

10<sup>th</sup> ANNUAL DEPARTMENT OF PATHOLOGY YOUNG INVESTIGATORS' DAY  
POSTER SESSION

POSTER #

25

(for Admin. use)

Thursday, April 17<sup>th</sup>, 2008  
TURNER CONCOURSE  
REGISTRATION FORM

Applicant's Name: Balasubramanyam Karanam Degree: Ph.D

Applicant's Division: Gynecological Pathology

Faculty Preceptor: Richard Roden  
(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 \* **Vaccination with TA-CIN (L2E6E7), with immune enhancer GPI-0100 elicits protective humoral as well as cell mediated immune response in mice and monkey**

Where has the work been presented? Beijing, China

Meeting Name 24th International Papillomavirus Conference and Clinical Workshop  
Meeting Date Nov 3-9,2007

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

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

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

In Preparation (Y) - Where? Journal of Virology

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

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**E-mail COMPLETED Registration form and abstract to:  
Stacey Morgan ([smorgan9@jhmi.edu](mailto:smorgan9@jhmi.edu)) on or before  
Friday, March 14th, 2008**

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

**Vaccination with TA-CIN (L2E6E7), with immune enhancer GPI-0100 elicits protective humoral as well as cell mediated immune response in mice and monkey.**

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**Abstract:** L1 virus-like particle (VLP) vaccines provide effective protection against Human papillomavirus (HPV) type from which the L1 was derived via the induction of neutralizing antibodies. While partial protection can occur against very closely related types, it is generally type-restricted and necessitates highly multivalent L1 VLP vaccines to obtain broad coverage. The minor capsid protein, L2, is emerging as an attractive alternative cross-protective antigen. Unfortunately, neither L1 VLP nor L2-based vaccines are effective against pre-existing disease, suggesting the need to develop therapeutic vaccines. Unlike the capsid proteins, the E6 and E7 oncoproteins are both required to maintain and expressed throughout cervical intraepithelial neoplasia (CIN) and cancer. TA-CIN, a vaccine comprising the HPV16 L2, E6 and E7 in a single tandem fusion protein, attempts to combine the advantages of broad cross-protection against HPV transmission with therapeutic responses targeting HPV16 early proteins. Here we test TA-CIN formulated along with GPI-0100, a semi-synthetic quillaja saponin analog, that was developed to promote both humoral and cellular immune responses. TA-CIN administered subcutaneously to mice three times at monthly intervals (125mg of clinical-grade protein) with 50mg GMP-grade GPI-0100 was found to elicit high titer antibodies that effectively neutralized not only HPV16 but also other oncogenic HPV types including HPV18, HPV31, HPV45, HPV58. Similarly, vaccination of pigtail macaques (*Macaca nemestrina*) with TA-CIN (three doses of 125mg of TA-CIN with 1000mg GMP-grade GPI-0100 at monthly intervals) was well tolerated and induced serum antibodies that neutralized HPV16, HPV18, and HPV31 in vitro. Notably, vaccination of mice with TA-CIN protected them from cutaneous HPV16 challenge as effectively as HPV16 L1 VLP. Combination of TA-CIN along with adjuvant GPI-0100 enhanced production of E7-specific, interferon gamma producing CD8+ T cell precursors by 20-fold. Vaccination with TA-CIN in adjuvant GPI-0100 completely prevented tumor growth after challenge with 5 x 10<sup>4</sup> HPV16 transformed TC-1 tumor cells. Protection of the mice immunized with TA-CIN plus GPI-0100 against TC-1 in a prophylactic setting was significantly more effective than TA-CIN alone or GPI-0100 alone. Patients vaccinated with TA-CIN alone develop weak HPV neutralizing antibody and E6/E7-specific T cell responses. GPI-0100 has been used safely as an adjuvant in several human trials suggesting that the combination of TA-CIN and GPI-0100 warrants further study.