Down-Regulation of miR-129-5p and the let-7 Family in Neuroendocrine Tumors and Metastases Leads to Up-Regulation of Their Targets Egr1, G3bp1, Hmga2 and Bach1

Down-Regulation of miR-129-5p and the let-7 Family in Neuroendocrine Tumors and Metastases Leads to Up-Regulation of Their Targets Egr1, G3bp1, Hmga2 and Bach1

Expression of miRNAs in Neuroendocrine Neoplasms (NEN) is poorly characterized. We therefore wanted to examine the miRNA expression in Neuroendocrine Tumors (NETs), and identify their targets and importance in NET carcinogenesis. miRNA expression in six NEN primary tumors, six NEN metastases and four normal intestinal tissues was characterized using miRNA arrays, and validated by in-situ hybridization and qPCR. Among the down-regulated miRNAs miR-129-5p and the let-7f/let-7 family, were selected for further characterization. Transfection of miR-129-5p inhibited growth of a pulmonary and an intestinal carcinoid cell line. Analysis of miRNA expression changes identified EGR1 and G3BP1 as miR-129-5p targets. They were validated by luciferase assay and western blotting, and found robustly expressed in NETs by immunohistochemistry. Knockdown of EGR1 and G3BP1 mimicked the growth inhibition induced by miR-129-5p. let-7 overexpression inhibited growth of carcinoid cell lines, and let-7 inhibition increased protein content of the transcription factor BACH1 and its targets MMP1 and HMGA2, all known to promote bone metastases. Immunohistochemistry analysis revealed that let-7 targets are highly expressed in NETs and metastases. We found down-regulation of miR-129-5p and the let-7 family, and identified new neuroendocrine specific targets for these miRNAs, which contributes to the growth and metastatic potential of these tumors.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Cognitive Systems, Rigshospitalet, University of Copenhagen, Memorial Sloan-Kettering Cancer Center, Næstved Hospital
Pages: 1-21
Publication date: 2014
Peer-reviewed: Yes

Publication information
Journal: Genes
Volume: 6
Issue number: 1
ISSN (Print): 2073-4425
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.49 SJR 1.82 SNIP 0.856
Web of Science (2017): Impact factor 3.191
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.62 SJR 1.951 SNIP 0.782
Web of Science (2016): Impact factor 3.6
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 3.18 SJR 1.743 SNIP 0.718
Web of Science (2015): Impact factor 3.242
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 1.33 SJR 0.838 SNIP 0.484
Web of Science (2014): Impact factor 1.151
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 1.36 SJR 0.807 SNIP 0.394
ISI indexed (2013): ISI indexed no
Scopus rating (2012): CiteScore 1.45 SJR 0.843 SNIP 0.406
ISI indexed (2012): ISI indexed no
Scopus rating (2011): CiteScore 0.94 SJR 0.473 SNIP 0.175
ISI indexed (2011): ISI indexed no
Original language: English
Keywords: GENETICS, MIDGUT CARCINOID-TUMORS, TRANSCRIPTION FACTOR, MICRORNA EXPRESSION, SIGNALING PATHWAY, BINDING PROTEINS, REAL-TIME, CANCER, GROWTH, CELLS, DOMAIN