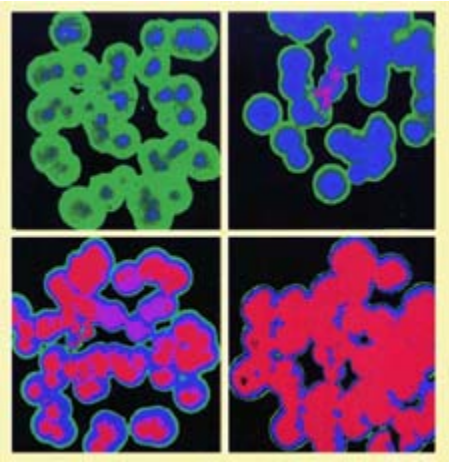
Research Statement

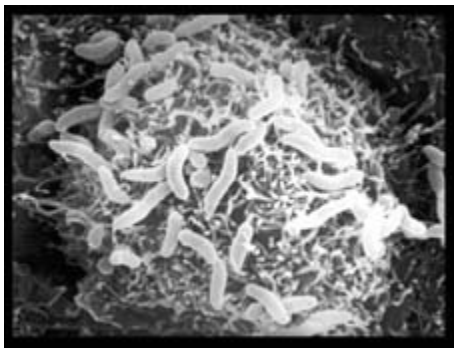
Enteric pathogenesis, immunology, and vaccine development; epitopes of cholera enterotoxins and related enterotoxins from Escherichia coli, genetically-engineered chimeras, and synthetic peptides; Vibrio cholerae adherence mechanisms and iron-regulated membrane proteins; bacterial zinc-containing metalloproteases; iron and bacterial-host interactions; antimicrobial activity of human and bovine milk; colonial morphology (phase variation) in choleragenic vibrios; choleraphage and choleracins; Burkholderia (Pseudomonas) pseudomallei.

Dr. Finkelstein's laboratory made major contributions to the understanding of the pathogenesis of cholera, including the first isolation and characterization of the cholera enterotoxin (CT), identification of Vibrio cholerae antigens and adhesive mechanisms, and development and evaluation of cholera vaccines. He has also isolated and characterized CT-related heat-labile enterotoxins (LTs) from Escherichia coli and developed rapid procedures for identifying LT-producing E. coli colonies. Dr. Finkelstein's group pioneered studies on the role of iron in virulence of several microbial pathogens, including the gonococcus, and produced the first evidence that V. cholerae grown in vivo express iron-regulated membrane proteins which are not expressed under iron-replete conditions in vitro. His laboratory has studied virulence mechanisms in V. cholerae, common and specific epitopes in the CT-related enterotoxins, antibacterial factors in human and bovine milk, and has recently cloned and sequenced the HA/protease, a zinc metalloprotease which is a putative virulence factor of V. cholerae. By genetic substitutions in the A subunit of CT, his laboratory created CT analogs which are not toxic and re-inserted them in V. cholerae as live vaccine candidates. He has most recently been involved in studies on colonial opacity phase variation in choleragenic vibrios (including the recently described O139 serogroup); choleraphage; cholera vibrio population dynamics; and choleracins (bacteriocins from V. cholerae)



Colonies of Vibrio cholerae of font varying opacity (increasing from top right, left bottom right) pseudocoloured to accentuate differences in gray-scale intensity. Of varying opacity (increasing from top left to top right, to bottom left to bottom right) pseudocoloured to accentuate differences in grey-scale intensity. Picture supplied by Richard A. Finkelstein,

Mary B.-Finkelstein, Dilip K. Sengupta, C. Michael Stanley and Thomas E. Phillips, University of Missouri-Columbia, MO, USA, and William J. Page, University of Alberta, Alberta, Canada. 1996. Microbiol. 142:213-448. (cover picture)



Adherence of Vibrio cholerare El Tor biotype strain C7258 to monolayers of HT29-18N2 cells at 1 h. V. cholerae organisms adhere in clusters

at hot spots scattered across the apical surface of the goblet cell monolayers as seen here by scanning electron microscopy. (Magnification ca 6200x)