Reviewer's report

Title: Cucurbitacin I blocks cerebrospinal fluid and platelet derived growth factor-BB stimulation of leptomeningeal and meningioma DNA synthesis

Version: 2 Date: 16 July 2013

Reviewer: Nitin Telang

Reviewer's report:

General Comments:
This study seeks to examine the anti-proliferative effects of Cucurbitacin-I (JSI-124) on the cell cultures from fetal leptomeningiomas and patent derived meningiomas, and to identify its mechanism of action. The major mechanism of action of Cucurbitacin-I appears to be via the regulation of the STAT-3 pathway. Carefully designed experimental strategy has generated scientifically robust phenomenological and mechanistic data.

Specific Comments:
1. The experimental strategy of using leptomeningeal cultures and patient derived Grade I and Grade II meningiomas represents an innovative direction. Commonly observed Inter-patient variation has been adequately addressed.
2. The efficacy of JSI-124 to inhibit DNA synthesis, and its interaction with CSF and PDGF-BB has been adequately interpreted and discussed.
3. The molecular targets and mechanistic pathways that are commonly up-regulated in cancer cells have been convincingly demonstrated to be functioning via regulation of STAT-3 status.
4. Overall, the study outcome has provided scientifically robust mechanistic evidence for the anti-proliferative effects of Cucurbitacin-I (JSI-124).

Minor Essential Revisions:
1. The cerebrospinal fluid (CSF) samples from patients with or without neurological disease have been used. It will therefore, be of considerable interest to know whether specific CSF samples have selective effects on DNA synthesis in samples from fetal leptomeningiomas, or from Grade I or Grade II meningiomas. This clarification needs to be included in the Discussion section.
2. P.12, Para 2, Line 9: The meningioma cells showed a but also---: there appears to be a typo in the part of sentence bold faced. This needs to be corrected.