Paola Grandi, J Antivir Antiretrovir 2014, 6:2
http://dx.doi.org/10.4172/1948-5964.S1.020

OMICS Group Conferences
Accelerating Scientific Discovery

4th World Congress on
Virology

October 06-08, 2014 Hilton San Antonio Airport, TX, USA

# Highly selective HSV virotherapy for glioblastoma

**Paola Grandi**
University of Pittsburgh, USA

Glioblastoma Multiforme (GBM) is an aggressive brain cancer for which there is no effective treatment. Oncolytic HSV vectors (oHSV) are attenuated lytic viruses that have shown promise in the treatment of human GBM models in animals. Although proven safe for treatment of GBM in patients, oHSVs efficacy has been limited, a consequence of poor intra-tumoral virus replication and spread. To counter these limitations, we have developed oHSVs whose selective replication in GBM cells does not rely on defective genes. This was accomplished by (i) full retargeting of oHSV to utilize the epidermal growth factor receptor (EGFR) for infection of human GBM tumor cells and (ii) further vector engineering to modify the essential HSV immediate early gene (ICP4) for sensitivity to repression by the microRNA mir-124. Mir-124 is highly expressed in neurons but virtually absent in GBM and highly conserved among different species. The mir-124-regulated vector was unable to replicate in nude mice following intracranial inoculation supporting vector safety and was shown to be effective in the treatment of human GBM in nude mice. To enhance vector intra-tumor vector spread, our EGFR retargeted-mir-124 controlled vector was further modified by vector arming with the matrix metalloproteinase gene encoding MMP9. MMP9 degrades collagen type IV, a major component of the extracellular matrix (ECM) and basement membranes of glioblastomas but absent in normal brain tissue. Studies are ongoing to determine whether MMP9 expression enhances vector spread in GBM neurospheres and as a therapeutic agent for enhanced treatment of human GBM in animals.

## Biography

Grandi received her Ph.D. from the University of Ferrara (Italy) and was a post-doctoral fellow in the Molecular Neurogenetics Department at the MGH-HMS (Boston). She is now an Assistant Professor in the Dept. of Neurosurgery at the University of Pittsburgh and has a joint appointment in the Department of Microbiology and Molecular Genetics.She has a long standing interest in the molecular biololgy of herpes simplex virus, mechanisms of virus replication and neuropathogenesis and virus host cells interactions that result in innate immune responses to infection.

pag24@pitt.edu