### List of original publications


I. Remitz A, Kyllönen H, Granlund H, Reitamo S: Tacrolimus ointment reduces staphylococcal colonization of atopic dermatitis lesions. J Allergy Clin Immunol 2001; 107: 196–197.

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III. Kyllönen H, Malmberg P, Remitz A, Rytilä P, Metso T, Helenius I, Haahtela T, Reitamo S. Respiratory symptoms, bronchial hyperresponsiveness, and eosinophilic airway inflammation in patients with moderate-to-severe atopic dermatitis. Clin Exp Allergy 2006; 36:192–197.

IV. Virtanen H, Kari O, Kari M, Reitamo S. Tacrolimus ointment in the treatment of atopic blepharoconjuntivitis. A retrospective study. Acta Ophth Scand 2006; 84: 693–695.

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# Antimicrobial Activities of Histidine-rich Glycoprotein and Cationic Peptides


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**Dr Victoria Rydengård from the Department of Dermatology and Venereology, Lund University, Sweden, defended her PhD thesis on 11 May, 2008 in Lund. The thesis was supervised by Associate Professor Artur Schmidtchen from the Department of Clinical Sciences, Lund University. The opponent was Professor Birgitta Agerberth from the Karolinska Institut in Stockholm.**

In an environment full of potential pathogens it is important for organisms to mount a fast and effective defence. Antimicrobial peptides are ancient and integral effector molecules of the innate immune system. They are found in all kinds of species, from bacteria to plants and animals, indicating their importance during evolution. They possess a broad-spectrum antimicrobial activity and some peptides can also participate in wound healing and connect the innate and adaptive immune systems.

Results presented in this thesis show that structural motifs connected with heparin-binding may confer antimicrobial activity on a given peptide. Peptides from various heparin-binding endogenous proteins exerted antimicrobial activity against Gram-positive and Gram-negative bacteria, and similar results were obtained with consensus sequences for heparin-binding. Furthermore, we demonstrated that replacement of lysine and arginine by histidine in the consensus motifs abrogated the antibacterial effects of these peptides. Antibacterial effects of the histidine-rich consensus peptides were restored by the addition of zinc ions ($Zn^{2+}$) or low pH. Similar results were obtained with histidine-rich peptides derived from domain 5 of kininogen and histidine-rich glycoprotein (HRGP).

HRGP, an abundant heparin-binding plasma protein, exerted antimicrobial effects against Gram-positive and Gram-negative bacteria and fungi. The antibacterial activity of HRGP was dependent on $Zn^{2+}$ ions or low pH, and the antifungal activity was increased under low pH conditions.

Electron microscopy demonstrated that HRGP induced lysis of bacteria and fungi. Truncated HRGP, devoid of the heparin-binding and histidine-rich domain, was not antimicrobial. In addition, HRGP was found to have antifungal effects *ex vivo* when bound to fibrin clots.

### List of original publications


1. Andersson E, Rydengård V, Sonesson A, Mörgelin M, Björck L, Schmidtchen A. Antimicrobial activities of heparin-binding peptides. Eur J Biochem 2004; 271: 1219–1226.
2. Rydengård V, Andersson Nordahl E, Schmidtchen A. Zinc potentiates the antibacterial effects of histidine-rich peptides against Enterococcus Faecalis FEBS J 2006; 273: 2399–2406.
3. Kacprzyk L, Rydengård V, Malmsten M, Schmidtchen A. Antimicrobial activity of histidine-rich peptides is dependent A of acidic conditions (manuscript).
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