

miRNA expression patterns of colorectal adenocarcinomas

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Introduction:

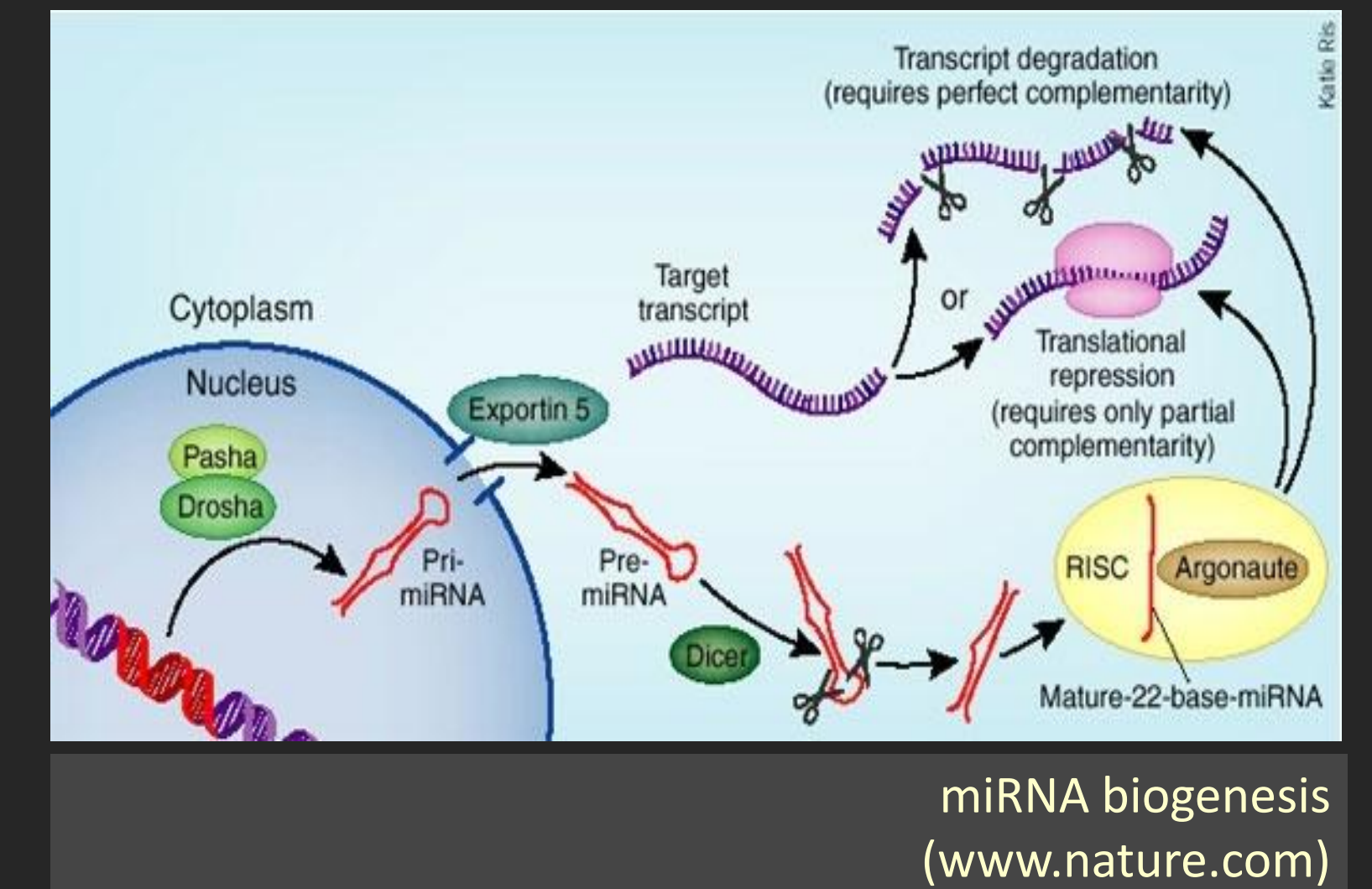
Recent advances in the field of RNA research provided evidence implicating non-coding RNA molecules in colorectal carcinogenesis. Epigenetic alterations in colorectal cancer that transform colon epithelial cells into adenocarcinoma cells include aberrant expression of miRNAs. We customized and tested a panel of miRNAs for human colorectal adenocarcinoma.

Materials and methods:

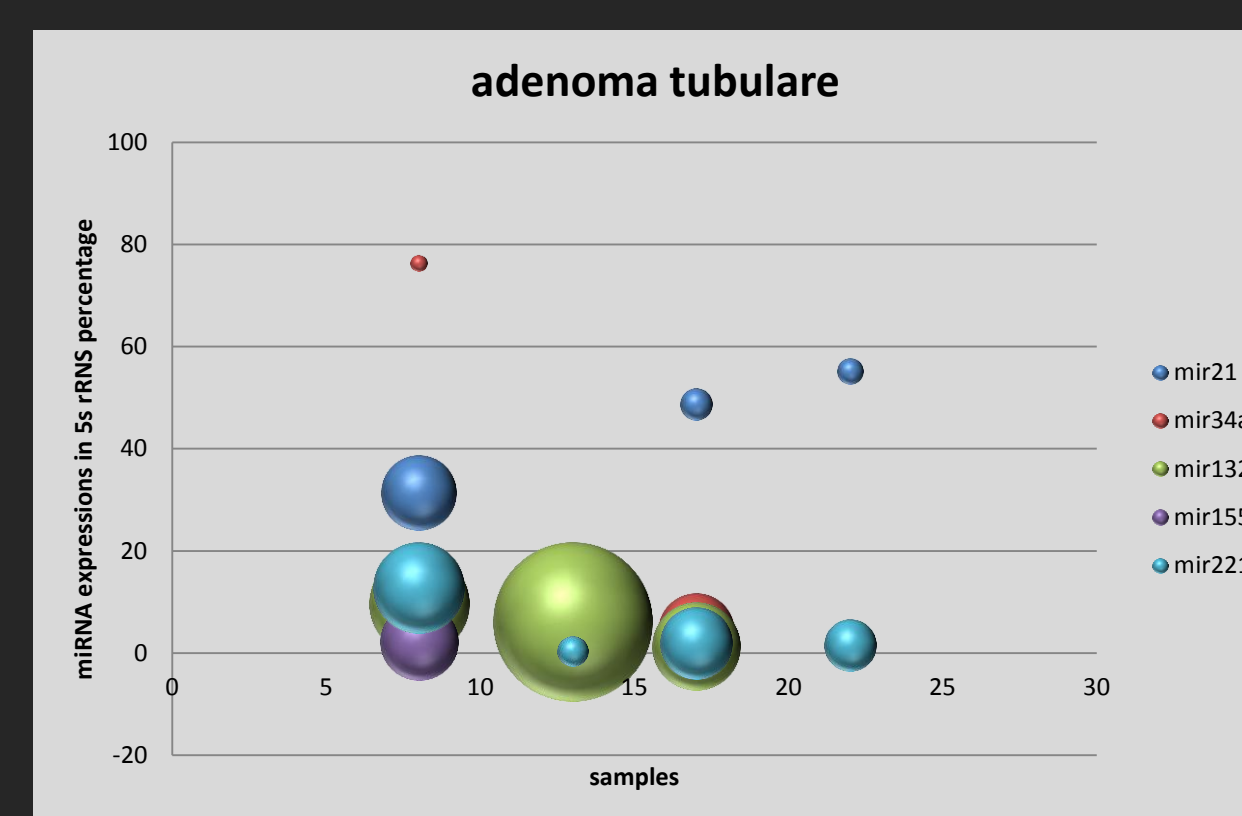
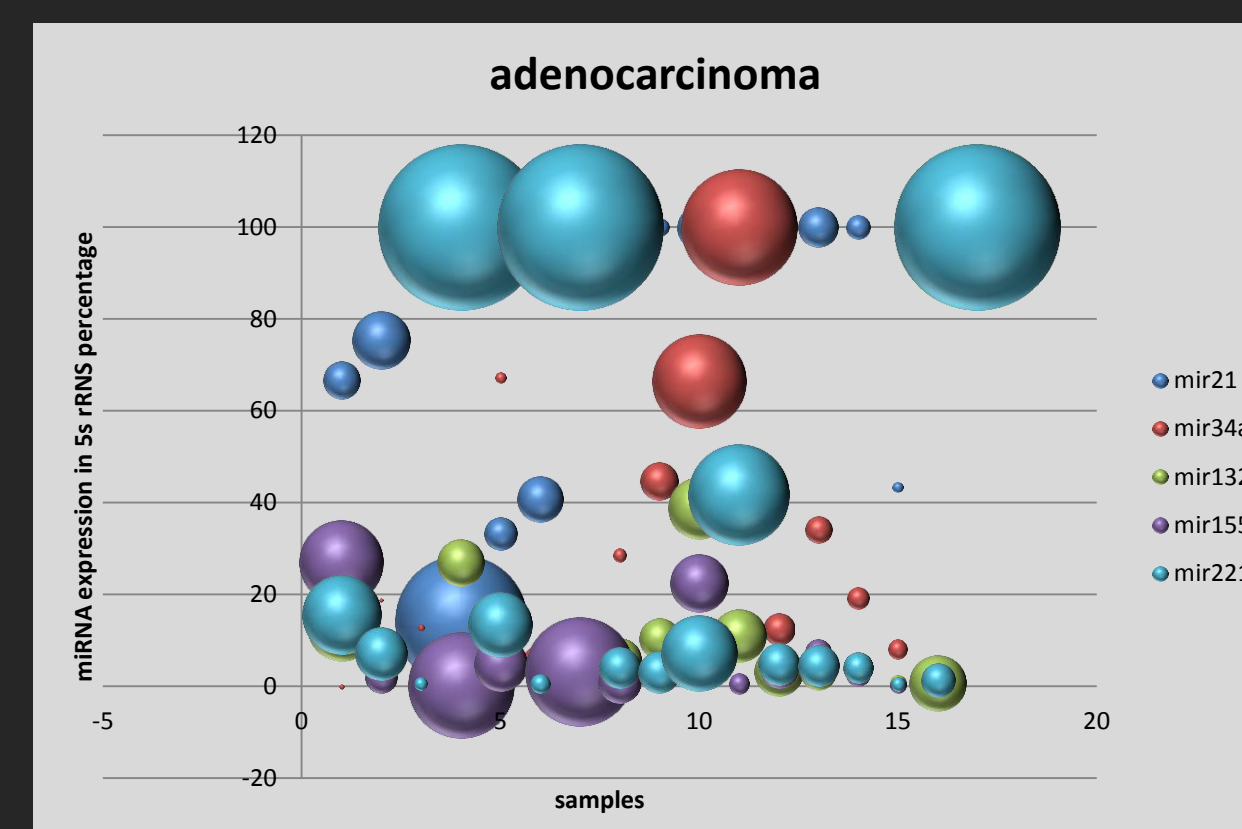
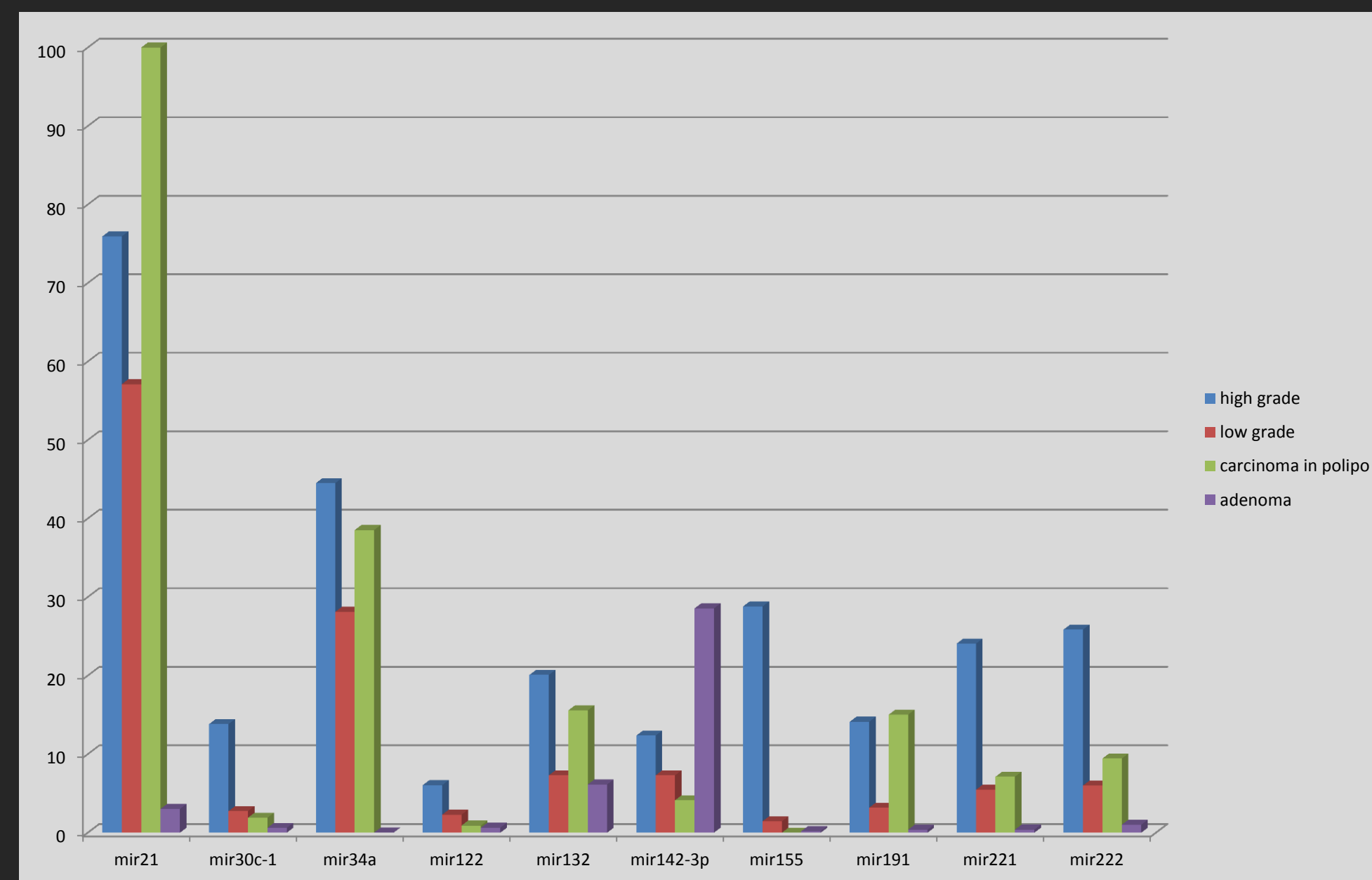
Different histopathological grades of colorectal adenocarcinoma, adenoma tubulare and normal colon epithelial samples (No:56) were obtained during colonoscopy from patients diagnosed at Pécs University Surgery Clinic. After histopathological evaluation tumors were analyzed in LightCycler 480 PCR system for the expressions of 10 pre-hsa-miRNAs (miR-21, miR-27a, miR-34a, miR-143, miR-146a, miR-196a, miR-155, miR-203, miR-205, miR-221) and 10 matured-hsa-miRNAs (miR-21, miR-30c, miR-34a, miR-122, miR-132, miR-142-3p, miR-191, miR-221, miR-222) compared to 5S rRNA and U6 snRNA as internal controls. Expression profiles were ordered and statistically evaluated according to clinical stage, histological grade and cancer location.

Results:

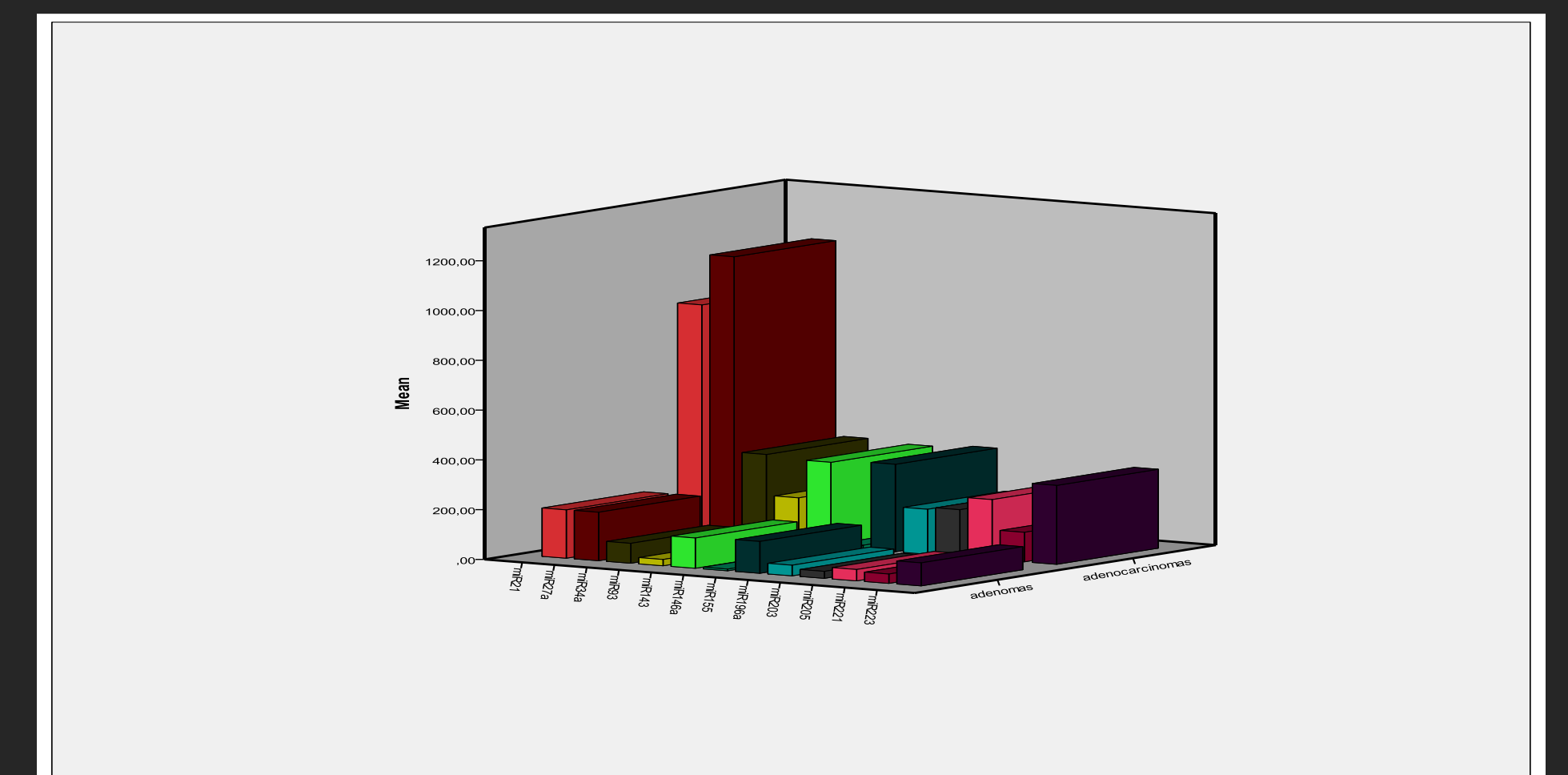
Expression pattern differences were more characteristic for distinguishing benign from malignant tissues and reached higher statistical significance in pre-miRNA expressions compared to matured miRNA. Pre-miRNA pattern correlations with the clinical stage and histology grade. High Grade T4N1M1- T3N0M0 tumors as well as the low grade T2N0M0, T1N0M0 adenocarcinomas showed significant over-expressions of miR-21, miR27a, miR-34a, miR155 and miR221 in paired two-sample t-tests. miR-146a and 196a were specific only for adenoma samples. Analysis of variance (ANOVA) of the significantly up-regulated miRNAs (miR-21, 27a, 34a and 155) was also found to be significant matching high grade tumors with low grade tumors ($p: 0,03$ CI: 3,75-4,49) and high grade adenoma ($p: 0,019$ CI: 1,744-3,362) tissues. A correlation between adenocarcinoma location and miR-155 expression was also observable, but it reached no statistical significance on the analysis.



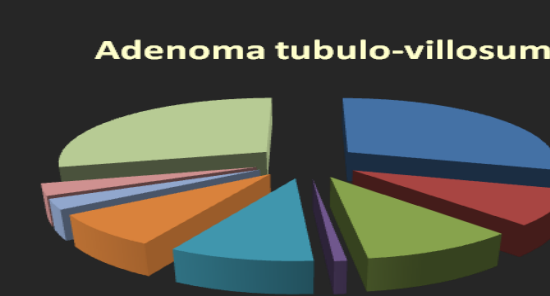
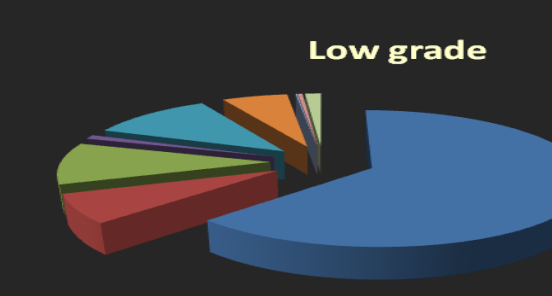
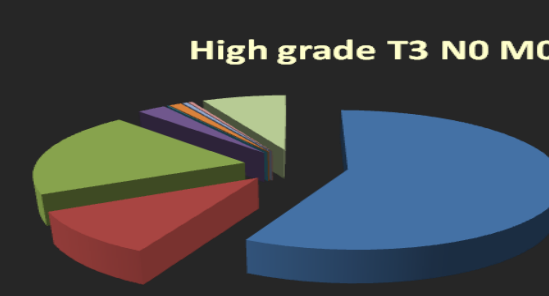
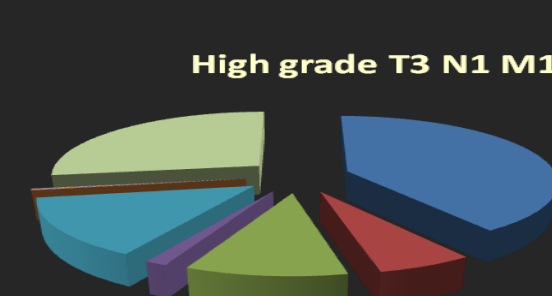
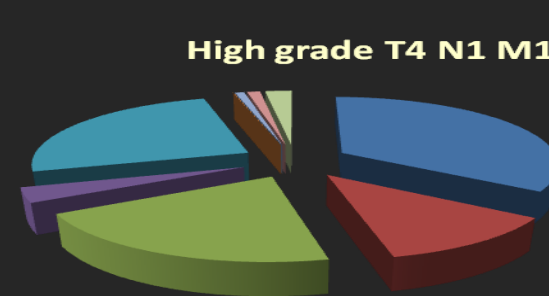
Mature miRNA expressions in benign adenomas and different grades of adenocarcinomas



Pre-miRNA expressions in benign adenomas and colorectal carcinomas



		Paired Samples Test							
		Paired Differences			95% Confidence Interval of the Difference		t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper			
Pair 1	var001 - var002	122,57500	146,89992	42,40636	29,23924	215,91076	2,890	11	,015
Pair 2	var003 - var004	349,82250	313,59614	90,52741	150,57302	549,07198	3,864	11	,003
Pair 3	var005 - var006	368,78575	461,16490	133,12684	75,77555	661,79595	2,770	11	,018
Pair 4	var007 - var008	382,63633	470,41345	135,79666	83,74989	681,52278	2,818	11	,017
Pair 5	var009 - var010	341,51742	389,98904	112,58014	93,73020	589,30463	3,034	11	,011
Pair 6	var011 - var012	188,28650	182,50059	52,68338	72,33115	304,24185	3,574	11	,004
Pair 7	var013 - var014	221,48575	178,35346	51,48621	108,16537	334,80613	4,302	11	,001
Pair 8	var015 - var016	346,89308	516,87847	149,20996	18,48417	675,30199	2,325	11	,040
Pair 9	var017 - var018	117,66092	149,94177	43,28446	22,39246	212,92937	2,718	11	,020
Pair 10	var019 - var020	350,56808	830,70959	239,80520	-177,23961	878,37577	1,462	11	,172
Pair 11	var021 - var022	252,14092	259,11451	74,79991	87,50741	416,77442	3,371	11	,006
Pair 12	var023 - var024	314,07958	515,65052	148,85548	-13,54913	641,70829	2,110	11	,059



Conclusions

MiRNA profiling is a suitable method for molecular characterization of colorectal adenocarcinoma, standing out as a potential new biomarker. Determining the causes and roles of epigenetic regulation in colorectal adenocarcinoma pathogenesis will lead to effective prevention and therapeutic strategies for colorectal cancer patients.