



\* Precursor cells are positive for each lineage markers and negative for other lineage markers but they may be all positive for P-PTEN, P-Akt, 14-3-3 $\beta$  and with nuclearly-localized  $\beta$ -catenin.

\*\* ISCs may express multiple downstream lineage markers including Chr-A, Muc-2, and Cryptdin with relative lower levels in comparing to mature cells. Whether ISCs express absorptive lineage marker is yet to be determined; and co-staining of the lineage markers at the ISC position is also required to verify the data.

**Supplementary Figure II. Model of the dual roles of PTEN in controlling ISC activation (A) and lineage fate determination (B).**

AP: Absorptive progenitor which express high levels of Myc and undergo fast proliferation. SP: Secretory progenitor which express much lower levels of Myc (data not shown) and undergo slow cycling. SP progenitor cells will potentially give rise to progenitor cells with biopotential, which in turn give rise to single lineage precursor cells.