

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

**Thursday, April 5th, 2007
TURNER CONCOURSE
REGISTRATION FORM**

**E-mail COMPLETED Registration form and abstract to:
Stacey Morgan (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)**

Applicant's Name: Eli Bar Degree: PhD.

Applicant's Division: Neuropathology

Faculty Preceptor: Charles G. Eberhart M.D PhD.
(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: Cyclopamine-Mediated Hedgehog Pathway Inhibition Depletes Cancer Stem Cells in Glioblastoma.

Where has the work been presented? This work hasn't been presented yet.

Meeting Name Annual AACR Meeting

Meeting Date 4/15/2007

Not Previously Presented The work hasn't been presented yet

Where is this work being published? Submitted to the journal **Oncogene**

Journal Name, Volume, Page, Date N/A

In Preparation

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

Cyclopamine-Mediated Hedgehog Pathway Inhibition Depletes Cancer Stem Cells in Glioblastoma

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Abstract

Brain tumors can arise following deregulation of signaling pathways normally activated during neural development. We found that Gli1, a key Hedgehog pathway target, was highly expressed in 5 of 19 primary GBMs and in 4 of 7 GBM cell lines. Shh was expressed in some primary tumors, and in GBM-derived neurospheres, suggesting a potential mechanism for pathway activation. Hedgehog pathway blockade by cyclopamine caused a 40-60% reduction in growth of glioma lines highly expressing Gli1, but not in those lacking evidence of pathway activity. Cyclopamine also removed an additional population of cells when given together with ionizing radiation, suggesting the possibility of combinatorial therapies. Given the requirement for Hedgehog in nonneoplastic neural stem cells, we investigated if Hedgehog blockade could target the stem-like population in GBM. Cyclopamine blocked formation of U87-MG colonies and GBM-derived neurospheres, suggesting clonogenic cells had been depleted. In addition, the stem-like fraction in gliomas, marked by Aldefluor and Hoechst dye excretion (side population) was significantly reduced or eliminated by cyclopamine. Finally, viable cells injected intracranially following Hedgehog blockade were no longer able to form tumors, suggesting a population critical for ongoing growth had been removed.