MIR-30E-5P DISCRIMINATES PATIENTS WITH IDIOPATHIC OSTEOPOROSIS AND LOW-TRAUMATIC FRACTURES

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BACKGROUND

- Circulating microRNAs (miRNAs) are a novel class of stable extracellular biomarkers. They are actively released from circulating cells or solid tissues, and have been shown to reflect the physiology of donor cells, or to modulate the behavior of their target cells. Several miRNAs were previously shown to regulate bone homeostasis in vitro and in vivo.
- The aim of this study was to explore changes in circulating miRNAs between subjects with a history of idiopathic osteoporotic fracture and age-matched control subjects.

	OPO	CTRL
No. of patients	36	39
preMP/postMP/male	10/10/16	12/11/16
Age (yr)	46.6 ± 13.0	46.6 ± 9.4
Height (cm)	170.3 ± 8.1	172.0 ± 10.3
Weight (kg)	71.3 ± 16.6	77.6 ± 13.6
Body mass index	24.6 ± 5.4	26.3 ± 4.4
Vertebral fractures, mean	1.9 ± 2.2	0
Peripheral fractures, mean	2.4 ± 4.4	0
Smoking (%)	36	23
Alcohol (%)	6	0
Family history f%)	22	0
Previous Treatment (%)	31	0
Lactose intolerance (%)	14	0

Table 1. Patient characteristics. PreMP, premenopausal women; PostMP, postmenopausal women; MIO, male idiopathic osteoporosis. No signifacant differences were found between subgroups.

METHODS

- Patients with low-traumatic fractures (46.6. ± 13.0 yrs) and comparable healthy controls (46.6 ± 9.4 yrs) were included (see table 1).
- Patients were considered as having idiopathic osteoporosis if they were premenopausal women or men age <50 years with low-traumatic fractures but had a normal medical history.
- miRNAs were also evaluated in postmenopausal osteoporosis.
- Reverse-Transcription quantitative PCR (RT-qPCR) analysis of 187 circulation microRNAs was conducted using custom-designed 384 well panels (Exiqon, Denmark).

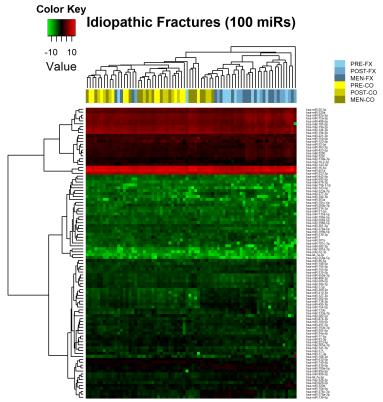

Figure 1. Heatmap with hierarchial clustering of all samples. 100 miRNAs with highest variation (SD) across all samples were considered for clustering.

RESULTS

- Unsupervised hierarchical clustering gave two main clusters, which largely corresponded to subjects with fractures and controls (Fig. 1). No subclusters corresponding to PreMP, PostMP and MiO were observed.
- MIO showed the highest number of regulated miRNAs (55), followed by PostMP (48) and PreMP (46).
- An overlap of 19 regulated miRNAs (16 down-regulated, 3 up-regulated in FX) was observed across all three subgroups (Fig. 2).
- miRNA 30e-5p was significantly down-regulated in patients with idiopathic osteoporosis (Fig. 3)
- ROC-analysis for miR-30e-5p showed excellent discriminatory power (AUC=0.96, p<0.0001, Fig. 3).
- Previous anti-resorptive treatment and weight did not influence miRNAs.

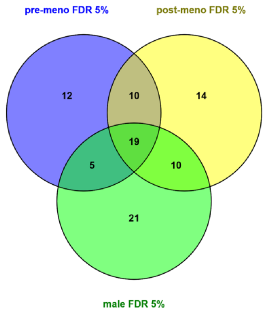

Figure 2. An overlap of 19 miRNAs regulated in all three subgroups were observed.

CONCLUSION

- Our data indicate that patients with male idiopathic osteoporosis as well as premenopausal and postmenopausal osteoporosis have a shared circulating miRNA profile regardless of age and sex, as indicated by the overlap of 19 regulated miRNAs.
- miR-30e-5p in particular discriminates patients with low-traumatic fractures from healthy controls independently of age, sex, weight and pretreatment.
- miR-30e-5p was previously reported to suppress osteogenic differentiation via IGF2 in vitro and in vivo.

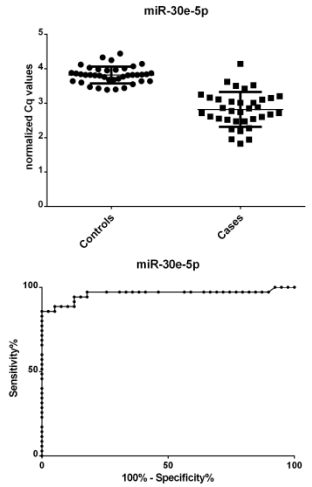

Figure 3. Top: Scatterplot depicting global-mean normalized miR-30e-5p levels in cases and controls. Bottom: ROC Curve Analysis.