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)

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(Must hold a primary appointment in Pathology)
Appointment Category:  _____House Staff  _____Clin Fellow  __X__Research Fellow
_____Medical Student  _____Graduate Student (Program:____________)
Register for:  _____ Clinical Research  _X__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.
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In Preparation
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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.