11th International Conference on
CANCER STEM CELLS AND ONCOLOGY RESEARCH
June 11-13, 2018 | Dublin, Ireland

TARGETING NOTCH4 IN OVARIAN CANCER RESULTS IN DECREASED NUMBER OF CANCER STEM CELLS AND INCREASED SURVIVAL WHEN USED IN COMBINATION WITH CISPLATIN IN PRE-CLINICAL MODELS

Elaine M Hurt, Suneetha B Thomas, Jon Chesebrough, Tim Hummer and **Peter Pavlik**
MedImmune LLC, USA

The Notch pathway plays a central role in the regulation of cellular growth and differentiation. There are 4 known receptors and 5 ligands in this pathway. While all receptors have been shown to be important in tumor biology, Notch4 continues to be implicated as a key mediator of cancer stem cell (CSC) biology. CSC-targeted biologics are an important part of a comprehensive oncology therapeutic strategy due to the role of CSCs in tumorigenesis, therapeutic resistance and patient relapse. Targeting this sub-population of cells is anticipated to lead to more durable patient responses. We have developed a human IgG1 antibody that targets the negative regulatory region of the Notch4 receptor, keeping it in an auto-inhibited state. We have determined Notch4 is expressed by CSCs of many solid tumors and is increased by cisplatin, a commonly used chemotherapy. Furthermore, uur anti-Notch4 antibody inhibits ovarian CSC growth *in vitro* and secondary tumor growth *in vivo*, consistent with depletion of CSCs. Combination of our anti-Notch4 antibody with cisplatin in ovarian tumor models demonstrates a more durable response than cisplatin alone, as expected with a CSC-combination therapeutic approach. Overall targeting Notch4 with an inhibitory antibody demonstrates superior ability, as compared with other Notch pathway inhibitors, to inhibit CSCs in preclinical models.

BIOGRAPHY

Elaine M Hurt received her PhD in Biochemistry, Molecular Biology and Biophysics from the University of Minnesota in 1999 where she studied estrogen receptor signaling cascades. She did her post-doctoral studies at the National Institutes of Health in the laboratory of Dr. Louis Staudt elucidating the molecular mechanisms governing therapeutic responses in lymphoma and multiple myeloma patients. In 2010, She-joined MedImmune to lead their cancer stem cell group. Prior to joining MedImmune, She was a Staff Scientist at the National Cancer Institute, where she focused primarily on identifying and targeting prostate cancer stem cells. In 2014, She became Adjunct Associate Professor in the Department of Biochemistry and Molecular Biology at the University of Maryland. She is the co-inventor on several patents, has been an invited speaker at numerous conferences, and has published over 50 scientific articles.

elaine.hurt@yahoo.com

Note: