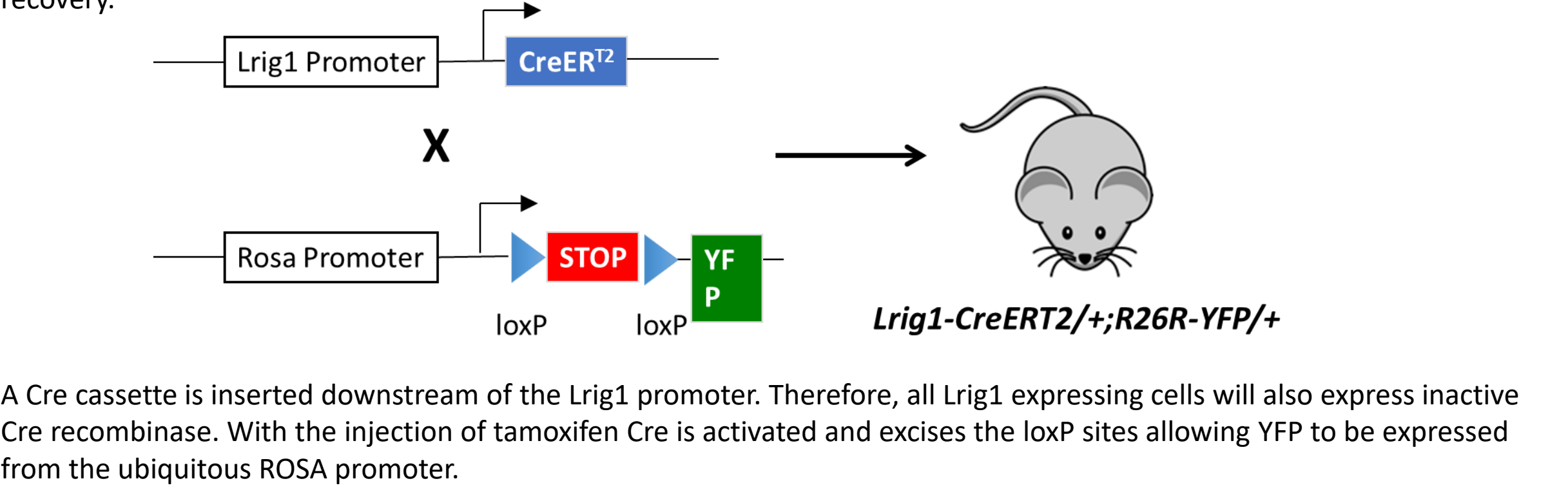
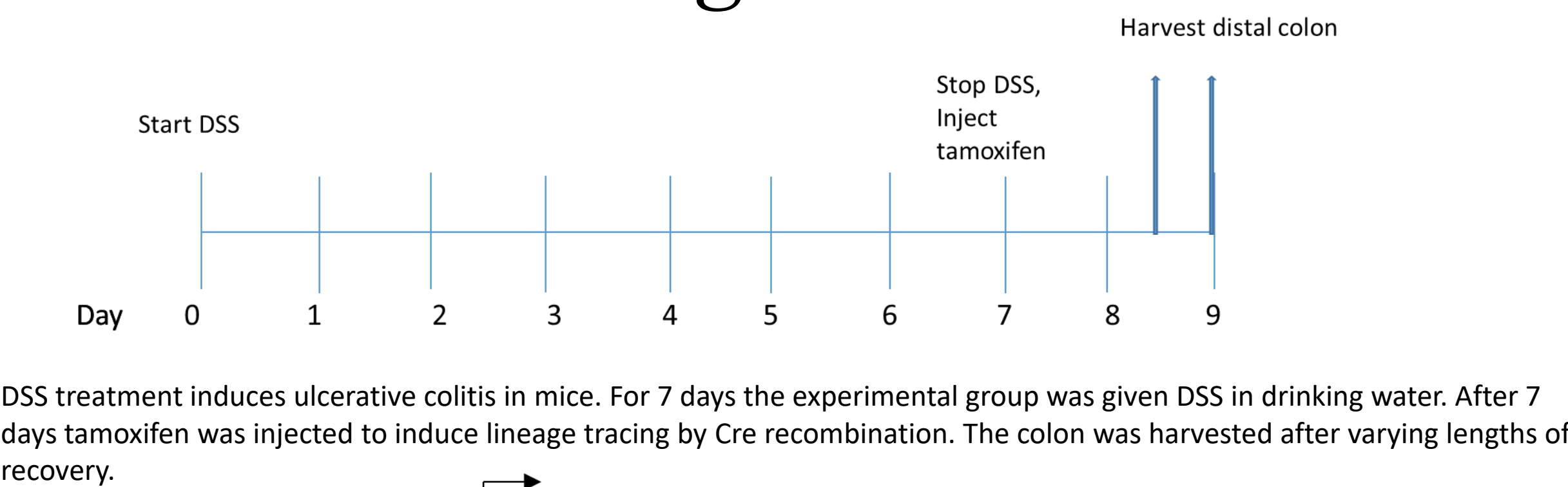


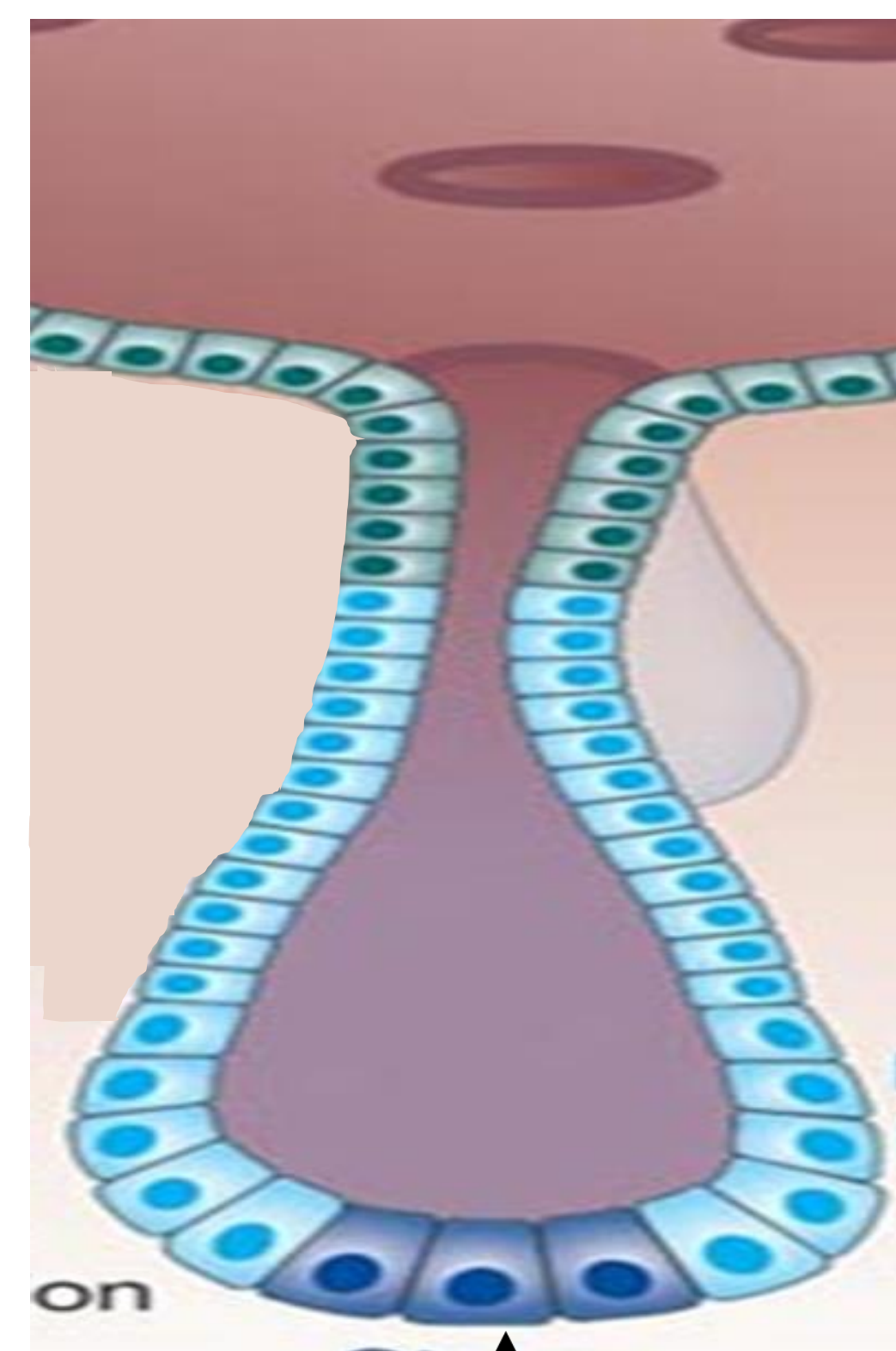
1 Abstract and Background

The intestine is a highly regenerative organ in humans and mice in which epithelial cells are replenished weekly and damage is rapidly repaired. Lrig1 protein has been shown to mark a population of quiescent stem cells residing in the base of the crypt that may be important for the recovery of the intestine from a disease state. Current knowledge about the stem cell populations involved in colonic injury and repair is sparse. To address this, we used Lrig1 as a marker for lineage tracing of the stem cells that reside at the base and the middle of the intestinal crypts. Lineage tracing of *Lrig1-Cre/ROSA26-YFP* mice was induced in animals treated with DSS to simulate ulcerative colitis in the distal colon. We performed immunohistochemistry analysis for lineage tracing and proliferation to examine the location of Lrig1-based cellular contribution in recovery after DSS-induced colitis. **We hypothesize that Lrig1 positive stem cells participate in the recovery of the intestine from damage caused by DSS induced colitis.**

2 DSS-induced colitis with an inducible gene construct



3 Structure and parameters of crypts and counts



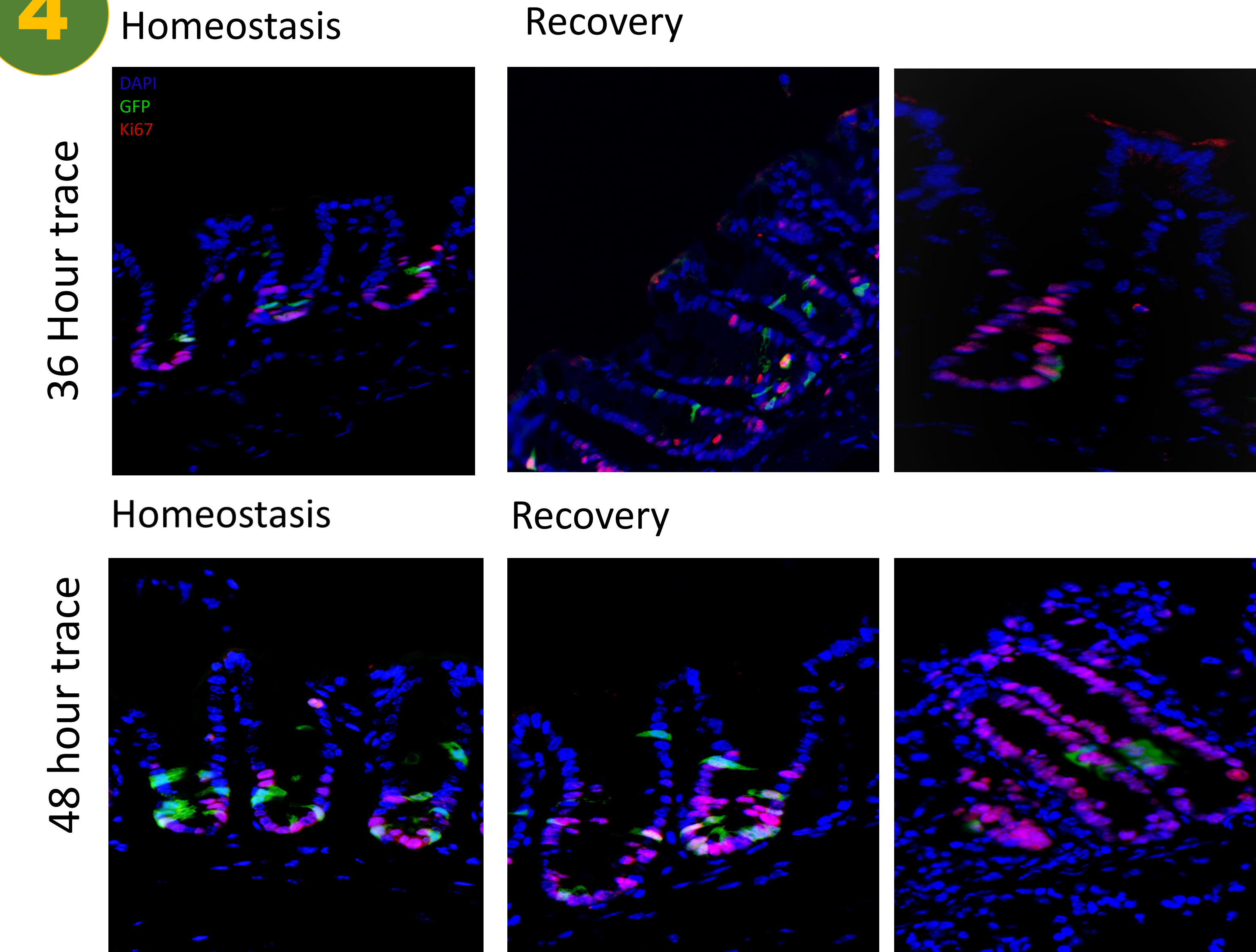
Green cytoplasm indicates GFP positivity. Blue (DAPI) nuclear stain confirms a cellular body.

A red nucleus is indicative of Ki67 which tags a protein expressed during cell division. This is a cell copositive for GFP and Ki67

Immunofluorescence via antibody staining allowed for the position of both lineage traced GFP positive cells and co positive GFP/Ki67 cells to be observed and recorded.

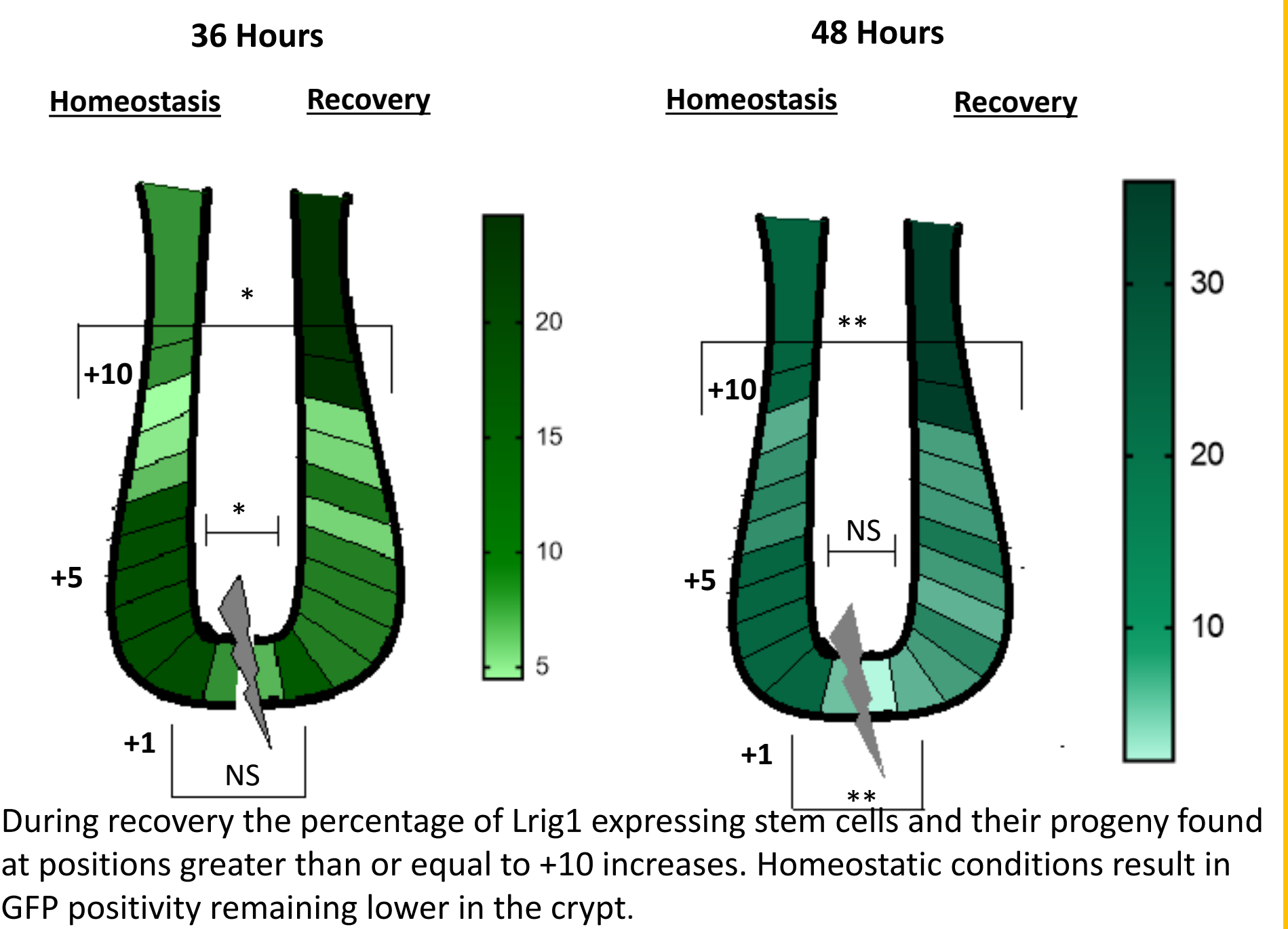
Reya, Clevers, 2005

4 Lrig1 Lineage Tracing Is Present During Homeostasis and DSS Recovery

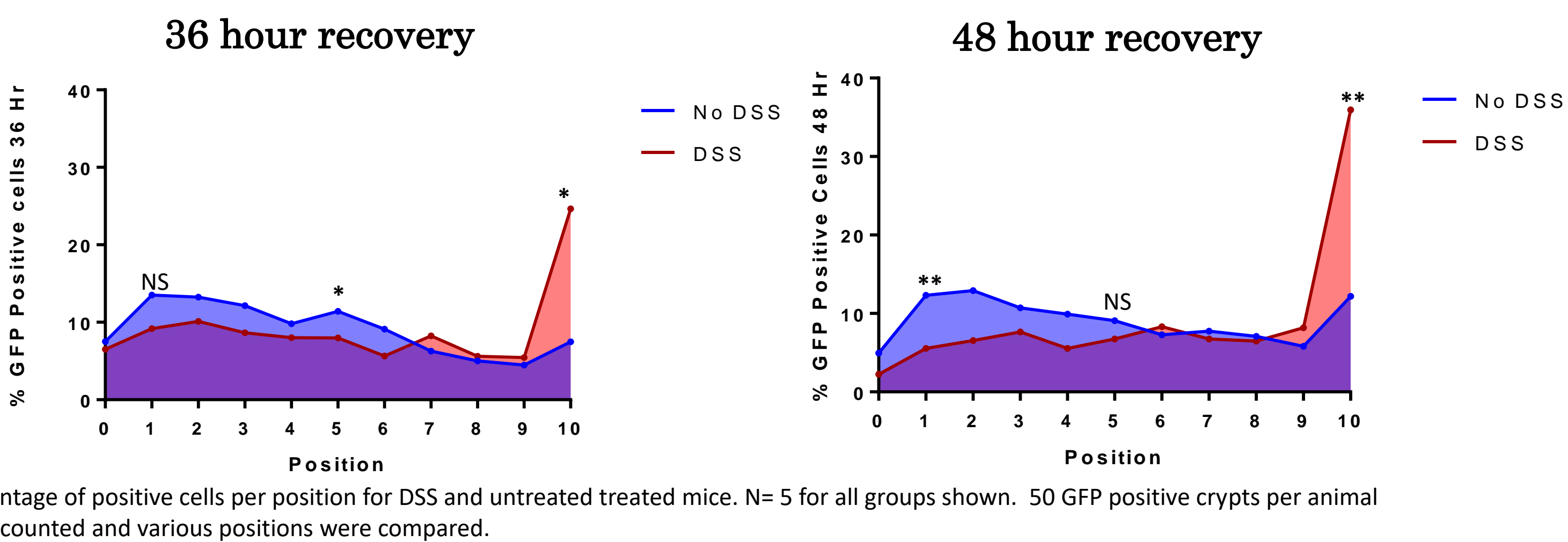


Lineage tracing during recovery of the epithelium from DSS-induced colitis was appreciable as quickly as 36 hours. Lrig1 expressing cells and their progeny are marked by GFP. Proliferating cells are marked by Ki67.

7 Lineage Tracing is more Prevalent Lower in the Crypt At 36 Hours and Higher during Recovery

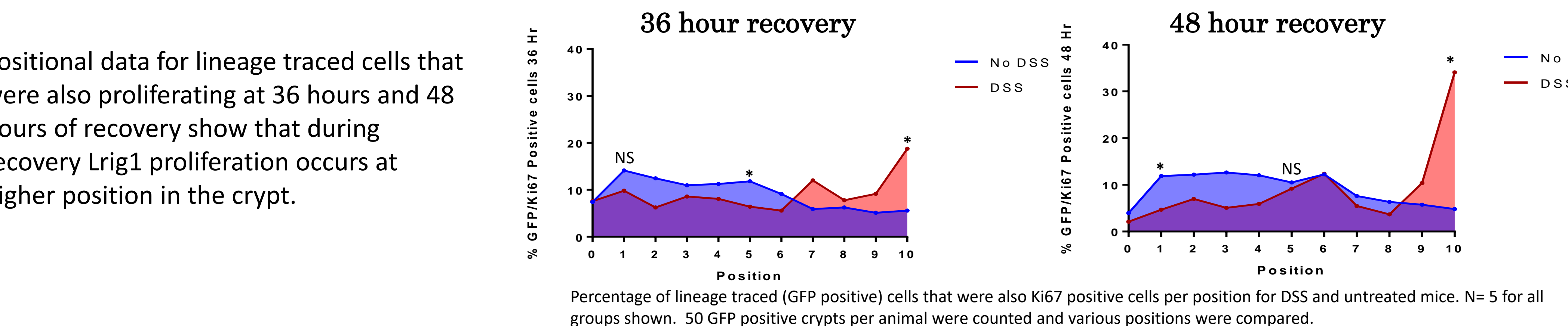


5 Lrig1 Positive Stem Cells and Progeny are Expressed Higher in the Crypt During DSS Recovery



Lineage tracing of Lrig1 positive stem cells and their progeny visualized by GFP expression at 36 hours and 48 hours of recovery indicate that as recovery is occurring GFP positive cells are found at higher positions in the crypt.

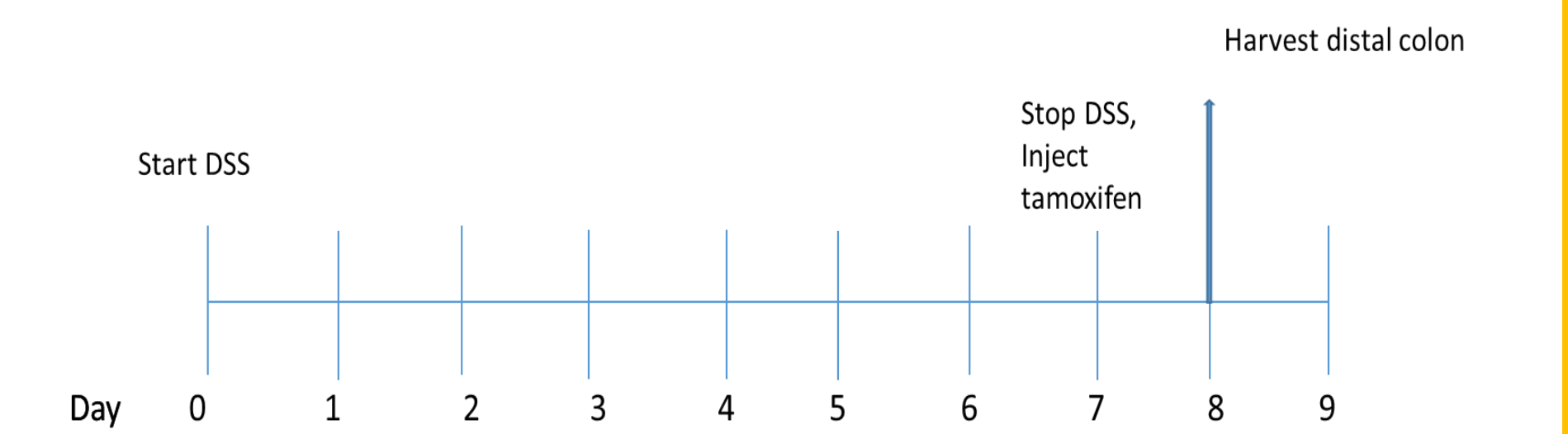
6 Proliferation of Lrig1 Positive Stem Cells and Progeny Occurs Higher in the Crypt During Recovery



8 Conclusions & Future Directions

Lrig1 lineage tracing of intestinal crypt stem cells during recovery from DSS induced colitis is appreciable as early as 36 hours of recovery. Recovery conditions stimulate migration of lineage traced cells in both 36 and 48 hours of recovery confirming that the quiescent population of stem cells in the crypt does participate in recovery from damage. At both timepoints the GFP positivity is found at higher positions in the crypt. Proliferation of lineage traced cells also follows these same trends. Together these results indicate that Lrig1 positive stem cells and their progeny are migrating up the crypt during recovery.

Future directions include using the same method to conduct a lineage trace but only allow 24 hours of recovery to assess if these trends continue. Our lab is also working on transcriptome profiling of Lrig1 expressing stem cells in order to understand what makes these stem cells function the way we are observing and how they manage to do so.



Acknowledgements

NIDDK The Powell Lab - University of Oregon
 OURS Program - University of Oregon