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# Effect of the synthetic NC-1059 peptide on diffusion of riboflavin across an intact corneal epithelium

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NC-1059 (KKKKAARVGLGITTVLVTTIGLGVRAA), a channel-forming peptide, alters ion transport across epithelia, transiently reducing barrier integrity of intact rabbit or chick corneal tissues, as well as cultured monolayers derived from human cornea (THCE). In cultured cells, NC-1059 causes a concentration-dependent increase in short circuit current, suggesting anion secretion and/or cation absorption, and an increase in transepithelial electrical conductance, suggesting paracellular permeation. These transient effects last < 90 min, with cell viability unaffected. During this period, the corneal epithelium is permeable to 5,6-Carboxyfluorescein and methotrexate, as well as FITC-labeled dextrans ranging in size from 10 to 70 kDa. Maximum transepithelial permeation appeared to reach a maximum approximately 30 min following a 5 min NC-1059 exposure. Histological examination of the ex vivo rabbit corneas revealed no apparent effect on cell ultrastructure, although the paracellular pathway was apparently opened. NC-1059 enhanced riboflavin (RF) diffusion across the corneal epithelium in chick embryos. RF irradiated with UV-A light is used clinically to cross-link corneal stroma collagen in patients with keratoconus. RF reaching a depth of 50 μm in stroma increased dramatically after exposure to NC-1059 for 10 minutes, reaching a plateau by 30 minutes. The concentrations of RF at stromal depths of 50, 100, and 150 μm were significantly greater in the presence of the peptide, approaching the magnitude of stromal permeation in preparations where the corneal epithelium was removed. These results support a model in which NC-1059 potentiates the movement of solutes across cell layers that typically form a barrier, blocking effective delivery of therapeutic compounds.

## Biography

Tomich has been designing and synthesizing bioactive peptides for more than 25 years. He has been the Director of the Biotechnology Core Lab at Kansas State University for 20 years. He has published more than 100 research articles. The work presented here has been supported by several NIH grants.

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