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Landes Highlights

A new method to identify microRNA targets: OrbID

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MicroRNAs (miRNAs) coordinate networks of mRNAs, but predicting specific sites of interactions is complicated due to the very few bases of complementarity needed for regulation. A recent report by Dr Glen Borchert and colleagues presents a novel approach to miRNA target identification. Previously, the molecular events responsible for the genomic formation of many miRNA loci from transposable element (TE) sequences have been described. This led the authors of the recent report to hypothesize that a miRNA and its mRNA target sites might actually be formed in parallel by ongoing colonization of a common ancestral TE. In light of this, they propose that limiting miRNA target searches to transcripts containing the TE initially giving rise to a miRNA can significantly facilitate target identification. The report outlines the methodology behind OrbID (Origin-based identification of microRNA targets). Interestingly, OrbID was found to be particularly efficacious at predicting the mRNA targets of miRNAs formed more recently in evolutionary time. This is in contrast to the principal miRNA target algorithms, which rely heavily on target site conservation across species and are therefore most effective at predicting targets for older miRNAs. After defining the TE origins of over 200 human miRNAs, OrbID successfully generated likely target sets for 191 predominately primate-specific human miRNA loci. While only a handful of the loci examined were well enough conserved to have been previously evaluated by existing algorithms, the authors find about 80 % of the targets for the oldest miRNA (miRNA-28) in their analysis contained within the principal Diana and TargetScan prediction sets. More importantly, four of the 15 OrbID miRNA-28 putative targets have been previously verified experimentally. Since OrbID proved best-suited for predicting targets for more recently formed miRNAs, the authors suggest that OrbID makes a logical complement to existing, conservation based, miRNA target algorithms.

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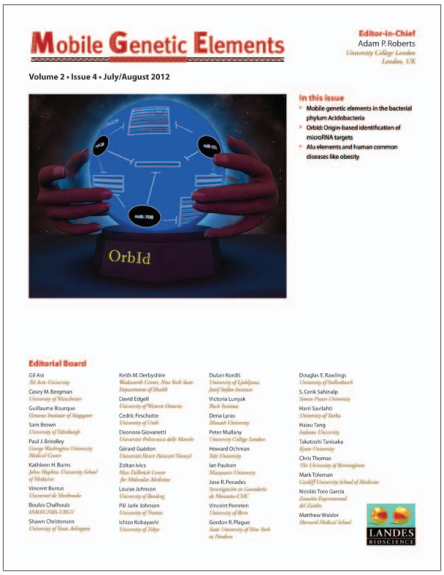

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Study of conserved miRNA family members with a single reagent

Xiangling Yang, Zina Jeyapalan Rutnam, Chunwei Jiao, Duo Wei, Yizhen Xie, Jun Du, Ling Zhong and Burton B. Yang

MicroRNAs are non-coding RNAs, 18-25 nucleotides in length, that are able to modulate gene expression, primarily negatively be either inducing the degradation or repressing translation of the target mRNAs. The binding specificity and efficiency is believed to be determined by a 6-7 nucleotide sequence near the 5′ region of miRNAs, the so called „seed sequence", which is the initial binding site of the miRNA to the 3′UTR of the target mRNA. The 12 members of the let-7 miRNA family have been extensively studied and classified as tumor suppressor miRNAs. They share identical seed regions, suggesting that they may target the same mRNAs. A new study set out to develop a means that can regulate the functions of all family members. Using a DNA synthesis technique, Dr Burton Yang and colleagues generated an anti-let-7 sponge aiming to modulate the function of all members. The anti-let-7 contruct could bind and inactivate all members of the let-7 family, producing decoy and decay effects. Stable expression of the anti-let-7 construct in two types of cancer cells increased cell survival, invasion and adhesion. This corroborates with known functions of let-7 family members. Further, the authors identified a novel target site across all species of the let-7 family in hyaluronan synthase 2 (HAS2). Overexpression of HAS2 produced similar effects as the anti-let-7 sponge. Silencing HAS2 expression by siRNAs produced opposite effects to anti-let-7 on cell survival and invasion. The ability of anti-let-7 to regulate multiple members of the let-7 family allowed the authors to observe their multiple functions using a single reagent. The authors suggest that this approach could be applied to other family members with conserved sequences.

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Role for miR-20a in the progression of human prostate cancer

Long Chen, Jane E. Dahlstrom, Sung-Hun Lee and Danny Rangasamy

The aberrant expression of microRNAs (miRNAs) has been found in various types of cancer. For instance, miRNAs have recently been shown to participate in the development, prognosis and chemo-resistance of prostate cancer. A new study by Dr Zhan-Song Zhou and co-workers found miR-20a to be significantly upregulated in prostate cancer compared with normal prostate tissues. The proliferation and colony formation assays revealed that the downregulation of miR-20a by miR-20a inhibitor suppresses the proliferation of prostate cancer cell line cells in vitro and also inhibits tumor growth in vivo. Furthermore, the gap junction protein α 1 (CX43) was identified as a direct target gene of miR-20a. These widely-expressed transmembrane proteins, known to form gap junction complexes, play critical roles in cell growth, tissue regeneration and carcinogenesis. As a member of gap junction channels, CX43 has previously been found to be disregulated in multiple types of cancer, and evidence suggests that CX43 may function as a tumor suppressor. In the current study, the upregulation of CX43 was detected in prostate cancer cell line cells after treatment with miR-20a inhibitor both in vitro and in vivo. In conclusion, the study findings show that miR-20a significantly contributes to the progression of prostate cancer by targeting CX43.

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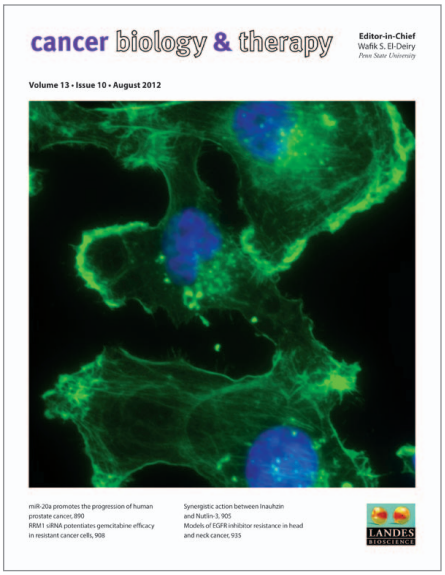

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