Supplementary Materials

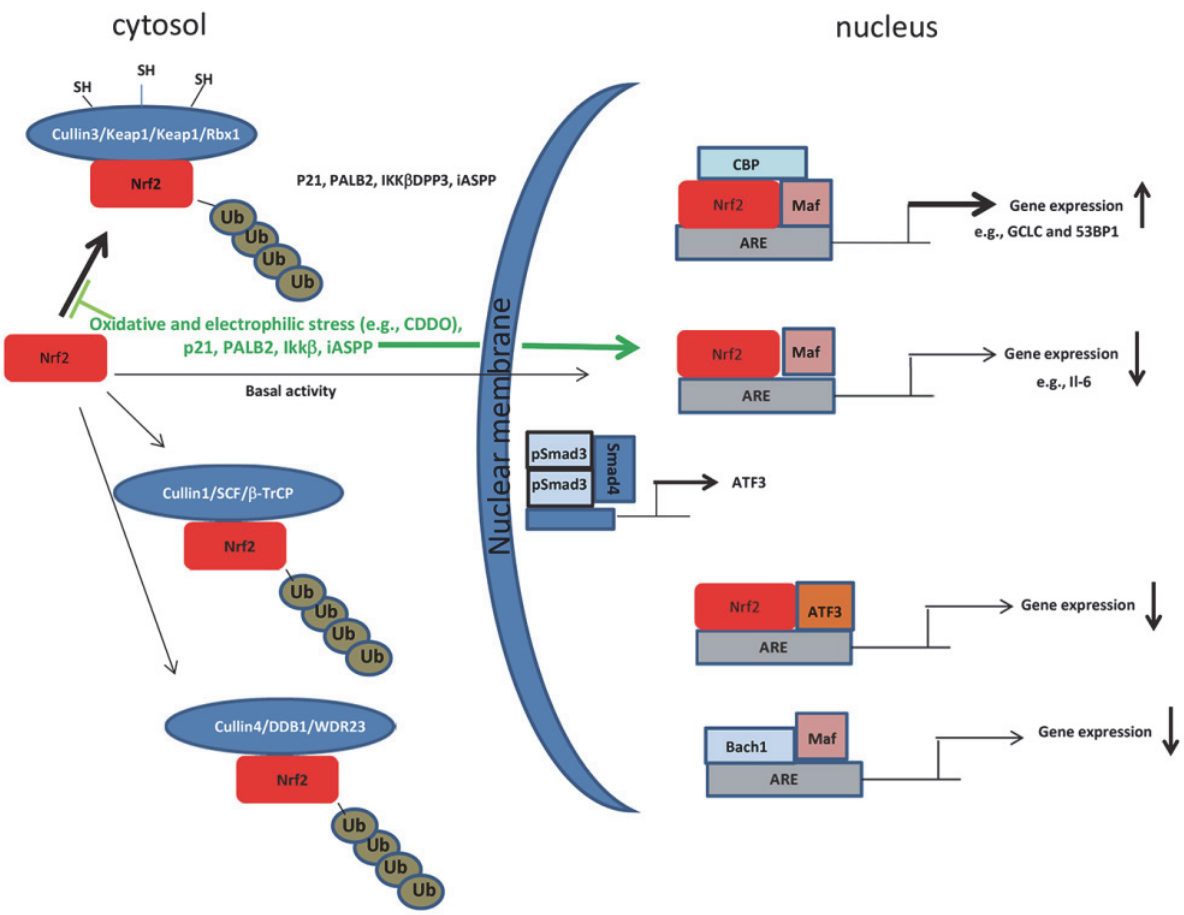

Fig S1 Under basal conditions Nrf2 undergoes rapid ubiquitination, a consequence of interactions with Cullin3/Keap1/Rbx1 (17, 18), Cullin1/SCF/□-TrCP (19), or Cullin4/DDB1/WDR23 (20) complexes. The major site of ubiquitination appears to be with the Cullin3/Keap1/Rbx1 complex. Oxidative and electrophilic stresses can block Keap1 function while p21 (23), p62, PALB2, IKKB, DPP3 (24)) and iASPP (25) can competitively bind to Keap1 and inhibit Nrf2 ubiquitination allowing newly synthesized Nrf2 to translocated to the nucleus (green arrow). Once in the nucleus Nrf2 heterodimerizes with partners such as small Maf transcription factors, binds at AREs present in the proximal promoter of target genes and either induces or suppresses gene expression. The figure also illustrates TGF□/pSMAD3 induction of ATF3 that heterodimerizes with Nrf2 to suppress Nrf2 target gene expression. Bach1 can heterodimerized with Maf transcription factors to suppress Nrf2-mediated gene expression.

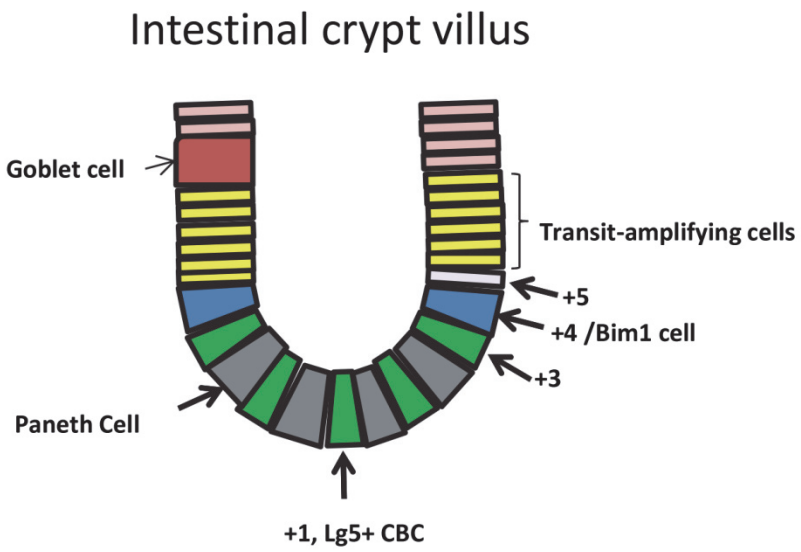

Fig S2 The figure illustrates the location of Lg5+ CBC cells (green), Paneth cells (gray), +4/Bim1 cells (blue), +5 cells (purple), transit-amplifying cells (yellow) and Goblet cells (red) (Adapted from Teteh et. al., Trends in Cell Biology 2015, 25(2): 100-8).