In situ Expression Patterns of miRNAs in High-grade Prostatic Carcinoma (PCa).

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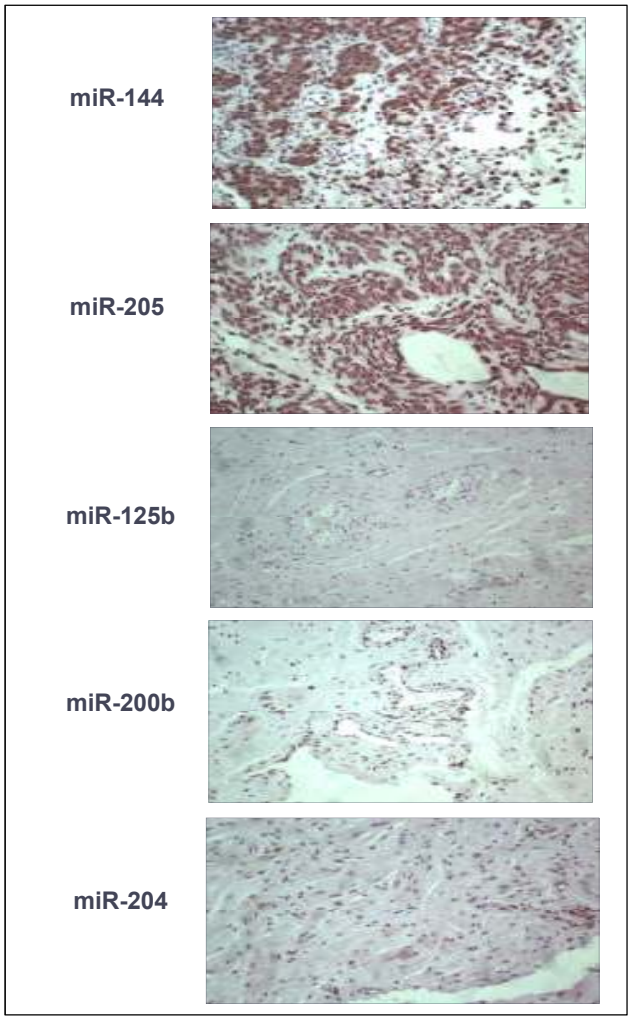
Background

MicroRNAs (miRNAs) are short, non-coding RNAs involved in post-transcriptional regulation of gene expression. Increasing data implicate dysregulation of miRNAs and their cognate targets as a fundamental property of diverse cancers. In prostatic carcinoma (PCa), miR-205 and miR-200b are both implicated as regulators of epithelial mesenchymal transition. miR-144 and miR-204 promote tumorigenesis while miR-125b regulates transcriptional signals, mediating proliferation, metastasis, and invasion. To date, interpretation of miRNA function in PCa has been limited by the inability to determine expression patterns in situ on a cellular level as profiling-based strategies using tissue homogenates may not adequately resolve expression differences in tumor microenvironment. Translation of any promising miRNA-based biomarkers would be greatly facilitated by their applicability to archival paraffin sections.

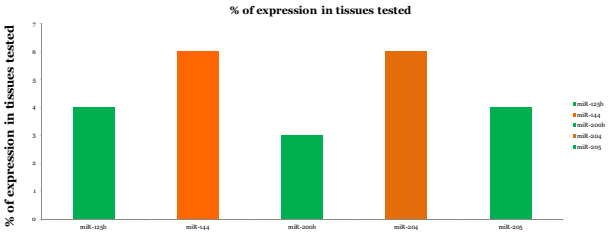
Design

Cases of high-grade PCa (n=10) were stained by chromogenic miRNA probes for miR-125b, miR-144, miR-200b, miR-204 and miR-205 (BioGenex) and visualized using Super Sensitive™ *in situ* Detection System (BioGenex, DF400-50K). Briefly, following dewaxing and rehydration, FFPE tissue slides were heated in Nucleic Acid Retrieval Solution I (NAR-I, BioGenex) for 20 min at 98ºC. After incubation with microRNA probe for 120 min at 52ºC, the signal was amplified with anti-fluorescein antibody . Nuclear staining was evaluated semi-quantitatively by intensity (low, no or weak stain; high, moderate to intense stain).

Results



Results



Benign prostatic glands (secretory & basal cells) showed strong immunoreactivity for all miRNAs (A). miR-125b, miR-200b, and miR-205 (B) were expressed at low levels in 33%, 44% and 44% of PCa cases, respectively, while down-regulation of 2 miRNAs was observed in 3 cases. miR-144 and miR-204 were expressed at higher levels in 22% and 44% cases, respectively.

Conclusion

Consistent with observations from model systems, suppressor miRNAs were expressed at low levels in high grade PCa while miRNAs implicated in disease progression were expressed at higher levels. Heterogeneity of expression was noted between cases and differing cell types, underscoring the importance of visualizing expression in situ on a cellular level. These observations demonstrate the feasibility and utility of determining miRNA expression on standard tissue sections. Candidate biomarker miRNAs may be tested prospectively and translated into diagnostic practice in a facile manner through this technology.