

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

POSTER #

21

(for Admin. use)

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

Applicant's Name: **SUBHASHINI JAGU** Degree: **Ph.D**

Applicant's Division: **Gyn-Pathology**

Faculty Preceptor: **Dr. Richard B 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 \* **Multitype L2 Fusion Protein as a Second Generation Prophylactic  
Human Papillomavirus Vaccine**

Where has the work been presented?

Meeting Name **Plenary talk at International Papillomavirus Conference, Beijing, China**

Meeting Date **November 3<sup>rd</sup>-9<sup>th</sup>, 2007**

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

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

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

In Preparation (Y/N) - Where? **Yes, Journal of Virology**

Author(s) (First & Last) **Subhashini Jagu, Richard B Roden**

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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))**

*(Paste abstract here)*

**Multitype L2 Fusion Protein as a Second Generation Prophylactic Human Papillomavirus Vaccine**

*Subhashini Jagu<sup>1</sup>, Balasubramanyam Karanam<sup>1</sup>, Nicole Malandro<sup>1</sup>, Ratish Gambhira<sup>1</sup>, Richard Roden<sup>1</sup>.*  
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The high cost and type-restricted protection by first generation HPV L1 virus-like particle vaccines necessitates the development of low cost and broadly protective second generation vaccines. Minor capsid protein L2 protects animals from papillomavirus challenge by the induction of neutralizing antibodies. While L2 induces antibodies that cross-neutralize diverse papillomavirus types, we observe that L2-specific antibodies typically neutralize related types more effectively than less evolutionarily related types. To enhance cross-protection we designed L2 fusion proteins consisting of known cross-neutralizing epitopes of divergent HPV types. Vaccination with HPV16 L2 polypeptides comprising residues 17-36, 1-88 or 11-200, was compared with three multitype L2 fusion proteins; 11-200x3 types (HPV6, 16, 18), 11-88x5 types (HPV1, 5, 6, 16, 18), 17-36x22 types (5 cutaneous, 2 mucosal low risk and 15 oncogenic types). Mice were vaccinated three times subcutaneously with 25ug of antigen in GPI-0100 adjuvant. Among all the monotype polypeptides, 11-200 generated the highest HPV16 neutralization titer. However, 11-200x3 induced the highest neutralization titer against HPV45 and HPV58 as well as with HPV16, HPV18, HPV6 as compared to other multitype and monotype fusion proteins. Immunized mice were challenged with HPV16 pseudovirus expressing luciferase. Vaccination with 11-200x3 protected mice against HPV16 challenge as well as HPV16 L1 VLP. Induction of HPV neutralizing antibodies upon vaccination with 25µg of 11-200x3 protein alone or with alum or 50ug or 200ug of GPI-0100, or 50ug GPI-0100 with Tween40 was compared. The presence of an adjuvant significantly boosted the humoral response to 11-200x3, but there was no significant difference among adjuvants. We conclude that vaccination with a single fusion protein comprising HPV6 L2 11-200, HPV16 L2 11-200 and HPV18 L2 11-200 produced in *E. coli* and formulated with an adjuvant is protective and induces broadly cross-neutralizing antibodies. NCI RAPID is preparing clinical grade 11-200x3 for early stage trials.