**Supplementary Figure 1.** Working hypothesis for MEN1 tumorigenesis including present clinical-genetic data and previous in vitro studies. The protein encoded by the \textit{MEN1} gene, MENIN, forms a transcriptional activation complex with the methyltransferase (MLL2) and RNA polymerase II and regulates the expression of the \textit{p27Kip1} (refs. 14,15,27,28). Inactivation of MENIN would lead to less p27 RNAm and a second germline hit as the V109, potentially related to p27 protein degradation by p38\textsuperscript{JAB1} (ref. 29), would trigger exacerbated development of multiple tumors (present study).