

# Keratins as modulators of epithelial stress responses and regeneration

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## Members of the research group

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## Description of the scientific aims

The aims of our studies are to understand the roles of epithelial intermediate filaments keratins on physiological and molecular levels in health, stress and disease of the intestine and endocrine pancreas. Epithelial diseases and disease models of interest in these studies are colorectal cancer, inflammatory bowel diseases and diabetes. Current pathways and cellular systems in our focus with keratins are the inflammasome, IL-22, Notch and HIF-signaling, differentiation, proliferation, regeneration, energy metabolism and mitochondrial, glucose stimulated insulin secretion, and protein targeting. We also develop *in vivo* imaging modalities for murine gut inflammation diagnostics as well as epithelial organoid culture systems.

## Selected publications 2010-

1. Misiorek JO, Lähdeniemi IA, Nyström JH, Paramonov VM, Gullmets JA, Saarento H, Rivero-Müller A, Husøy T, Taimen P, Toivola DM. Keratin-8 deletion induced colitis predisposes to murine colorectal cancer enforced by the inflammasome and IL-22 pathway. *Carcinogenesis*, 37(8):777-86, 2016.
2. Helenius TO, Misiorek JO, Nyström JH, Fortelius LE, Habtezion A, Liao J, Asghar MN, Zhang H, Azghar S, Omary MB, Toivola DM. Keratin 8 absence downregulates colonocyte HMGCS2 and modulates colonic ketogenesis and energy metabolism. *Mol Biol Cell*, 26(12):2298-310, 2015.
3. Asghar MN, Emani R, Alam C, Helenius TO, Grönroos TJ, Sareila O, Din MU, Holmdahl R, Hänninen A, Toivola DM. In vivo imaging of reactive oxygen and nitrogen species in murine colitis. *Inflamm Bowel Dis*, 20 (8):1435-47, 2014.
4. Alam CM, Silvander JSG, Daniel EN, Tao G-Z, Kvarnström SM, Alam P, Omary MB, Hänninen A, Toivola DM. Keratin 8 modulates  $\beta$ -cell stress responses and normoglycaemia. *J Cell Sci*, 126(24):5635-44, 2013.
5. Toivola DM, Alam C, Boor P, Strnad P. Keratins in health and disease. *Curr Opin Cell Biol*, 32C:73-81, 2015.