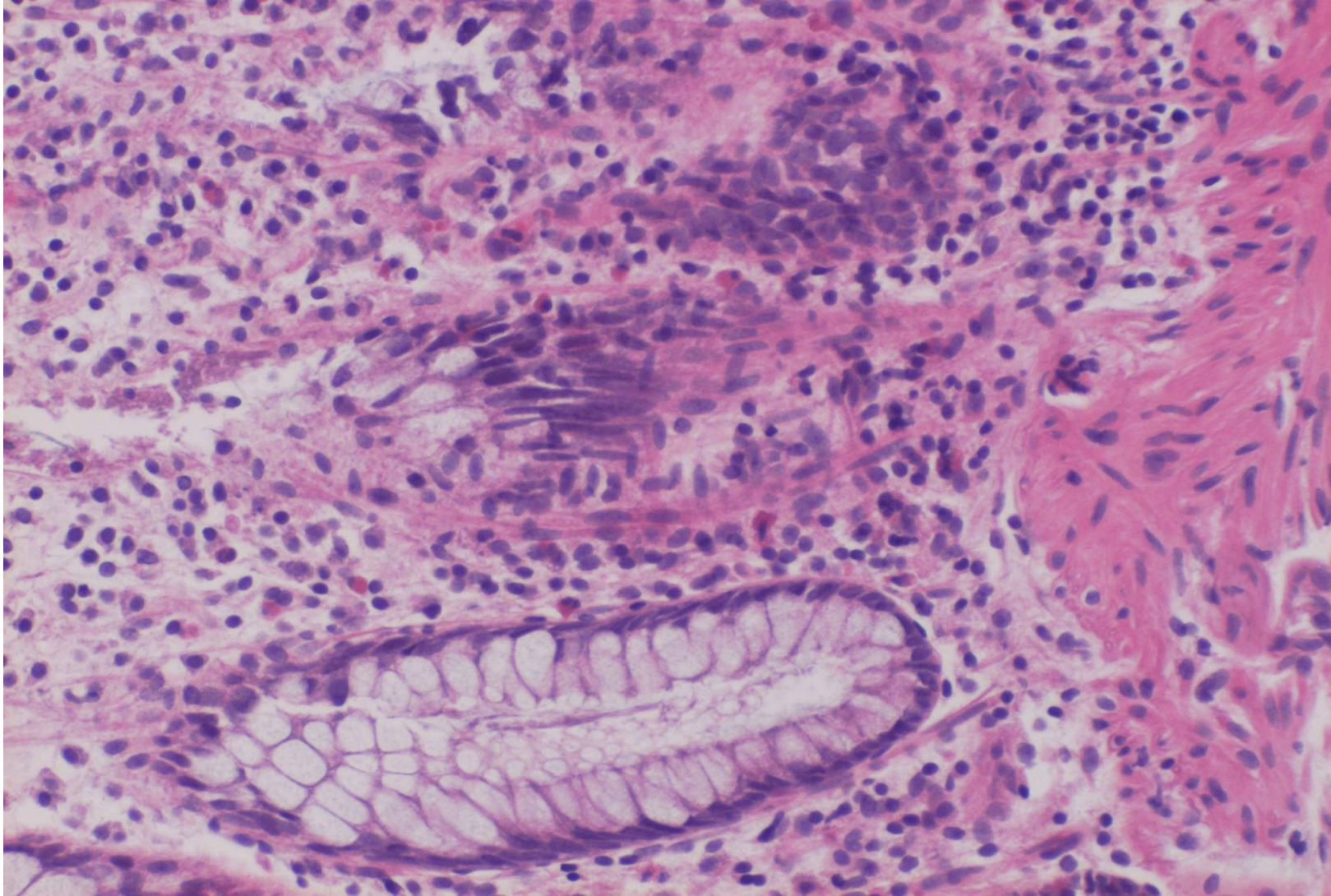
Wnt- β -catenin signaling plays a pivotal role in the homeostasis of the intestinal epithelium by promoting stem cell renewal. In the small intestine, Paneth cells secrete Wnt ligands and thus adopt the function of the stem cell niche to maintain epithelial homeostasis. In the colon, subepithelial mesenchymal GLI1-expressing cells (“pericryptic subepithelial myofibroblasts”) form the essential niche. Blocking Wnt secretion from GLI1-expressing cells prevents colonic stem cell renewal.

Ref.-1: Sipos F, et al. Physiological and pathological role of local and immigrating colonic stem cells. *World J Gastroenterol* 2012; 18(4): 295-301. doi: 10.3748/wjg.v18.i4.295

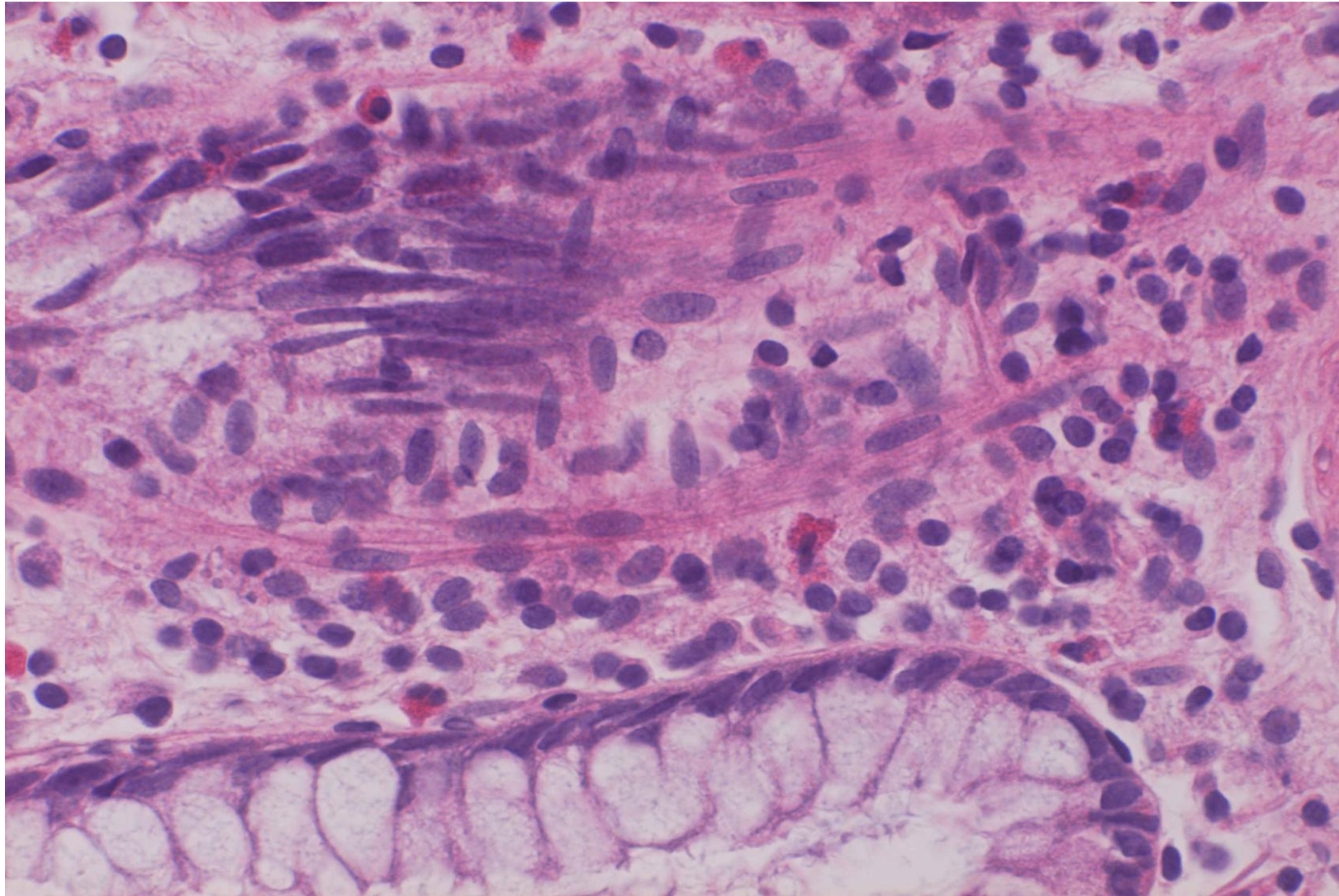
Ref.-2: Degirmenci B, et al. GLI1-expressing mesenchymal cells form the essential Wnt-secreting niche for colon stem cells. *Nature* 2018; 558: 449-453. doi: 10.1038/s41586-018-0190-3



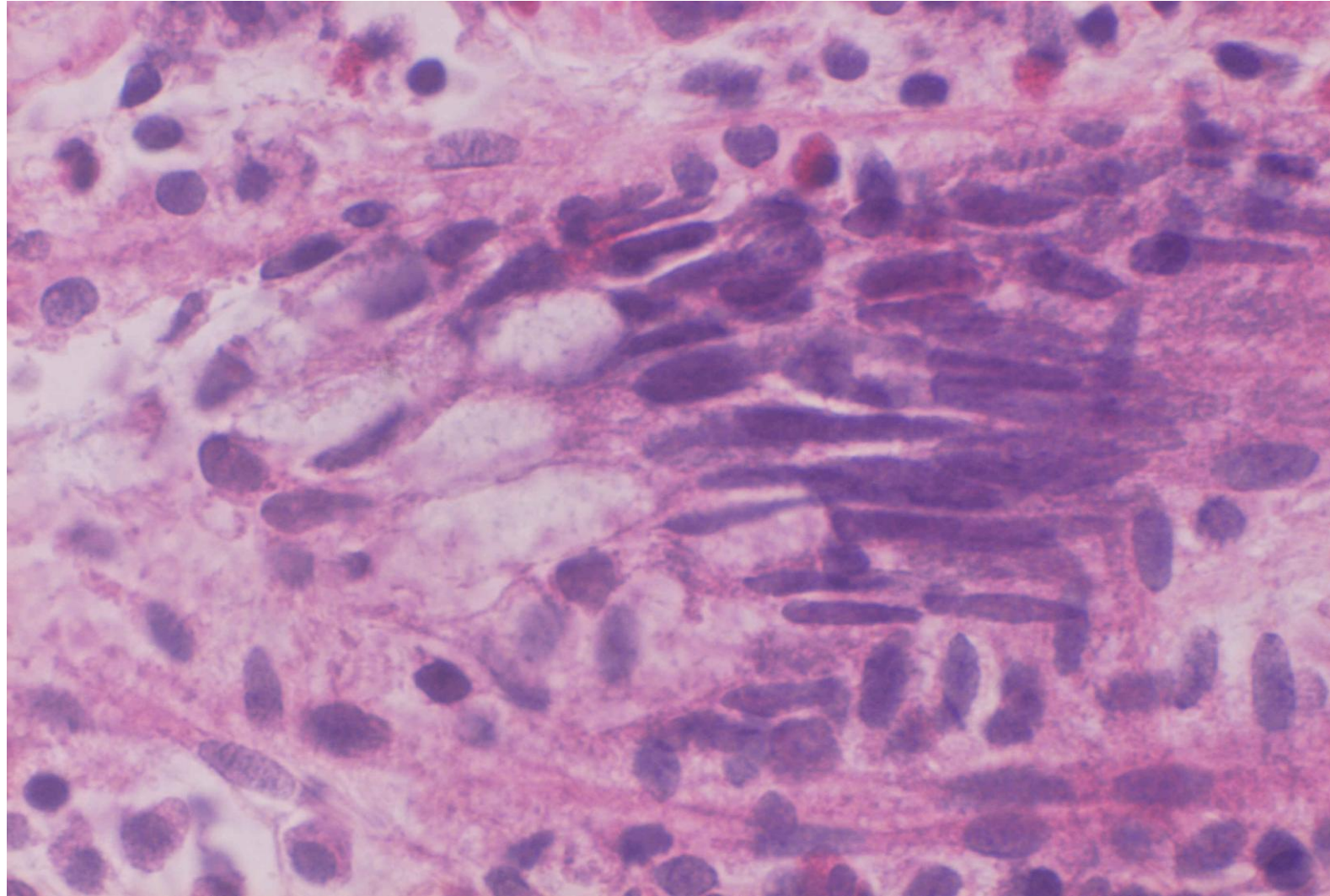
In the normal crypt of the colonic mucosa (biopsy from a male patient aged 40's), fibroblastic spindle cells are located just adjacent to the crypt epithelial cells (arrow). They may belong to “pericryptic subepithelial myofibroblasts”, playing an important role as a subepithelial stem cell niche. H&E-1



In the normal crypt of the colonic mucosa (biopsy from a male patient aged 40's), fibroblastic spindle cells are located just adjacent to the crypt epithelial cells. A tangential section just outside the crypt shows clustering of spindled cells along the colonic crypt. They may belong to "pericryptic subepithelial myofibroblasts". H&E-2



In the normal crypt of the colonic mucosa (biopsy from a male patient aged 40's), fibroblastic spindle cells are located just adjacent to the crypt epithelial cells. A tangential section just outside the crypt shows clustering of spindled cells along the colonic crypt. They may belong to "pericryptic subepithelial myofibroblasts". H&E-3



In the normal crypt of the colonic mucosa (biopsy from a male patient aged 40's), fibroblastic spindle cells are located just adjacent to the crypt epithelial cells. A tangential section just outside the crypt shows clustering of spindled cells along the colonic crypt. They may belong to "pericryptic subepithelial myofibroblasts". H&E-4