Keren Cohen, J Cell Sci Ther 2014, 5:4
http://dx.doi.org/10.4172/2157-7013.S1.029

OMICS Group Conferences
Accelerating Scientific Discovery

4th World Congress on
Cell Science & Stem Cell Research
June 24-26, 2014 Valencia Conference Centre, Valencia, Spain

Non-RGD-based strategies to target the thyroid-αvβ3 integrin axis: Lesson from multiple myeloma

Keren Cohen
Tel Aviv University, Israel

Introduction: αvβ3 integrin is a cell surface receptor with a pivotal role in cancer, attaching proteins through an RGD (Arg-Gly-Asp) recognition site and acting as a true signaling molecule. Recently, a non RGD site, binding L-thyroxine (T4) and 3, 5, 3'-triiodo-L-thyronine (T3), has been described, initiating proliferative activities, mainly via the MAPK pathway. It has recently been shown that similar activation occurs in multiple myeloma (MM), a hematological disease with poor prognosis despite all approaches. This novel non RGD site can be blocked by tetraiodothyroacetic acid (tetrac), a natural deaminated T4 analog. In the present work, tetrac mechanism of action is characterized, for the first time in MM.

Methods: MM cell lines (CAG, RPMI 8226,ARK, ARP-1, U266) and primary cells, were grown with T3/T4 with/without tetrac (100 nM-50 μM) and analyzed for: cell counts (FACS, CyQuant), viability (WST-1), cell cycle (FACS, PI), cell death (Annexin-PI±pan-caspase inhibitor, ZVAD, FACS; cleaved Caspase 3, cleaved PARP, westerns), DNA damage response (pATM and PARP, westerns) and apoptotic genes (Real-Time PCR).

Results: An early (4-8 hours) and late (24 hours) effect by tetrac was observed. In the early phase, tetrac reduced cell proliferation ($p<0.05$) and induced DNA damage response (ATM and PARP) and apoptosis (Cleaved caspase 3 and cleaved PARP). After 24 hours, tetrac reduced significantly ($p<0.05$) cell number and cell viability and induced apoptotic cell death with a parallel increase in apoptotic genes expression.

Conclusion: The non RGD-αvβ3 integrin site in myeloma is a valid target for inhibition and examining potential blockers is pioneering.

Biography

Keren Cohen has completed her MSc at the age of 27 years and directly continued towards a PhD degree at the Translational Hemato-Oncology Laboratory. She published 2 articles and is supported by a Tel-Aviv University Student Fellowship for Excellence.

kerencohe@gmail.com