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CELLULAR AND MOLECULAR GASTROENTEROLOGY AND HEPATOLOGY

Rebuttal to: Digesting the Importance of Cell Fusion in the Intestine

See Point-Counterpoint articles on pages 299 and 304.

We read with interest the commentary by Sutton et al on the occurrence of cell fusion in the intestine. The authors eloquently presented their point of view that cell fusion is an important physiological mechanism in homeostasis and diseases of the gut. Importantly, we do not question the underlying data that support fusion events. Although avoiding false-positive calls can be technically challenging,[1] evidence for the exchange of genetic material between cell types might be detected. Instead, our critique mainly focuses on the presumed important function of this phenomenon in the intestine.

In our view the extensive evidence backing intestinal plasticity as the primary source of regeneration and repair eliminates the need for cell fusion as an accessory and redundant mechanism.[2] This point of view is shown elegantly by the fact that deletion of *Ascl2* in intestinal epithelial cells fully abrogates the ability of this tissue to regenerate after irradiation because *Ascl2* is a critical mediator of cell plasticity in this tissue.[3] In our opinion these results cannot be reconciled with a significant role of cell fusion in tissue regeneration, by either directly serving as a source for repair, or even by simply restoring functional *Ascl2* in the intestinal epithelial compartment.

Similarly, we conclude that the contribution of cell fusion to tumor initiation and progression in the gut is limited at best. Colorectal cancer is the result of a stepwise accumulation of genetic aberrations that grants selective advantage to the mutant clone.[4] Loss of tumor-suppressor genes, in the intestine most notably *APC* and *TP53*, drives initiation and progression of the disease. We acknowledge that fusion events are likely to occur in cancers. However, we proposed that the fusion event would more likely rescue the loss of tumor-suppressor function rather than promote carcinogenesis. Indeed, in classic experiments by Harris et al,[5] hybrid cells resulting from fusion between normal murine fibroblasts and various types of cancer cells reverted the malignant phenotype.

In short, cell fusion might occur sporadically in the intestine and in colorectal cancers, but that it would represent a key biological process in these tissues we find hard to digest.

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Conflicts of interest
The author discloses no conflicts.