

Appendices

Appendix 1

Table 1. Search history (-2011.03.18). For this review, search strategy 18 was employed.

Search	Term	PubMed Results	ISI Results	EMBASE Results
1	colorectal.mp.	75879	99978	99823
2	colon/ or colon.mp.	131565	>100000	197449
3	rectal.mp.	77743	48772	66952
4	rectum/ or rectum.mp.	48114	19111	81312
5	1 or 2 or 3 or 4	258166	>100000	338107
6	cancer.mp.	2484181	>100000	1517375
7	neoplasm/ or neoplasm.mp.	2259486	30985	203146
8	tumor/ or tumor.mp.	2515356	>100000	1486779
9	carcinoma/ or carcinoma.mp.	602767	>100000	600127
10	malignancy.mp.	2247094	59722	91624
11	adenoma/ or adenoma.mp.	88080	26849	62624
12	6 or 7 or 8 or 9 or 10 or 11	2759755	>100000	2539091
13	microRNA.mp.	10680	8193	13883
14	miRNA.mp.	10431	5453	6478
15	miR.mp.	8049	7776	7034
16	let-7.mp.	375	9	473
17	13 or 14 or 15 or 16	15261	14341	16280
18	5 and 12 and 17	284	455	582

Appendix 2

Studies excluded from this review because of:

a. miRs and radiation therapy, chemotherapy (n=10), [1-10]

- 1 Ahmed FE, Vos PW, Jeffries C, Wiley JE, Weidner DA, Mota H, et al. Differences in mRNA and microRNA microarray expression profiles in human colon adenocarcinoma HT-29 cells treated with either Intensity-modulated Radiation Therapy (IMRT), or Conventional Radiation Therapy (RT). *Cancer Genomics Proteomics* 2009;6:109-27.
- 2 Zhou J, Zhou Y, Yin B, Hao W, Zhao L, Ju W, et al. 5-Fluorouracil and oxaliplatin modify the expression profiles of microRNAs in human colon cancer cells in vitro. *Oncol Rep* 2010;23:121-8.
- 3 Song B, Wang Y, Xi Y, Kudo K, Bruheim S, Botchkina GI, et al. Mechanism of chemoresistance mediated by miR-140 in human osteosarcoma and colon cancer cells. *Oncogene* 2009;28:4065-74.
- 4 Borralho PM, Kren BT, Castro RE, da Silva IB, Steer CJ, Rodrigues CM. Rodrigues CMP. MicroRNA-143 reduces viability and increases sensitivity to 5-fluorouracil in HCT116 human colorectal cancer cells. *Febs Journal* 2009;276:6689-700.
- 5 Graziano F, Canestrari E, Loupakis F, Ruzzo A, Galluccio N, Santini D, et al. Genetic modulation of the Let-7 microRNA binding to KRAS 3'-untranslated region and survival of metastatic colorectal cancer patients treated with salvage cetuximab-irinotecan. *Pharmacogenomics J* 2010;10:458-64.

- 6 Svoboda M, Izakovicova L, Sefr R , Vrtkova I, Kocakova I, Tichy B, et al. Micro-RNAs miR125b and miR137 are frequently upregulated in response to capecitabine chemoradiotherapy of rectal cancer. *Int J Oncol* 2008;33:541-7.
- 7 Rossi L, Bonmassar E, Faraoni I. Modification of miR gene expression pattern in human colon cancer cells following exposure to 5-fluorouracil in vitro. *Pharmacol Res* 2007;56:248-53.
- 8 Nakajima G, Hayashi K, Xi Y, Kudo K, Uchida K, Takasaki K, et al. Non-coding MicroRNAs hsa-let-7g and hsa-miR-181b are Associated with Chemoresponse to S-1 in Colon Cancer. *Cancer Genomics Proteomics* 2006;3:317-24.
- 9 Kitade Y, Akao Y. MicroRNAs and Their Therapeutic Potential for Human Diseases: MicroRNAs, miR-143 and -145, Function as Anti-oncomirs and the Application of Chemically Modified miR-143 as an Anti-cancer Drug. *J Pharmacol Sci.* 23 Sep 2010.
- 10 Mudduluru G, George-William JN, Muppala S, Asangani IA, Kumarswamy R, Nelson LD, et al. Curcumin regulates miR-21 expression and inhibits invasion and metastasis in colorectal cancer. *Biosci Rep* 2010; 31:185-97..

b. miRs in cell line (n=9), [11-19]

- 11 Gaur A, Jewell DA, Liang Y, Ridzon D, Moore JH, Chen C, et al. Characterization of microRNA expression levels and their biological correlates in human cancer cell lines. *Cancer Research* 2007;67:2456-68.
- 12 Park CW, Zeng Y, Zhang X, Subramanian S, Steer CJ. Mature microRNAs

- identified in highly purified nuclei from HCT116 colon cancer cells. *RNA Biol* 2010;7:606-14.
- 13 Ma YL, Zhang P, Wang F, Moyer MP, Yang JJ, Liu ZH, et al. Human embryonic stem cells and metastatic colorectal cancer cells shared the common endogenous human microRNA-26b. *J Cell Mol Med*. 10 Sep 2010.
- 14 Chai H, Liu M, Tian R, Li X, Tang H. miR-20a targets BNIP2 and contributes chemotherapeutic resistance in colorectal adenocarcinoma SW480 and SW620 cell lines. *Acta Biochim Biophys Sin (Shanghai)*. 2011;43:217-25.
- 15 Mader RM, Wieser M, Berger W, Kalipcayan M, Hackl M, Steger GG, et al. Relevance of microRNA modulation in chemoresistant colon cancer in vitro. *Int J Clin Pharmacol Ther* 2011;49:67-8.
- 16 Akao Y, Noguchi S, Iio A, Kojima K, Takagi T, Naoe T. Dysregulation of microRNA-34a expression causes drug-resistance to 5-FU in human colon cancer DLD-1 cells. *Cancer Lett* 2011; 300:197-204.
- 17 Wang CJ, Stratmann J, Zhou ZG, Sun XF. Suppression of microRNA-31 increases sensitivity to 5-FU at an early stage, and affects cell migration and invasion in HCT-116 colon cancer cells. *BMC Cancer* 2010;10:616.
- 18 Ragusa M, Majorana A, Statello L, Maugeri M, Salito L, Barbagallo D, et al. Specific alterations of microRNA transcriptome and global network structure in colorectal carcinoma after cetuximab treatment. *Mol Cancer Ther* 2010;9:3396-409.
- 19 Tili E, Michaille JJ, Alder H, Volinia S, Delmas D, Latruffe N, et al. Resveratrol

modulates the levels of microRNAs targeting genes encoding tumor-suppressors and effectors of TGF β signaling pathway in SW480 cells. *Biochem Pharmacol* 2010;80:2057-65.

c. miR-related gene polymorphisms (n=3), [20-22]

20 Lee HC, Kim JG, Chae YS, Sohn SK, Kang BW, Moon JH, et al. Prognostic impact of microRNA-related gene polymorphisms on survival of patients with colorectal cancer. *Journal of Cancer Research and Clinical Oncology* 2010;136:1073-8.

21 Landi D, Gemignani F, Naccarati A, Pardini B, Vodicka P, Vodickova L, et al. Polymorphisms within micro-RNA-binding sites and risk of sporadic colorectal cancer. *Carcinogenesis* 2008;29:579-84.

22 Chen H, Sun LY, Chen LL, Zheng HQ, Zhang QF. A variant in microRNA-196a2 is not associated with susceptibility to and progression of colorectal cancer in Chinese. *Intern Med J.* 2011 Jan 17.

d. miRs and their targeting mRNA, acid, enzymes, protein or genes (n=59), [23-81]

23 Asangani IA, Rasheed SA, Nikolova DA, Leupold JH, Colburn NH, Post S, et al. MicroRNA-21 (miR-21) post-transcriptionally downregulates tumor suppressor Pcd4 and stimulates invasion, intravasation and metastasis in colorectal cancer. *Oncogene* 2008;27:2128-36.

24 Chintharlapalli S, Papineni S, Abdelrahim M, Abudayyeh A, Jutooru I,

- Chadalapaka G, et al. Oncogenic microRNA-27a is a target for anticancer agent methyl 2-cyano-3, 11-dioxo-18beta-olean-1, 12-dien-30-oate in colon cancer cells. *Int J Cancer* 2009;125:1965-74.
- 25 Grady WM, Parkin RK, Mitchell PS, Lee JH, Kim YH, Tsuchiya KD, et al. Epigenetic silencing of the intronic microRNA hsa-miR-342 and its host gene EVL in colorectal cancer. *Oncogene* 2008;27:3880-8.
- 26 Gregersen LH, Jacobsen AB, Frankel LB, Wen J, Krogh A, Lund AH. MicroRNA-145 targets YES and STAT1 in colon cancer cells. *PLoS One*. 21 Jan 2010.
- 27 Guo C, Sah JF, Beard L, Willson JK, Markowitz SD, Guda K. The noncoding RNA, miR-126, suppresses the growth of neoplastic cells by targeting phosphatidylinositol 3-kinase signaling and is frequently lost in colon cancers. *Genes Chromosomes Cancer* 2008;47:939-46.
- 28 Hu M, Xia M, Chen X, Lin Z, Xu Y, Ma Y, et al. MicroRNA-141 Regulates Smad Interacting Protein 1 (SIP1) and Inhibits Migration and Invasion of Colorectal Cancer Cells. *Digestive Diseases and Sciences* 2010;55:2365-72.
- 29 Wu J, Qian J, Li C, Kwok L, Cheng F, Liu P, et al. miR-129 regulates cell proliferation by downregulating Cdk6 expression. *Cell Cycle* 2010;9:1809-18.
- 30 Kim MS, Oh JE, Kim YR, Park SW, Kang MR, Kim SS, et al. Somatic mutations and losses of expression of microRNA regulation-related genes AGO2 and TNRC6A in gastric and colorectal cancers. *J Pathol* 2010;221:139-46.
- 31 Kim S, Choi M, Cho KH. Identifying the target mRNAs of microRNAs in

- colorectal cancer. *Comput Biol Chem* 2009;33:94-9.
- 32 La Rocca G, Badin M, Shi B, Xu SQ, Deangelis T, Sepp-Lorenzino L, et al. Mechanism of growth inhibition by MicroRNA 145: the role of the IGF-I receptor signaling pathway. *J Cell Physiol* 2009;220:485-91.
- 33 Liu M, Lang N, Qiu M, Xu F, Li Q, Tang Q, et al. miR-137 targets Cdc42 expression, induces cell cycle G1 arrest and inhibits invasion in colorectal cancer cells. *Int J Cancer*. 12 May 2010.
- 34 Yamakuchi M, Lotterman CD, Bao C, Hruban RH, Karim B, Mendell JT, et al. P53-induced microRNA-107 inhibits HIF-1 and tumor angiogenesis. *Proc Natl Acad Sci U S A*. 2010;107:6334-9.
- 35 Valeri N, Gasparini P, Fabbri M, Braconi C, Veronese A, Lovat F, et al. Modulation of mismatch repair and genomic stability by miR-155. *Proc Natl Acad Sci U S A*. 2010;107:6982-7.
- 36 Nagel R, le Sage C, Diosdado B, van der Waal M, Oude Vrielink JA, Bolijn A, et al. Regulation of the adenomatous polyposis coli gene by the miR-135 family in colorectal cancer. *Cancer Res* 2008;68:5795-802.
- 37 Nakagawa Y, Iinuma M, Naoe T, Nozawa Y, Akao Y. Characterized mechanism of alpha-mangostin-induced cell death: caspase-independent apoptosis with release of endonuclease-G from mitochondria and increased miR-143 expression in human colorectal cancer DLD-1 cells. *Bioorg Med Chem* 2007;15:5620-8.
- 38 Nakano H, Miyazawa T, Kinoshita K, Yamada Y, Yoshida T. Functional screening identifies a microRNA, miR-491 that induces apoptosis by targeting Bcl-X(L) in

- colorectal cancer cells. *Int J Cancer* 2010;127:1072-80.
- 39 Schetter AJ, Nguyen GH, Bowman ED, Mathé EA, Yuen ST, Hawkes JE, et al. Association of inflammation-related and microRNA gene expression with cancer-specific mortality of colon adenocarcinoma. *Clin Cancer Res* 2009;15:5878-87.
- 40 Shi B, Sepp-Lorenzino L, Prisco M, Linsley P, deAngelis T, Baserga R. Micro RNA 145 targets the insulin receptor substrate-1 and inhibits the growth of colon cancer cells. *J Biol Chem* 2007;282:32582-90.
- 41 Slaby O, Hrstka R, Sobkova K, et al. Knockdown of oncogenic microRNA-21 displays cytotoxicity in p53 wild-type colon cancer cells. *Ejc Supplements* 2008;6:78.
- 42 Song B, Wang Y, Kudo K, Gavin EJ, Xi Y, Ju J.. miR-192 Regulates Dihydrofolate Reductase and Cellular Proliferation through the p53-microRNA Circuit. *Clini Cancer Res* 2008;14:8080-6.
- 43 Strillacci A, Griffoni C, Sansone P, Paterini P, Piazzini G, Lazzarini G, et al. MiR-101 downregulation is involved in cyclooxygenase-2 overexpression in human colon cancer cells. *Exp Cell Res* 2009;315:1439-47.
- 44 Sureban SM, May R, Ramalingam S, Subramaniam D, Natarajan G, Anant S, et al. Selective blockade of DCAMKL-1 results in tumor growth arrest by a Let-7a MicroRNA-dependent mechanism. *Gastroenterology* 2009;137:649-59.e2.
- 45 Tazawa H, Tsuchiya N, Izumiya M, Nakagama H. Tumor-suppressive miR-34a induces senescence-like growth arrest through modulation of the E2F pathway in

- human colon cancer cells. *Proc Natl Acad Sci U S A* 2007;104:15472-7.
- 46 Tsang WP, Kwok TT. The miR-18a* microRNA functions as a potential tumor suppressor by targeting on K-Ras. *Carcinogenesis* 2009;30:953-9.
- 47 Tsang WP, Ng EK, Ng SS, Jin H, Yu J, Sung JJ, et al. Oncofetal H19-Derived miR-675 Regulates Tumor Suppressor RB in Human Colorectal Cancer. *Carcinogenesis*. 2010;31:350-8.
- 48 Vidic S, Markec B, Sersa G, Coer A, Kamensek U, Tevz G, et al. MicroRNAs targeting mutant K-ras by electrotransfer inhibit human colorectal adenocarcinoma cell growth in vitro and in vivo. *Cancer Gene Ther* 2010;17:409-19.
- 49 Wang P, Zou F, Zhang X, Li H, Dulak A, Tomko RJ Jr, et al. microRNA-21 Negatively Regulates Cdc25A and Cell Cycle Progression in Colon Cancer Cells. *Cancer Res* 2009;69:8157-65.
- 50 Xi Y, Edwards JR, Ju J. Investigation of miRNA Biology by Bioinformatic Tools and Impact of miRNAs in Colorectal Cancer-Regulatory Relationship of c-Myc and p53 with miRNAs. *Cancer Inform* 2007;3:245-53.
- 51 Xi Y, Shalgi R, Fodstad O, Pilpel Y, Ju J. Differentially regulated micro-RNAs and actively translated messenger RNA transcripts by tumor suppressor p53 in colon cancer. *Clin Cancer Res* 2006;12:2014-24.
- 52 Zhang W, Winder T, Ning Y, Pohl A, Yang D, Kahn M, et al. A let-7 microRNA-binding site polymorphism in 3'-untranslated region of KRAS gene predicts response in wild-type KRAS patients with metastatic colorectal cancer

- treated with cetuximab monotherapy. *Ann Oncol* 2011;22:104-9.
- 53 Hu G, Chen D, Li X, Yang K, Wang H, Wu W. et al. miR-133b regulates the MET proto-oncogene and inhibits the growth of colorectal cancer cells in vitro and in vivo. *Cancer Biol Ther* 2010;10:190-7.
- 54 To KKW, Zhan ZR, Litman T, Bates SE. Regulation of ABCG2 expression at the 3' untranslated region of its mRNA through modulation of transcript stability and protein translation by a putative MicroRNA in the s1 colon cancer cell line. *Molecular and Cellular Biology* 2008;28:5147-61.
- 55 Zhang B, Wang XK, Wang Y. Altered gene expression and miRNA expression associated with cancerous IEC-6 cell transformed by MNNG. *Journal of Experimental & Clinical Cancer Research* 2009;28:56.
- 56 Wang XY, Wu MH, Li Y, Li N, Li GY, et al. Differential miRNA expression and their target genes between NGX6-positive and negative colon cancer cells. *Mol Cell Biochem* 2010;345:283-90.
- 57 Cottonham CL, Kaneko S, Xu L. miR-21 and miR-31 converge on TIAM1 to regulate migration and invasion of colon carcinoma cells. *J Biol Chem* 2010;285:35293-302.
- 58 Li LN, Zhang HD, Zhi R, Yuan SJ. Down-regulation of some miRNAs by degrading their precursors contributes to anti-cancer effect of mistletoe lectin-I. *Br J Pharmacol* 2011;162:349-64.
- 59 Zhang J, Guo H, Zhang H, Wang H, Qian G, Fan X, et al. Putative tumor suppressor miR-145 inhibits colon cancer cell growth by targeting oncogene

- friend leukemia virus integration 1 gene. *Cancer*. 24 Aug 2010.
- 60 Kalimutho M, Minutolo A, Grelli S, Formosa A, Sancesario G, Valentini A, et al. Satraplatin (JM-216) mediates G2/M cell cycle arrest and potentiates apoptosis via multiple death pathways in colorectal cancer cells thus overcoming platinum chemo-resistance. *Cancer Chemother Pharmacol*. 24 Aug 2010.
- 61 Feng L, Xie Y, Zhang H, Wu Y. Down-regulation of NDRG2 gene expression in human colorectal cancer involves promoter methylation and microRNA-650. *Biochem Biophys Res Commun*. 2011 Feb 23.
- 62 Mudduluru G, Ceppi P, Kumarswamy R, Scagliotti GV, Papotti M, Allgayer H. Regulation of Axl receptor tyrosine kinase expression by miR-34a and miR-199a/b in solid cancer. *Oncogene*. 2011 Feb 14.
- 63 Hu S, Dong TS, Dalal SR, Wu F, Bissonnette M, Kwon JH, et al. The microbe-derived short chain fatty acid butyrate targets miRNA-dependent p21 gene expression in human colon cancer. *PLoS One* 2011;6:e16221.
- 64 Sun K, Wang W, Zeng JJ, Wu CT, Lei ST, Li GX. MicroRNA-221 inhibits CDKN1C/p57 expression in human colorectal carcinoma. *Acta Pharmacol Sin* 2011;32:375-84.
- 65 Zhang W, Labonte MJ, Lenz HJ. KRAS let-7 LCS6 SNP predicts cetuximab efficacy in KRASwt metastatic colorectal cancer patients: Does treatment combination partner matter? *Ann Oncol* 2011;22:484-5.
- 66 Gao JS, Zhang Y, Tang X, Tucker LD, Tarwater PM, Quesenberry PJ, et al. The Evi1, microRNA-143, K-Ras axis in colon cancer. *FEBS Lett* 2011;585:693-9.

- 67 Noratto GD, Kim Y, Talcott ST, Mertens-Talcott SU. Flavonol-rich fractions of yaupon holly leaves (*Ilex vomitoria*, Aquifoliaceae) induce microRNA-146a and have anti-inflammatory and chemopreventive effects in intestinal myofibroblast CCD-18Co cells. *Fitoterapia* 2011 Jan 22.
- 68 Mongroo PS, Noubissi FK, Cuatrecasas M, Kalabis J, King CE, Johnstone CN, et al. IMP-1 Displays Cross-Talk with K-Ras and Modulates Colon Cancer Cell Survival through the Novel Proapoptotic Protein CYFIP2. *Cancer Res* 2011;71:2172-82.
- 69 Loboda A, Nebozhyn MV, Watters JW, Buser CA, Shaw PM, Huang PS, et al. EMT is the dominant program in human colon cancer. *BMC Med Genomics* 2011;4:9.
- 70 Vogt M, Munding J, Grüner M, Liffers ST, Verdoodt B, Hauk J, et al. Frequent concomitant inactivation of miR-34a and miR-34b/c by CpG methylation in colorectal, pancreatic, mammary, ovarian, urothelial, and renal cell carcinomas and soft tissue sarcomas. *Virchows Arch* 2011;458:313-22.
- 71 Liu M, Lang N, Chen X, Tang Q, Liu S, Huang J, et al. miR-185 targets RhoA and Cdc42 expression and inhibits the proliferation potential of human colorectal cells. *Cancer Lett* 2011;301:151-60.
- 72 Dickey JS, Zemp FJ, Altamirano A, Sedelnikova OA, Bonner WM, Kovalchuk O. H2AX phosphorylation in response to DNA double-strand break formation during bystander signalling: effect of microRNA knockdown. *Radiat Prot Dosimetry* 2011;143:264-9.

- 73 Pathi SS, Jutooru I, Chadalapaka G, Sreevalsan S, Anand S, Thatcher GR, et al. GT-094, a NO-NSAID, Inhibits Colon Cancer Cell Growth by Activation of a Reactive Oxygen Species-MicroRNA-27a: ZBTB10-Specificity Protein Pathway. *Mol Cancer Res* 2011;9:195-202.
- 74 Zhang H, Li W, Nan F, Ren F, Wang H, Xu Y, et al. MicroRNA expression profile of colon cancer stem-like cells in HT29 adenocarcinoma cell line. *Biochem Biophys Res Commun* 2011;404:273-8.
- 75 Venkatachalam R, Verwiel ET, Kamping EJ, Hoenselaar E, Görgens H, Schackert HK, et al. Identification of candidate predisposing copy number variants in familial and early-onset colorectal cancer patients. *Int J Cancer*. 2010 Dec 2.
- 76 Sarver AL, Li L, Subramanian S. MicroRNA miR-183 functions as an oncogene by targeting the transcription factor EGR1 and promoting tumor cell migration. *Cancer Res* 2010;70:9570-80.
- 77 Valeri N, Gasparini P, Braconi C, Paone A, Lovat F, Fabbri M, et al. MicroRNA-21 induces resistance to 5-fluorouracil by down-regulating human DNA MutS homolog 2 (hMSH2). *Proc Natl Acad Sci U S A* 2010;107:21098-103.
- 78 Nielsen BS, Jørgensen S, Fog JU, Søkilde R, Christensen IJ, Hansen U, et al. High levels of microRNA-21 in the stroma of colorectal cancers predict short disease-free survival in stage II colon cancer patients. *Clin Exp Metastasis* 2011;28:27-38.
- 79 Kim H, Watkinson J, Varadan V, Anastassiou D. Multi-cancer computational analysis reveals invasion-associated variant of desmoplastic reaction involving

- INHBA, THBS2 and COL11A1. BMC Med Genomics 2010;3:51.
- 80 Wong CC, Wong CM, Tung EK, Au SL, Lee JM, Poon RT, et al. The microRNA miR-139 suppresses metastasis and progression of hepatocellular carcinoma by down-regulating Rho-kinase 2. Gastroenterology 2011;140:322-31.
- 81 Ruzzo A, Canestrari E, Galluccio N, Santini D, Vincenzi B, Tonini G, et al. Role of KRAS let-7 LCS6 SNP in metastatic colorectal cancer patients. Ann Oncol 2011;22:234-5.
- e. miRs and methylation (n=5), [82-86]*
- 82 Bandres E, Agirre X, Bitarte N, Ramirez N, Zarate R, Roman-Gomez J, et al. Epigenetic regulation of microRNA expression in colorectal cancer. Int J Cancer 2009;125:2737-43.
- 83 Ng EK, Tsang WP, Ng SS, Jin HC, Yu J, Li JJ, et al. MicroRNA-143 targets DNA methyltransferases 3A in colorectal cancer. British Journal of Cancer 2009;101:699-706.
- 84 Balaguer F, Link A, Lozano JJ, Cuatrecasas M, Nagasaka T, Boland CR, et al. Epigenetic Silencing of miR-137 Is an Early Event in Colorectal Carcinogenesis. Cancer Res 2010;70:6609-18.
- 85 Toyota M, Suzuki H, Sasaki Y, Maruyama R, Imai K, Shinomura Y, et al. Epigenetic silencing of microRNA-34b/c and B-cell translocation gene 4 is associated with CpG island methylation in colorectal cancer. Cancer Res 2008;68:4123-32.

86 Pavicic W, Perkiö E, Kaur S, Peltomäki P. Altered Methylation at MicroRNA-Associated CpG Islands in Hereditary and Sporadic Carcinomas: MS-MLPA-Based Approach. Mol Med. 2011 Feb 9.

f. methods of detecting miRs in CRC (n=5), [87-91]

87 Lodes MJ, Caraballo M, Suci D, Munro S, Kumar A, Anderson B. Detection of cancer with serum miRNAs on an oligonucleotide microarray. PLoS One 2009;4:e6229.

88 Schuster C, Budczies J, Faber C, Kirchner T, Hlubek F. MicroRNA expression profiling of specific cells in complex archival tissue stained by immunohistochemistry. Lab Invest 2010. 26 Jul 2010.

89 Wang B, Wang XF, Howell P, Qian X, Huang K, et al. A personalized microRNA microarray normalization method using a logistic regression model. Bioinformatics 2010;26:228-34.

90 Wang S, Wang L, Zhu T, Gao X, Li J, Wu Y, et al. Improvement of tissue preparation for laser capture microdissection: application for cell type-specific miRNA expression profiling in colorectal tumors. BMC Genomics 2010;11:163.

91 Kore AR, Hodeib M, Hu ZT. Chemical synthesis of LNA-mCTP and its application for microRNA detection. Nucleosides Nucleotides & Nucleic Acids 2008;27:1-17.

g. data normalizations in miRs studies (n=1), [92]

92 Chang KH, Mestdagh P, Vandesompele J, Kerin MJ, Miller N. et al. MicroRNA expression profiling to identify and validate reference genes for relative quantification in colorectal cancer. *BMC Cancer* 2010;10:173.

h. miRs from stool samples (n=2), [93, 94]

93 Link A, Balaguer F, Shen Y, Nagasaka T, Lozano JJ, Boland CR, et al. Fecal MicroRNAs as novel biomarkers for colon cancer screening. *Cancer Epidemiol Biomarkers Prev* 2010;19: 1766-74.

94 Koga Y, Yasunaga M, Takahashi A, Kuroda J, Moriya Y, Akasu T, et al. MicroRNA Expression Profiling of Exfoliated Colonocytes Isolated from Feces for Colorectal Cancer Screening. *Cancer Prev Res (Phila)*. 2010;3:1435-42.

i. critical data can not be derived (n=12), [95-106]

95 Bandres E, Cubedo E, Agirre X, Malumbres R, Zárate R, Ramirez N, et al. Identification by Real-time PCR of 13 mature microRNAs differentially expressed in colorectal cancer and non-tumoral tissues. *Mol Cancer* 2006;5:29.

96 Chen X, Ba Y, Ma L, Cai X, Yin Y, Wang K, et al. Characterization of microRNAs in serum: a novel class of biomarkers for diagnosis of cancer and other diseases. *Cell Res* 2008;18:997-1006.

97 Lagerstedt KK, Kristiansson E, Lönnroth C, Andersson M, Iresjö BM, Gustafsson A, et al. Genes with relevance for early to late progression of colon carcinoma based on combined genomic and transcriptomic information from the same

- patients. *Cancer Inform* 2010;9:79-91.
- 98 Meiri E, Levy A, Benjamin H, Ben-David M, Cohen L, Dov A, et al. Discovery of microRNAs and other small RNAs in solid tumors. *Nucleic Acids Res* 2010;38:6234-46.
- 99 Michael MZ, O' Connor SM, van Holst Pellekaan NG, Young GP, James RJ. Reduced accumulation of specific microRNAs in colorectal neoplasia. *Molecular Cancer Research* 2003;1:882-891.
- 100 Schimanski CC, Frerichs K, Rahman F, Berger M, Lang H, et al. High miR-196a levels promote the oncogenic phenotype of colorectal cancer cells. *World J Gastroenterol* 2009;15:2089-96.
- 101 Yamamichi N, Shimomura R, Inada KI, Sakurai K, Haraguchi T, Ozaki Y, et al. Locked Nucleic Acid In situ Hybridization Analysis of miR-21 Expression during Colorectal Cancer Development. *Clinical Cancer Research* 2009;15:4009-16.
- 102 Akao Y, Nakagawa Y, Naoe T. MicroRNAs 143 and 145 are possible common onco-microRNAs in human cancers. *Oncol Rep* 2006;16:845-50.
- 103 Akao Y, Nakagawa Y, Naoe T. let-7 microRNA functions as a potential growth suppressor in human colon cancer cells. *Biol Pharm Bull* 2006;29:903-6.
- 104 Diaz R, Silva J, Garcia JM, Lorenzo Y, García V, Peña C, et al. Deregulated expression of miR-106a predicts survival in human colon cancer patients. *Genes Chromosomes Cancer* 2008;47:794-802.
- 105 Lin M, Chen W, Huang J, Gao H, Ye Y, Song Z, et al. MicroRNA expression profiles in human colorectal cancers with liver metastases. *Oncol Rep*. 20 Dec

2010.

106 Slattery ML, Wolff E, Hoffman MD, Pellatt DF, Milash B, Wolff RK.

MicroRNAs and colon and rectal cancer: Differential expression by tumor location and subtype. *Genes Chromosomes Cancer* 2011;50:196-206.

j. no healthy controls (n=5), [107-111]

107 Baffa R, Fassan M, Volinia S, O'Hara B, Liu CG, Palazzo JP, et al. MicroRNA

expression profiling of human metastatic cancers identifies cancer gene targets. *J Pathol* 2009;219:214-21.

108 Huang ZM, Yang J, Shen XY, Zhang XY, Meng FS, Xu JT, et al. MicroRNA

expression profile in non-cancerous colonic tissue associated with lymph node metastasis of colon cancer. *J Dig Dis* 2009;10:188-94.

109 Yantiss RK, Goodarzi M, Zhou XK, Rennert H, Pirog EC, Banner BF, et al.

Clinical, pathologic, and molecular features of early-onset colorectal carcinoma. *Am J Surg Pathol* 2009; 33:572-82.

110 Lanza G, Ferracin M, Gafa R, Veronese A, Spizzo R, Pichiorri F, et al.

mRNA/microRNA gene expression profile in microsatellite unstable colorectal cancer. *Mol Cancer* 2007;6:54.

111 Nishida N, Yokobori T, Mimori K, Sudo T, Tanaka F, Shibata K, et al. MicroRNA

miR-125b is a prognostic marker in human colorectal cancer. *Int J Oncol*. 2011 Mar 10.

k. multitissuse combined analysis (n=1), [112]

112 Mascellani N, Tagliavini L, Gamberoni G, et al. Using miRNA expression data for the study of human cancer. *Minerva Biotechnologica* 2008;20:23-30.

l. Animal experiment (n=2), [113-114]

113 Davidson LA, Wang N, Shah MS, Lupton JR, Ivanov I, Chapkin RS. n-3 Polyunsaturated fatty acids modulate carcinogen-directed non-coding microRNA signatures in rat colon. *Carcinogenesis*. 2009;30:2077-84.

114 Shah MS, Schwartz SL, Zhao C, Davidson LA, Zhou B, Lupton JR, et al. Integrated microRNA and mRNA expression profiling in a rat colon carcinogenesis model: Effect of a chemo-protective diet. *Physiol Genomics*. 2011 Mar 15.