

9th ANNUAL DEPARTMENT OF PATHOLOGY YOUNG INVESTIGATORS' DAY  
 POSTER SESSION

Thursday, April 5<sup>th</sup>, 2007  
 TURNER CONCOURSE  
REGISTRATION FORM

E-mail COMPLETED Registration form and abstract to:  
 Stacey Morgan ([smorgan9@jhmi.edu](mailto:smorgan9@jhmi.edu)) on or before  
Friday, March 16th, 2007

If you have questions or problems regarding your submission, please contact Stacey Morgan via e-mail ([smorgan9@jhmi.edu](mailto:smorgan9@jhmi.edu))

Applicant's Name: Jose C. Garcia-Garcia Degree: Ph.D.

Applicant's Division: Medical Microbiology

Faculty Preceptor: J. Stephen Dumler  
 (Must hold a primary appointment in Pathology)

Appointment Category:  House Staff  Clin Fellow  Research Fellow  
 Medical Student  Graduate Student (Program: \_\_\_\_\_)

Register for:  Clinical Research  Translational Research  Basic Research

Full Poster Title \* Epigenetic Control of Host Cell Gene Expression by *Anaplasma phagocytophilum* AnkA Protein

Where has the work been presented?

Meeting Name American Society for Rickettsiology

Meeting Date September 2006

Not Previously Presented \_\_\_\_\_

Where is this work being published? \_\_\_\_\_

Journal Name, Volume, Page, Date \_\_\_\_\_

In Preparation \_\_\_\_\_

Author(s) (First & Last) \_\_\_\_\_

In-House Address: Ross 624  
 (Room # and Building Name, Lab, etc.)

Telephone: 410-955-8654 Beeper: \_\_\_\_\_

Fax: \_\_\_\_\_ E-mail: jgarci17@jhmi.edu

**\*INCLUDE A ONE-PAGE ABSTRACT (including title and all authors) OF THE WORK YOU WILL BE PRESENTING**

\*\*\*\*\*

Epigenetic Control of Host Cell Gene Expression by *Anaplasma phagocytophilum* AnkA Protein

Author: J. C. Garcia-Garcia, A. M. Milstone, J. S. Dumler;  
Johns Hopkins University School of Medicine, Baltimore, MD.

Abstract:

Intracellular pathogens, through a long-standing association with host cells, have evolved mechanisms that allow survival within the often hostile environment of their hosts by affecting vital host cell processes either directly or by interfering with signal transduction pathways. Recent work in our lab, using the rickettsial pathogen *Anaplasma phagocytophilum* as a model, has focused on a novel mechanism by which intracellular bacteria interact with the host cell at the nuclear interface. During *A. phagocytophilum* infection of neutrophils, changes in host gene transcription lead to down-regulation of antimicrobial mechanisms. Our recent data show that *A. phagocytophilum* produces one protein, AnkA, which is translocated into the host cell nucleus and interacts with host chromatin. We hypothesized that this interaction of AnkA with host chromatin leads to transcriptional changes mediated in part by alterations in chromatin structure. Using cell fractionation, we studied accumulation kinetics of AnkA in the nuclei of *A. phagocytophilum*-infected cells. AnkA accumulation correlated with downregulated transcription of *CYBB* and upregulated *IL8* transcription and protein expression. Similar transcriptional changes were also observed when HL-60 cells were transfected with purified AnkA or with an AnkA mammalian expression plasmid. Using chromatin immunoprecipitation with AnkA mab, AnkA bound host cell chromatin matrix attachment regions (MARs), such as a MAR in the *CYBB* promoter overlapping transcriptional activator binding sites. Histone acetylation, associated with transcriptional activity, decreased dramatically around the AnkA binding site. Changes in chromatin structure may presage downregulated expression of this locus during infection. These data strongly support the hypothesis that AnkA effects epigenetic host cell gene regulation. Identification of this novel pathogenicity mechanism improves understanding of the molecular basis for bacterial manipulation of host cells and facilitates future design of strategies for prevention and treatment of intracellular bacterial infections.