conferenceseries.com

4th International Conference on

Integrative Biology

July 18-20, 2016 Berlin, Germany

Protein replacement therapy for mitochondrial disorders: New hopes for incurable diseases

Haya Lorberboum-Galski[1], **Rapoport M**[1], **Marcus D**[1], **Erlich T**[1], **Hadad R, Greif H**[2] and **Lichtenstein M**[1]
[1]Hebrew University of Jerusalem, Israel
[2]BioBlast-Pharma Ltd., Israel

Modern medicine offers no cure for genetic mitochondrial disorders and the usual treatment is mostly palliative. We developed a novel concept for the treatment of mitochondrial disorders using Cell/Organelle-Directed Protein Replacement Therapy; the delivery of a wild type mitochondrial protein/enzyme directly to its sub-cellular location and into its natural complexes, in the form of a fusion protein. Our approach is to fuse a wild type mitochondrial protein, including the Mitochondrial Targeting Sequence (MTS) with the delivery peptide TAT [HIV-transactivator of transcription (TAT) peptide], which will lead the protein/enzyme into the cells and their mitochondria, where it will substitute for the mutated endogenous protein. We tested this novel approach using a number of mitochondrial proteins, implicated in mitochondrial human diseases: Lipoamide Dehydrogenase (LAD), C6ORF66 and Frataxin were evaluated *in vitro*, in patients' cells and *in vivo*, in mouse models. TAT-MTS-Mitochondrial fusion proteins are rapidly and efficiently internalizing into cells and their mitochondria both in patients' cells and in mice tissues, including the brain. Treatment with the new TAT-MTS-Mitochondrial fusion proteins, improves mitochondrial functions and life span in animal models. Interestingly, when we replaced the MTS sequence of the exogenous protein with a heterogeneous MTS sequence, both mitochondrial penetration and biological activity significantly increased. This novel approach may open new inroads in the management of many incurable mitochondrial diseases.

Biography

Haya Lorberboum-Galski is a full Professor of Biochemistry at the Department of Biochemistry and Molecular Biology, Institute for Medical Research Israel-Canada (IMRIC), Faculty of Medicine, the Hebrew University of Jerusalem, Israel. She has published over 60 publications in peer-reviewed journals in her fields of expert, as well as review articles and edited a book on chimeric proteins. She serves as an ad-hoc Referee for peer-reviewed journals. She is currently the Chairman of the Institute for Medical Research Israel-Canada (IMRIC).

hayag@ekmd.huji.ac.il

Notes: