Genome Biology

POSTER PRESENTATION Open Access

Reprogramming the human cancer cell nucleus

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From Beyond the Genome: The true gene count, human evolution and disease genomics
Boston, MA, USA. 11-13 October 2010

Background

The human cancer cell nucleus contains 46 or more chromosomes, each bearing portions of the human genome. During the initiation and progression of the neoplastic state, chromosome portions can be duplicated, deleted, translocated or inverted, and these lesions often aggravate the rate of progression and metastasis of the cells. During gene transcription, two or more chromosomes can form gene clusters at specific gene sites, and such clusters regulate the rate of gene transcription and replication. Gene clusters are often sensitive to the immediate effects of ligand microRNAs (miRNAs) and other transcribed ultra-conserved noncoding RNAs (T-UCRs). Recent studies have reported 481 species of T-UCRs within human neuroblastoma cells, mostly from intragenic exon and/or intron sequences within the Ref-seq genome, but 37% were found transcribed from noncoding intergenic sites in the neoplastic cell genome [1]. In 237 of the 481 T-UCRs, intra-nuclear functions were completely independent of those within coding and other nuclear RNAs, and were increased in neuroblastomas of an aggressive type. Most of the T-UCRs could be found in linked regions of 4 major gene clusters, associated with the 4 nuclear processes of neoplastic proliferation, apoptosis, differentiation, and patient survival. Similar T-UCR RNA patterns in normal human fibroblast BJ cells were also observed [1]. Earlier observations had demonstrated a specific deficiency of let-7 RNA microRNA species within human lung and breast neoplasms, that was reversed by the addition of let-7 RNA species to the neoplastic cells in culture [2,3].

Conclusion

It appears that microRNAs and perhaps T-UCRs may well be able to reverse the neoplastic state within animals with metatstatic neoplasms, and these RNAs can be delivered as liposomal exosomes [4].

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Published: 11 October 2010

References

1. Mestdagh E, *et al*: **An integrative genomics screen uncovers ncRNA T-UCR functions in neuroblastoma tumours.** *Oncogene* 2010, **29**:3583-3592.
2. Takamizawa J, *et al*: **Reduced Expression of the let-7 MicroRNAs in Human Lung Cancers in Association with Shortened Postoperative Survival.** *Cancer Res* 2004, **64**:3753-3756.
3. Kumar MS, *et al*: **Suppression of non-small cell lung tumor development by the let-7 microRNA family.** *Proc Natl Acad Sci USA* 2008, **105**:3903-3908.
4. Kosaka N, *et al*: **Secretory Mechanisms and Intercellular Transfer of MicroRNAs in Living Cells.** *J. Biol. Chem* 2010, **285**:17442-17452.

doi:10.1186/1465-6906-11-S1-P14
Cite this article as: Frenster and Hovsepian: Reprogramming the human cancer cell nucleus. *Genome Biology* 2010 **11**(Suppl 1):P14.

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