



Fig. S1. Possible mechanisms and pathways in the pathogenesis of rosacea. In response to environmental exogenous trigger factors (temperature changes, microbes, mites, spicy food) or endogenous trigger factors (exercise with subsequent vasodilation, ethanol, microbiota imbalance), TLRs and other pattern recognition receptors induce release of cathelicidin, kallikreins (e.g. (KLK)-5), matrix metalloproteinases (MMPs), reactive oxygen species (ROS), nitric oxides (NO), cytokines, and chemokines, which initiate and perpetuate inflammation. The dermal structure is modified by these effectors through vascular changes (prolonged vasodilation, plasma extravasation, later also angiogenesis) and also leads to extracellular matrix (especially collagen) degeneration, probably induced by MMPs. Infiltrated macrophages and mast cells, as well as T cells, produce more effector molecules, resulting in chronic inflammation. TLRs: Toll-like receptors. (Modified from Steinhoff et al. (1), Steinhoff et al. (9), Aubdool & Brain (13), Schwab et al. (16), Yamasaki & Gallo (20), Forton (23), Melnik (28), Buhl et al. (36), Yamasaki et al. (40), Schaubert et al. (99), Picardo & Ottaviani (100), Schafer & Werner (101), Huggenberger & Detmar (102), Helfrich et al. (103), Muto et al. (104), Liu et al. (105)).