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Innovations in drug delivery technology: Improvements in long-term herpes treatment

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Abstract

Herpesviruses are ubiquitous pathogens that infect many different animal species worldwide. The human herpesviruses HSV-1, HSV-2, and VZV are of particular clinical importance because of their frequency and the debilitating sequalae associated with their uncontrolled recurrences. Current antiviral interventions consist of multiple oral daily doses of drugs such as acyclovir (ACV), valacyclovir, or famciclovir; these frequent dosings keep adequately suppressive levels of drug in the tissues to abrogate recrudescence, yet require strict patient compliance. Such adherence to the dosing regimen is required because only 10-20% of ACV is absorbed from the gut and the drug itself has only a 3 hour half-life in vivo; any variance in administration could result in drug troughs that permit virus replication, which could result in the spontaneous appearance of drug-resistant mutants.

Previous research in our lab established that ACV can be delivered with near zero-order kinetics from a non-biodegradable silicone implant. The resulting device is also capable of suppressing HSV-1 reactivations in a mouse model over ten weeks. Our current research explores the development of bioerodable drug delivery devices, using polycaprolactone (PCL) as the matrix material. Furthermore, we herein report a novel fabrication method, VASE (volatile acid-solvent evaporation), that most likely results in a molecularly homogeneous mix of polymer and drug and, more significantly, improves stability, longevity, and drug delivery characteristics from the matrix. We expect that VASE will prove to be an important method for more perfect drug dispersion in delivery matrices for other acid-stable drugs in the future.

Biography

Margulies received B.S. at the Massachusetts Institute of Technology, where he did research with Drs. Eyal Ron and Robert Langer in controlled release technology. He earned his Ph.D. at the Johns Hopkins University School of Medicine under the tutelage of Dr. Wade Gibson, where he studied the G protein-coupled receptors encoded by human cytomegalovirus. He did his post-doctoral studies also at the Johns Hopkins University School of Medicine, with Dr. Janice Clements, studying CD4-independent entry of human and simian immunodeficiency viruses. He has been a faculty member at Towson University since 2001, where he established the Towson University Herpes Virus Lab. His research encompasses studies in the molecular biology of human cytomegalovirus and human herpes virus–6, and new methods for the long-term prevention of recurrent outbreaks of herpes simplex viruses-1 and -2, varicella zoster virus, and feline herpes virus-1.