

Association of miR-146a-5p and miR-21-5p with prognostic features in melanoma subtypes

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Objective

To verify the association between the expression of miR-146a-5p and miR-21-5p and different melanoma features associated with patients' prognosis.

Methods

FFPE slices of 170 samples from patients with cutaneous melanoma were provided by Dermatopathology unit of Bologna University Hospital. RNA was isolated using miRNeasy kit and, after the extraction, RNA samples were converted to cDNA using miRCURY LNA RT kit. Starting from data obtained by CFX Manager software, the levels of miR-146a-5p and miR-21-5p were calculated. The association of miRNAs expression with selected histo-pathological features was considered significant for values of two-sided P less or equal to 0.05. For all categorical variables, differences across the groups were analyzed using Mann-Whitney or unpaired t-test according to D'Agostino-Pearson Test for normality.

Results

MiR-146a-5p and miR-21-5p expression was significantly higher in all tumors with higher **mitotic rate** ($\geq 1/\text{mm}^2$). Considering the **ulceration** status, we assessed that miR-146a-5p and miR-21-5p expression was significantly higher in ulcerated melanomas (Fig.1). We did not observe any difference in miRNAs expression when we considered all subtypes and their **regression** status (Fig.2). We then stratified miRNAs combined expression in different melanoma subtypes and surprisingly the MiR-146a-5p and miR-21-5p expression was lower in **lentigo maligna melanoma (LMM)** than in all the other histotypes (OHT). Moreover, given the recognized association of miR-146a-5p and miR-21-5p with **Breslow Thickness (BT)**, we also stratified the tumors according to both BT and tumor histotype and miR-146a-5p and miR-21-5p expression was lower even in LMM with BT ≥ 0.8 when compared to all the other histotypes with same BT (Fig.3).

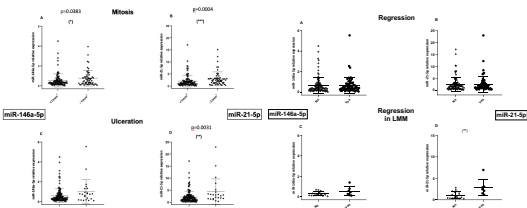


Fig.1 Analysis of miR-146a-5p and miR-21-5p expression in melanoma prognostic group: (A), (B): Scatter plots showing a significant difference in miR-146a-5p ($p=0.0383$) and miR-21-5p ($p=0.0004$) expression in samples with mitotic rate $\geq 1/\text{mm}^2$ and $< 1/\text{mm}^2$. (C) The plots show a higher miR-146a-5p expression and (D) a significantly higher miR-21-5p expression ($p=0.0031$) in ulcerated samples compared to samples without presence of ulceration.

Fig.2 Analysis of miR-146a-5p and miR-21-5p expression and regression status: (A) and (B) miR-146a-5p and miR-21-5p did not show different expression between samples with presence and absence of regression when both considering all subtypes. (C) No difference was found in miR-146a-5p expression in LMM subtype with or without regression (D), but a significant increased expression ($p=0.0030$) of miR-21-5p was observed in LMM subtype with presence of regression.

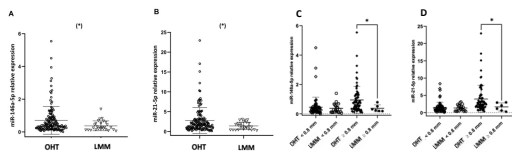


Fig.3 Differential miR-146a-5p and miR-21-5p expression in association with tumor histotypes (LMM vs OHT): (A), (B) Scatter plot graphs representation of miR-146a-5p and miR-21-5p relative expression in LMM vs OHT. A significantly difference in miRNA expression was found both for miR-146a-5p ($p=0.0189$) and miR-21-5p ($p=0.0247$) expression in the two groups. (C), (D) Scatter plots of miR-146a-5p and miR-21-5p relative expression LMM with BT ≥ 0.8 mm or OHT with BT < 0.8 mm (OBL ≥ 0.8 mm, OBL < 0.8 mm). Significantly lower expression was observed both for miR-146a-5p ($p=0.0331$) and miR-21-5p ($p=0.0473$) in LMM with BT ≥ 0.8 mm compared to OHT with BT ≥ 0.8 mm.

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