Krt19(+)/Lgr5(-) Cells Are Radioresistant Cancer-Initiating Stem Cells in the Colon and Intestine.

Abstract:
Epithelium of the colon and intestine are renewed every 3 days. In the intestine there are at least two principal stem cell pools. The first contains rapid cycling crypt-based columnar (CBC) Lgr5(+) cells, and the second is composed of slower cycling Bmi1-expressing cells at the +4 position above the crypt base. In the colon, however, the identification of Lgr5(-) stem cell pools has proven more challenging. Here, we demonstrate that the intermediate filament keratin-19 (Krt19) marks long-lived, radiation-resistant cells above the crypt base that generate Lgr5(+)/CBCs in the colon and intestine. In colorectal cancer models, Krt19(+) cancer-initiating cells are also radioresistant, while Lgr5(+) stem cells are radiosensitive. Moreover, Lgr5(+) stem cells are dispensable in both the normal and neoplastic colonic epithelium, as ablation of Lgr5(+) stem cells results in their regeneration from Krt19-expressing cells. Thus, Krt19(+) stem cells are a discrete target relevant for cancer therapy.