



Fig.S24 Topical Rapamycin treatment effectively alleviates Paget's Disease-associated pathological symptoms in a cohort of human EMPD patients – Patient 2. **a** Gross image of erythematous lesion of skin around the genital region of an 81-year-old patient (Patient ID: EMPD02) with penile EMPD before and after two weeks of topical Rapamycin treatment. The 81-year-old male patient was pathologically diagnosed with scrotal EMPD in 2009. It recurred in May 2018 after three local surgical excisions in 2009, 2011, and 2017. **b** Histopathology of EMPD skin from patient EMPD02 before and after two weeks of topical Rapamycin treatment. **c-f** PAS and immunohistochemical staining against CEA, CAM5.2 and pS6 in EMPD skin from patient EMPD02 before and after two weeks of topical Rapamycin treatment. **g** Reflectance confocal microscopy of lesioned skin from patient EMPD02 before and after two weeks of topical Rapamycin treatment. **h** Ultrasound images of affected skin from patient EMPD02 before and after two weeks of topical Rapamycin treatment. Representative images are shown. Epidermis and dermis are demarcated with broken line. Scale bar: **c-f** – 50 μm .