From chromosomal instability to metastases- H19's role in cancer progression and its clinical significance

Eli Raveh

Hebrew University of Jerusalem, Israel

Abstract

The oncofetal H19 long non-coding RNA (lnc RNA) is normally expressed in the embryo and down regulated at birth; however its expression is re-elicited in human tumors of almost every type. Accumulating data by us and others consolidate into a paradigm according to which H19 is in the center of a mammalian "selfish survival pathway" activated by the cancerous cell in order to cope with stress conditions. P53 nullification or dysfunction, hypoxia, serum starvation, chemotherapy and other stress inducers up-regulate H19 expression. H19 in turn supports tumor growth and enhances proliferation in response to hypoxia and p53 mutations. We have also recently proven that H19 RNA significantly contributes to epithelial to mesenchymal transition (EMT), a process which is known to emerge as a response to a multitude of stress conditions. Surprisingly, studies indicate that H19 is involved also in the further, apparently converse steps of mesenchymal to epithelial transition to support colonization and proliferation in the secondary tumor site. In view of the paradigm suggested above, H19's unique expression in cancers and the active involvement of H19 in almost every deleterious aspect of cancer progression, H19 should serve as a state of the art target for highly selective cancer therapy. Indeed, we currently use a DNA-plasmid based drug that harnesses H19 regulatory elements to drive the expression of Diphtheria toxin – a translational regulated therapy designed to selectively kill cancer cells with no collateral damage to the healthy surrounding tissues. We will comprehensively review recent studies that align with our paradigm and demonstrate how understanding of H19 expression and biology is translated into promising results in bladder, pancreas and ovarian cancer clinical trials.

Biography

Eli Raveh earned his PhD in Developmental Biology from the Hebrew University of Jerusalem (HUJI) in 2011, specializing in Hair & Skin Development. Since then he is serving as a Research Assistant in Prof. Avraham Hochberg's Laboratory at the department of biological chemistry, HUJI, which focuses on cancer therapy research based on the H19 gene involvement in cancer.