

MEET THE GUEST EDITOR

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Alexander Cole has been investigating two aspects of innate host defense. The first area examines the natural ability of human airway secretions to prevent pathogenic bacterial colonization and aims to identify the host substances that mediate the innate resistance to colonization. His group is examining the host defense of the airways of donors who are healthy and donors who are persistent nasal carriers of *Staphylococcus aureus*. Their studies to date suggest that a defect exists in the nasal fluid of carriers that permits the colonization of *S. aureus* in their nasal passages. Ongoing studies to resolve the molecular determinants of *S. aureus* nasal carriage include a proteomic approach to identify molecules that are dysregulated in *S. aureus* carrier fluid. Their second focus is based on the reconstruction (from an expressed pseudogene) of a human antimicrobial peptide, called "retrocyclin", homologous to rhesus monkey circular minidefensins. The peptide had a remarkable ability to inhibit proviral DNA formation and to protect immortalized and primary human CD4⁺ lymphocytes from in vitro infection by both X4 and R5 strains of HIV-1. Current goals include characterizing retrocyclin's antiretroviral mechanism of action, testing the activity, stability and toxicity of retrocyclin in human fluids, and constructing next-generation analogs for use as antimicrobial therapeutics and preventatives.

REPRESENTATIVE PUBLICATIONS

1. **Cole, A.M.**, T. Hong, L.M. Boo, T. Nguyen, C. Zhao, G. Bristol, J.A. Zack, A.J. Waring, O.O. Yang, and R.I. Lehrer. (2002). Retrocyclin: a primate peptide that protects cells from infection by T- and M-tropic strains of HIV-1. *Proc. Natl. Acad. Sci. USA* 99(4): 1813-1818.
2. **Cole, A.M.**, H-I. Liao, O. Stuchlik, J. Tilan, J. Pohl, and T. Ganz. (2002). Cationic polypeptides are required for antimicrobial activity of human airway fluid. *J. Immunol.* 169(12): 6985-6991.
3. Ganz, T., V. Gabayan, H-I. Liao, L. Liu, A. Oren, T. Graf, and **A.M. Cole**. (2003). Increased pathogenicity of *Micrococcus luteus* in lysozyme M-deficient mice. *Blood* 101(6): 2388-2392.
4. **Cole, A.M.** and R.I. Lehrer. (2003). Minidefensins: antimicrobial peptides with activity against HIV-1. *Curr. Pharm. Des.* 9(18): 1463-1473.
5. **Cole, A.M.** (2003). Minidefensins and other antimicrobial peptides: candidate anti-HIV microbicides. *Expert Opin. Therapeut. Targets.* 7(3): 329-341.
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7. Münk, C., G. Wei, O.O. Yang, A.J. Waring, W. Wang, T. Hong, R.I. Lehrer, N.R. Landau and **A.M. Cole**. (2003). The theta-defensin, Retrocyclin, inhibits HIV-1 entry. *AIDS Res. Hum. Retroviruses* 19(10): 875-882.
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10. **Cole, A.M.**, W. Wang, A.J. Waring, and R.I. Lehrer. (2004). Retrocyclins: using past as prologue. *Curr. Prot. & Peptide Sci.* 5(5): 373-381.