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Synergistic combinations of chromatin modifiers as a potential treatment approach for gliomas

A series of seminal discoveries made over the last decade have shown that critical changes in cancer cells, such as silencing of tumor suppressor genes and activation of oncogenes, are caused not only by genetics but also by epigenetic mechanisms. Although epigenetic changes are somatically heritable, in contrast to genetic changes, they are potentially reversible, making them good targets for therapeutic intervention. Covalent modifications of chromatin, such as methylation and acetylation of histones and methylation of DNA,are important components of epigenetic machinery. Several recent studies have shown that epigenetic modifiers are candidates for potent new drugs in multiple cancers therapies, including gliomas, and several clinical trials are ongoing. However, as with other chemotherapeutic drugs, toxicity is one of the main concerns with some of the potent epigenetic drugs. Synergistic combinations of these agents are one approach to overcoming toxicity issues and enhancing efficacy. In our previous studies, we demonstrated that specific combinations of histone methyltransferase (HMT) and deacetylase (HDAC) inhibitors significantly attenuated the viability of D54 cells, but had only a small effect on normal stem cell growth. Recently, we demonstrated that these combinations exhibit a similar effect also on other glioma cell lines. All these studies suggest that specific combinations of histone covalent modifiers could be an effective treatment option for several types of gliomas.

Biography

Arshak R Alexanian (PhD, VMD) is a founder and Chief Scientific Officer at Cell Reprogramming and Therapeutics LLC. He is also holding an Adjunct Associate Professor position in the Department of Medicine at the Medical College of Wisconsin (MCW). Previously, he held faculty positions in the Departments of Neurosurgery at MCW (2000-2013) and in the Departments of Anatomy and Neurobiology, as well as in Biochemistry and Molecular Biology, at Colorado State University (1997-2000). He has received training at universities and centers worldwide, including the Pasteur Institute and the University of Montpelier in France, the University of Saarland in Germany, Institute of Biochemistry in Armenia, Russia, and China. His research funded by the government grants such as National Institute of Health (NIH) and Veterans Affairs, as well as other organizations such as Spinal Cord Society, Quadracci, Bryon Riesch Paralysis Foundation, AOSpine North America and International, Hansjorg Wyss and others. The main focus of his current research activities (supported by NIH SBIR and other funding agencies) are 1) elucidation of epigenetic mechanism governing normal and cancer cells self-renewal, pluri- and multipotency, lineage commitment, differentiation and 2) development of new safe and cost-effective cell reprogramming technologies for generation of desired neural subtypes that can be used for the treatment of several neurological disorders including CNS injuries, age-related neurological disorders and brain cancers.

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