doi: 10.4172/1948-5956.10000S12

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

SNS01- An eIF5A-based biologic with significant anti-tumoral activity following systemic administration in a murine model of multiple myeloma

John E. Thompson[1,2], Catherine Taylor[1] and Richard Dondero[2]

[1]Department of Biology, University of Waterloo, Canada
[2]Senesco Technologies Inc., USA

Eukaryotic translation initiation factor 5A (eIF5A) is post-translationally modified to hypusine-eIF5A and is the only known protein to contain hypusine. Recent studies have indicated that unhypusinated eIF5A is strongly pro-apoptotic, initiating both mitochondrial and death receptor mediated apoptosis, whereas hypusine-modified eIF5A has a pro-survival function

SNS01 has two therapeutic components: (1) an RNAi-resistant plasmid with a B-cell-specific (B29) promoter encoding $eIF5A^{K50R}$, a mutant of eIF5A that cannot be hypusinated; and (2) an siRNA that selectively suppresses endogenous hypusinated eIF5A which promotes growth of cancer cells. SNS01 nanoparticles are formed by complexing these therapeutic nucleic acids with polyethylenimine (PEI), a synthetic cationic polymer that serves as a delivery vehicle. SNS01 induces apoptosis in both IL-6-responsive (KAS-6/1) and IL-6-independent (U266) myeloma cell lines and exhibits anti-tumoral activity when administered systemically to SCID mice bearing subcutaneous human multiple myeloma (KAS-6/1) tumors. Control mice treated with PEI nanoparticles containing a non-expressing plasmid and a non-targeting siRNA had an average tumour volume of 284 mm^3 at the time of sacrifice, whereas mice treated with 1.5 mg/kg or 0.75 mg/kg SNS01 exhibited significant tumor regression and had average tumor volumes of 13 mm^3 (95 % inhibition; *p = 0.026) and 24.5 mm^3 (91 % inhibition; *p = 0.03), respectively. TUNEL-labeling of tumor tissue indicated that tumor regression induced by SNS01 is attributable to apoptosis. Bio-distribution studies have indicated that that SNS01 nanoparticles are also taken up by B cells in the bone marrow. Thus SNS01 may be an effective treatment option for multiple myeloma patients.

Biography

John Thompson is Professor of Biology and Associate Vice-president, Research at the University of Waterloo, Chief Scientific Officer for Senesco Technologies Inc and a Fellow of the Royal Society of Canada.

Catherine Taylor is a Senior Research Associate in John Thompson's laboratory.

Richard Dondero is Vice-president, Research and Development at Senesco Technologies Inc.