



**NEWS RELEASE**  
July 19, 2004

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## **2004 GRANTS ANNOUNCED**

The Alternatives Research & Development Foundation (ARDF) announced today that \$155,000 has been awarded to conduct four research projects nationwide in its 2004 Alternatives Research Grant Program.

The purpose of the annual grant program is to stimulate development of new techniques for conducting basic biomedical research, testing, or education that do not rely on animal models. Past grants have helped improve the accuracy and efficiency of experiments that benefit human health, while successfully replacing or reducing animal use in broad areas of research, such as the production of monoclonal antibodies.

The 2004 grant cycle brings to a total more than \$1.25 million given since the inception of the program to support qualified scientists in the development of non-animal alternative methods.

ARDF is pleased to announce the recipients of the 2004 Alternatives Research Grant Program:

### **1. Dr. Luca Cucullo**

Department of Neurosurgery  
The Cleveland Clinic Foundation / Cleveland, Ohio

#### **Project: A new DIV-BBB\* For Extensive Pharmacological Study at the Blood Brain Barrier**

*\*Dynamic In Vitro Blood Brain Barrier [device]*

It often happens that new drugs designed to treat various brain disorders appear very promising in the laboratory but fail when put into human trials. Dr. Cucullo is addressing this gap between performance in initial phases of development (generally done in animals) and in final human clinical trials. He will use human cells in a device that cleverly mimics the layers and dynamics of the blood-brain barrier, a hurdle in achieving effective treatment. By using human cells outside the body rather than rodent brains, which react differently, Dr. Cucullo expects to develop a more accurate test to assess effectiveness of drugs during early stages of development.

In addition, Dr. Cucullo plans to test this model in a specific application as a predictor of the responsiveness of human brain tumors to chemotherapy.

### **2. Dr. David T. Curiel**

Gene Therapy Center  
University of Alabama Birmingham / Birmingham, Alabama

#### **Project: Human Tissue Slices as an Alternative for Mouse Models in the Evaluation of Gene Therapy Vectors**

The rapid development of gene therapy as a new approach for a wide spectrum of diseases has stimulated research in virtually every leading medical center. Dr. Curiel's team has made considerable progress in analysis of targeted gene therapy vectors to deliver the

gene, utilizing *in vitro* assays with human cells as well as the traditional use of animals. However, he questions the fidelity of mouse and rat systems with respect to the human counterparts of disease.

In this study, Dr. Curiel plans to utilize a special device to obtain precisely cut human tissue slices to develop a new *in vitro* test that will go beyond the preliminary human cell analysis and create the ability to assay the vectors in three-dimensional human tissue. He expects to use this new model to demonstrate a better representation of human disease and more accurate prediction of the effectiveness of gene therapy that, if widely adopted, will considerably reduce the number of animals use in gene therapy research.

### **3. Dr. Richard Lee Gregory**

Department of Oral Biology  
Indiana University / Indianapolis, Indiana

#### **Project: An Alternative *In Vitro* Biofilm Model for Dental Caries Study**

Studies of tooth decay and plaque formation have traditionally involved rats who experience considerable suffering as a result of the manipulations of the experiments, often including removal of their salivary glands. Dr. Gregory, who has conducted non-animal studies for the successful company Tom's of Maine, expects to demonstrate the usefulness of a method that mimics oral conditions in humans on a Biofilm Flow device, introducing a new and important parameter of fluid-shear stress.

Dr. Gregory expects that a green fluorescent protein (GFP) genetic marker will provide a reporter system to monitor gene expression and aid in the study of the attachment and detachment processes of oral bacteria.

### **4. Dr. Michael J. Rybak**

Anti-Infective Research Laboratory  
Wayne State University / Detroit, Michigan

#### **Project: Evaluation of an *In Vitro* Pharmacodynamic Model for Antibiotic Assessment: A comparison and potential replacement of a murine model of infection**

Models of infection to assess efficacy of antibiotic agents have traditionally used large numbers of animals in tests such as the murine (mouse) thigh model, where mice are first treated to damage their immune system and then injected with bacteria before being given an antibiotic. These experiments not only raise ethical issues, but have practical disadvantages as well, including the difference of pharmacokinetics in mice versus humans.

Dr. Rybak will develop an *in vitro* model consisting of a two compartment hollow fiber bioreactor that will closely simulate a three-dimensional site of infected animal and human tissue. He expects that the system will be able to elucidate how quickly the drug is able to attack the bacteria and how effective it is in doing so in order to predict results in humans. To demonstrate comparability for important uses such as drug approvals, he plans to compare with previously published data obtained in the animal methods.

Because of its practicality, lower cost, and rapid turn around, this system could enjoy quick adoption as a method of antibiotic assessment if this project is successful.

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