Infectious Agents and Cancer

Poster presentation

Open Access

AKT/TSC/mTOR activation by the Kaposi's sarcoma-associated herpesvirus G protein-coupled receptor: novel therapeutic targets for the treatment of Kaposi's sarcoma

S Montaner*[1,2], R Chaisuparat[1], J Hu[1] and BC Jham[1]

Address: [1]Department of Oncology and Diagnostic Sciences, University of Maryland, Baltimore, Maryland, USA and [2]Greenebaum Cancer Center, University of Maryland, Baltimore, Maryland, USA

* Corresponding author

from 11th International Conference on Malignancies in AIDS and Other Acquired Immunodeficiencies (ICMAOI): Basic, Epidemiologic, and Clinical Research
Bethesda, MD, USA. 6–7 October 2008

Published: 17 June 2009

Infectious Agents and Cancer 2009, **4**(Suppl 2):P29 doi:10.1186/1750-9378-4-S2-P29

This abstract is available from: http://www.infectagentscancer.com/content/4/S2/P29

The identification of the Kaposi's sarcoma (KS)-associated herpesvirus (KSHV) as the viral etiologic agent for KS has provided an opportunity to uncover its molecular pathogenesis and to identify new therapeutic targets for this neoplasm. The expression of only one KSHV gene, *vGPCR*, is able to induce KS-like sarcomas in mice, suggesting that *vGPCR* may be the viral gene responsible for the development of KS.

Here, we demonstrate that dysregulation of Akt/TSC2/mTOR by the KSHV vGPCR is essential for KS sarcomagenesis. *In vitro*, cells overexpressing vGPCR showed constitutive signaling of Akt/TSC/mTOR. Immunohistochemical analysis of vGPCR experimental and human KS tissues revealed high levels of phosphorylated Akt and S6 ribosomal protein. Of interest, the treatment of allografts established upon injection of endothelial cells overexpressing KSHV vGPCR with the specific mTOR inhibitor, rapamycin, blocked tumor growth, providing a molecular explanation of the efficacy of rapamycin in the regression of KS lesions in patients with iatrogenic KS. Moreover, a novel dual inhibitor of PI3Kα and mTOR, PI-103, was able to inhibit vGPCR tumorigenesis *in vitro* and *in vivo*. Exposure of vGPCR expressing cells to this compound blocked the phosphorylation of Akt, its downstream substrates, and mTOR suggesting that combinatorial inhibition of mTOR and p110α may represent an effective therapeutic alternative for KS patients. All together, these results suggest that specific inhibitors of Akt/TSC/mTOR represent valuable therapeutic alternatives for Kaposi's sarcoma.