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Use of the Synthetic Copolymer PSMA as a Component in a Combination Microbicide Active Against HIV-1

Jin Qian¹, Shendra Miller¹, Mary L Ferguson¹, Lori Schlipf¹,
Mohamed E Labib², Robert F Rando², Brian Wigdahl¹ and Fred C Krebs^{*†1}

Address: ¹Department of Microbiology and Immunology, and Institute for Molecular Medicine and Infectious Disease, Drexel University College of Medicine, Philadelphia, PA, USA and ²Novaflux Biosciences, Inc., Princeton, NJ, USA

Email: Fred C Krebs* - fred.krebs@drexel.edu

* Corresponding author †Presenting author

from 2005 International Meeting of The Institute of Human Virology
Baltimore, USA, 29 August – 2 September 2005

Published: 8 December 2005

Retrovirology 2005, 2(Suppl 1):S96 doi:10.1186/1742-4690-2-S1-S96

The remarkable successes achieved using combination therapy to treat systemic human immunodeficiency virus type 1 (HIV-1) infection suggest that combination microbicides, which include two or more active ingredients, may also provide a particularly effective means to prevent HIV-1 transmission. We have recently identified the compound PSMA, an alternating copolymer of polystyrene (PS) and maleic anhydride (MA), as a potential partner for our candidate microbicide polyethylene hexamethylene biguanide (PEHMB), a member of the polybiguanide family of compounds. *In vitro* studies of PSMA demonstrated that this compound is minimally cytotoxic and highly effective against both macrophage- and T cell-tropic strains of HIV-1. We hypothesize that the dissimilar mechanisms of action of PSMA and PEHMB may provide additive or synergistic activity against HIV-1. Experiments are now underway to identify optimal combinations of PSMA and PEHMB to be used in experiments to assess toxicity, anti-HIV-1 activity, and formulation strategies. These investigations will be used to confidently advance the preclinical development of PSMA and a combination microbicide containing both compounds toward human trials.