miR-146a Expression in Cervical Squamous Cell Carcinoma

Conference Paper · January 2013

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miR-146a Expression in Cervical Squamous Cell Carcinoma

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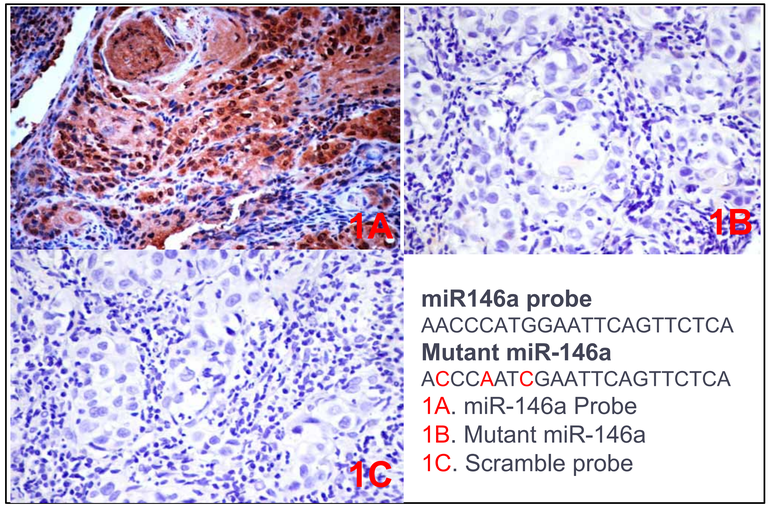
Background

MicroRNA (miRNA) are short single stranded RNA molecules that act as post-transcriptional regulators by binding to complementary sequences on target messenger RNA transcripts. miR-146a, initially characterized as playing an important role in innate immune response to microbial infection, has been implicated in recent studies in control of cell growth, differentiation and survival. Lower miR-146a expression has been associated with more extensive lymph node metastasis and venous invasion in gastric and breast carcinoma. However, the expression of miR-146a in cervical squamous cell carcinoma (SCC-Cx) and its role in prognosis is not fully established. It has been reported that miR-218 levels in patients with high-risk CIN were lower than in those with low-risk CIN. In this study, we have examined the expression of miR-146a and miR-218 in SCC-Cx.

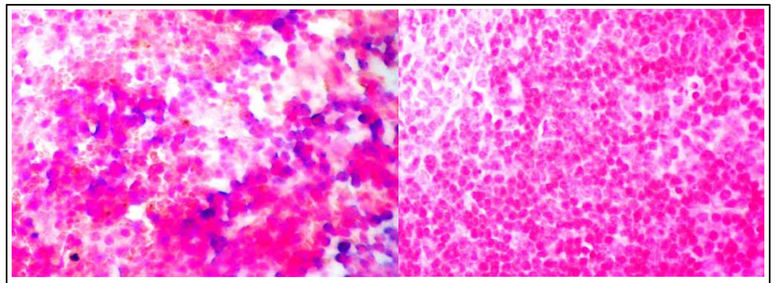
Design

Tissue microarrays were constructed from 60 cases of SCC-Cx and 10 normal Cx biopsies. FAM-labeled scramble probe (BioGenex, PR032), miR-146a (BioGenex, HM146A), mutant miR-146a (BioGenex, HM146AM), miR-218 (BioGenex, HM218) and One-step ISH Detection Kit (BioGenex, DF400) were used in this study. Briefly, following dewaxing and rehydration, FFPE tissue slides were heated in Nucleic Acid Retrieval Solution I (NAR-I, Biogenex) for 10 min at 92C. After incubation with 40 nM of microRNA probe for 60 min at 50 C, the signal was amplified with anti-fluorescein antibody .

Results

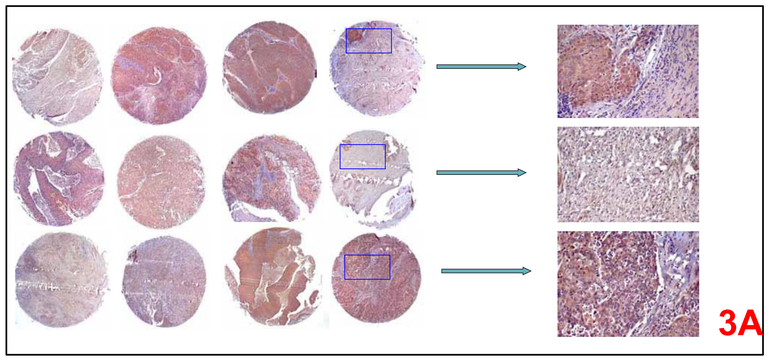


miR146a probe
AACCCATGGAATTCAGTTCTCA
Mutant miR-146a
ACCCAATCGAATTCAGTTCTCA
1A. miR-146a Probe
1B. Mutant miR-146a
1C. Scramble probe



2A. miR-146a staining in WT mouse spleen

2B. miR-146a staining in KO mouse spleen



Results

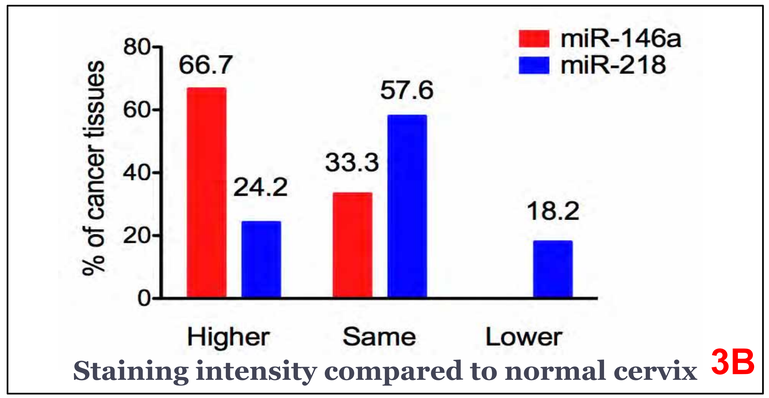


Figure 1. In SCC-Cx, miR-146a staining was observed only with miR-146a probe, but not with mutant miR-146a or scramble probe.

Figure 2. The microRNA staining was observed in wild-type mouse spleen (blue color from the chromogen BCIP), but not in miR-146a knockout mouse spleen tissues.

Figure 3. Using the cervical cancer assay, we found that the expression of miR-146a was up-regulated in 66.7% of cancer samples compared with normal cervical tissues with a trend towards increased expression in moderate to poorly differentiated cases. But another microRNA, miR-218, did not show significant difference (Array data not shown).

Conclusion

SCC-Cx cases showed upregulation of miR-146a in the majority of cases and showed a trend towards increased expression in moderately to poorly differentiated SCC-Cx. miR-218 expression was decreased or similar compared to normal controls in most SCC-Cx cases. Larger studies to examine the prognostic implications of these two markers are warranted.