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Selective myeloperoxidase-bacteria binding and killing: Mechanism for establishing and maintaining lactic acid bacteria (LAB) as normal flora

Lactic acid bacteria (LAB) lack cytochrome synthesis and the electron transport mechanisms required for efficient oxygen-based metabolism. LAB redox activity is flavoenzyme-based and metabolism is fermentative resulting in production of lactic acid, and in many cases, hydrogen peroxide (H_2O_2). LAB occupy dominant positions within the normal flora of the mouth, vagina and lower gastrointestinal tract in man. Neutrophil leukocytes and monocytes provide innate immune defense against infecting pathogens. These phagocytes synthesize relatively large quantities of myeloperoxidase (MPO), a unique microbicidal haloperoxidase that catalyzes the H2O2-dependent oxidation of chloride (Cl^-) to hypochlorite (OCl^-); OCl^- can directly react with a second H_2O_2 producing singlet molecular oxygen ($^1O_2$*), a metastable electronically excited state of oxygen with a microsecond half-life that restricts its potent electrophilic reactivity to within a radius of about 0.2 micron from its generation. A healthy human adult generates about a hundred billion neutrophils per day. Inflammation, infection and G-CSF treatment greatly increase neutrophil production and the concentration of MPO/neutrophil. After a short circulating lifetime, neutrophils leave the blood and migrate into body spaces including the mouth, vagina, et cetera. Neutrophils lavaged from the mouth of healthy humans are in proportion to the blood neutrophil count. MPO selectively binds to all Gram-negative and many Gram-positive bacteria we have tested. However, MPO does not show significant binding to LAB. Migration of neutrophils to body spaces delivers MPO into a milieu conditioned by LAB fermentative action. The acid and H2O2 drive extra-phagocyte MPO microbicidal action against MPO-bound microbes. Selectivity of MPO binding results in selective killing, and provides a mechanism for establishing and maintaining LAB as the normal flora of man.

Biography

Robert C Allen has completed his PhD and MD degrees from Tulane University (1970 to 1977). He practiced infectious disease and later clinical pathology. He is a Fellow in the College of American Pathologists (FCAP) and is presently a Professor in the Department of Pathology of Creighton University School of Medicine.

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