

**Die Fakultät für Chemie  
und die  
Gesellschaft Deutscher Chemiker  
gemeinsam mit**

**SFB 613: Physik von Einzelmolekülprozessen und  
molekularer Erkennung in organischen Systemen**

**International Graduate School of Chemistry and  
Biochemistry**

**laden ein zum Vortrag von**

**Prof. Dr. Paul Saftig**

**Christian-Albrecht Universität Kiel**

**“Shedding New Light on the Function of  
Lysosomal Membrane Proteins”**

One crucial role of the membrane limiting late endosomes and lysosomes is to separate the potent activities of lysosomal acid hydrolases from other cellular constituents. Several highly glycosylated proteins of the lysosomal membrane have been identified (1). Lysosomal associated membrane proteins (LAMPs) and Lysosomal integral membrane proteins (LIMPs) are the most abundant proteins of the lysosomal membrane. Experiments on knockout mice have demonstrated that these proteins are important for normal cell physiology and they can be involved in pathological conditions (2-6). Recent studies have implicated both LAMP proteins to be of major importance for the lysosomal motility and phagosomal maturation (7, 8). LIMP-2 as a type-III transmembrane protein may be involved in endocytotic membrane traffic. A deficiency of this protein causes ureteric abnormalities, deafness and peripheral neuropathy associated with an impaired vesicular trafficking and distribution of apically expressed proteins (5, 9). This presentation will focus on a newly discovered role of the LIMP-2 protein in targeting certain hydrolases to the lysosomal compartment. In vitro and in vivo experiments support an important role for LIMP-2 as a mannose-6 phosphate independent receptor in lysosomal biogenesis.

1. Eskelinen, E.L., Tanaka, Y., and Saftig, P. 2003. At the acidic edge: emerging functions for lysosomal membrane proteins. *Trends Cell Biol* 13:137-145.

2. Andrejewski, N., Punnonen, E.L., Guhde, G., Tanaka, Y., Lullmann-Rauch, R., Hartmann, D., von Figura, K., and Saftig, P. 1999. Normal lysosomal morphology and function in LAMP-1-deficient mice. *J Biol Chem* 274:12692-12701.

3. Tanaka, Y., Guhde, G., Suter, A., Eskelinen, E.L., Hartmann, D., Lüllmann-Rauch, R., Janssen, P.M.L., Blanz, J., von Figura, K., and Saftig, P. 2000. Accumulation of autophagic vacuoles and cardiomyopathy in LAMP-2 -deficient mice. *Nature* 406:902-906.
4. Eskelinen, E.L., Illert, A.L., Tanaka, Y., Blanz, J., von Figura, K., and Saftig, P. 2002. Role of LAMP-2 in lysosome biogenesis and autophagy. *Mol Biol Cell* 13:3355-3368.
5. Gamp, A., Tanaka, Y., Lullmann-Rauch, R., Wittke, D., D'Hooge, R., De Deyn, P., Moser, T., Maier, H., Hartmann, D., Reiss, K., et al. 2003. LIMP-2/LGP85 deficiency causes ureteric pelvic junction obstruction, deafness and peripheral neuropathy in mice. *Hum Mol Genet* 12:631-646.
6. Eskelinen, E.L., Schmidt, C.K., Neu, S., Willenborg, M., Fuertes, G., Salvador, N., Tanaka, Y., Lullmann-Rauch, R., Hartmann, D., Heeren, J., et al. 2004. Disturbed cholesterol traffic but normal proteolytic function in LAMP-1/LAMP-2 double-deficient fibroblasts. *Mol Biol Cell* 15:3132-3145.
7. Huynh, K.K., Eskelinen, E.L., Scott, C.C., Malevanets, A., Saftig, P., and Grinstein, S. 2007. LAMP proteins are required for fusion of lysosomes with phagosomes. *Embo J* 26:313-324.
8. Binker, M., Cosen-Binker, L., Terebiznik, M.R., Mallo, G.V., McCaw, S.E., Eskelinen, E.L., Willenborg, M., Brumell, J., Saftig, P., Grinstein, S., et al. 2007. Arrested maturation of Neisseria-containing phagosomes in the absence of the lysosome-associated membrane proteins, LAMP-1 and LAMP-2 *Cellular Microbiology* in press.
9. Knipper, M., Claussen, C., Ruttiger, L., Zimmermann, U., Lullmann-Rauch, R., Eskelinen, E.L., Schroder, J., Schwake, M., and Saftig, P. 2006. Deafness in LIMP2-deficient mice due to early loss of the potassium channel KCNQ1/KCNE1 in marginal cells of the stria vascularis. *J Physiol* 576:73-86.

**Universitätsgebäude, Hörsaal 3,  
Donnerstag, den 6. Dezember 2007 um 17 Uhr  
c.t.**

**gez. Prof. Dr. Thomas Koop, Prof. Dr. Uwe Manthe, Prof. Dr. Jochen Mattay**