



Fig.S27 Working model of Msi1-induced conversion of keratinocytes to Paget and Paget-like cells. *Msi1* overexpression in mouse epidermis partially recapitulates features associated with human Paget's Disease. *Msi1* overexpression in basal keratinocytes activates mTOR signaling pathway via Pten and Cmtm5/Her2 cascades, resulting in formation of Paget and Paget-like cells in mouse and human skin epidermis. Human EMPD skin contains high inflammatory profile in epithelial cells and an increase of immune cells. Paget cells express novel biomarkers *S100A9*, *SHROOM3*, *TSLP* and *ALCAM*. Blockage of mTOR via Rapamycin alleviates Paget-like phenotype in mice and topical Rapamycin-treatment is an effective therapeutic strategy against human EMPD.