UNIVERSITI PUTRA MALAYSIA

EXPRESSION AND ASSOCIATION OF miR-181a AND miR-663 AND THEIR TARGET GENES IN HEAD AND NECK CANCER

YAGHMA MASOOD

FPSK(p) 2018 45

EXPRESSION AND ASSOCIATION OF miR-181a AND miR-663 AND THEIR TARGET GENES IN HEAD AND NECK CANCER

By

YAGHMA MASOOD

Thesis submitted to the School of Graduate Studies, Universiti Putra Malaysia, in fulfillment of the requirements for the Degree of Doctor of Philosophy

February 2018

COPYRIGHT

To my parents, husband and daughters

For their unconditional love and support

This accomplishment belongs to you all as well

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirement for the degree of Doctor of Philosophy

EXPRESSION AND ASSOCIATION OF miR-181a AND miR-663 AND THEIR TARGET GENES IN HEAD AND NECK CANCER

By

YAGHMA MASOOD

February 2018

Chair: Cheah Yoke Kqueen, PhD
Faculty: Medicine and Health Sciences

Head and neck cancer is the sixth most common malignancy worldwide and the fifth most common cancer in peninsular Malaysia. The over five-year survival rate for patients with HNC is only 40-50% because of distant metastasis, loco-regional recurrences, and secondary primary tumours. miRNAs have been shown to be able to regulate many cellular processes, including proliferation, differentiation, angiogenesis, cell development, etc. There is strong evidence that miRNAs may represent different targets for anticancer therapies. The aberrant expression of human microRNA-181a-2-3p and miR-663 has been implicated in the pathogenesis of various cancers. However, the role of hsa-miR-181a-2-3p and hsa-miR-663 in the pathogenesis of head and neck cancer and its clinical significance are still unclear. This study is the continuation of previous work done by our research group where novel expression of hsa-miR-181a-2-3p was found in head and neck cancer. To check and compare the expression of hsa-miR-181a-2-3p, hsa-miR-663 was selected, which already has established expression in HNC. Therefore, the aim of this study was to search for the molecular targets of hsa-miR-181a -2-3p and hsa-miR-663 and determine their expression and their common predicted targets in HNC. So, it was hypothesised that hsa-miR-181a-2-3p and hsa-miR-663 may play an important role in the progression of head and neck cancer and co-regulate few common targets which lead to the activation of cancer pathways in HNC development. To predict the targets of hsa-miR-181a -2-3p and hsa-miR-663, three different algorithms were used, including TargetScan, miRanda-mirSVR and RNA22 HAS. Two algorithms, TarBase and miRTarBase, were used to identify the validated targets of hsa-miR-181a-5p (a mature product of hsa-miR-181a) and hsa-miR-663. To further narrow down the list of targets identified from the *in silico* analysis, the target genes of hsa-miR-181a-2-3p and hsa-miR-663 were further validated by published literature, before using them in this research project. The web-based Database for Annotation, Visualization and Integrated Discovery tool (DAVID) was used to provide biological functional

interpretation of the validated targets of hsa-miR-181a-5p and hsa-miR-663. A total of 70 formalin-fixed paraffin embedded (FFPE) tissue specimens and 4 fresh frozen (FF) tissue samples from HNC patients (26 stage I,15 stage II, 11 stage II and 22 stage IV HNC cases), and 12 non-cancerous FF samples were collected from the Peninsular Malaysian population. The expression of these miRNAs and their common predicted targets were determined by doing q-PCR in HNC cell line, non-cancerous samples and HNC samples.

Bioinformatic studies have showed that hsa-miR-181a and hsa-miR-663 might regulate a large number of target genes that are important in the regulation of critical cell processes, such as cell fate, cell survival, metabolism, and cell death. To date, 584 targets of hsa-miR-181a have been validated; and 61 of these targets are cancer genes. In addition, it was identified that 101 targets of hsa-miR-663 have been validated; and 15 of these targets are cancer genes. The precision of predictions by all the algorithms for hsa-miR-181a-2-3p and hsa-miR-663 targets was low. Based on the DAVID and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis, it is concluded that many of these genes are involved in tumorigenesis of various cancers, including HNC. Besides this, the main cancer pathways regulated by hsa-miR-181a and hsa-miR-663 could be PI3K/Akt, MAPK, and Wnt signaling pathways in head and neck cancer. Based on the amalgamation of *in silico* analysis and published literature, nine common predicted targets (ATM, BCL2, BCL2L2, CDKN1A, CDKN1B, DDIT4, p53, p73 and PARP1) of hsa-miR-181a-2-3p and hsa-miR-663 were chosen for further experimental investigation. Moreover, results in this study showed that advanced HNC had a significant higher expression level of hsa-miR-181a-2-3p and hsa-miR-663 than that in early stage of HNC, suggesting that it may have a critical role in tumor metastasis of advanced HNC. It was also found that BCL2 and PARP1 were also upregulated along with upregulation of hsa-miR-181a-2-3p and hsa-miR-663 in HNC compared to that in non-cancerous tissues. However, ATM, CDKN1A, CDKN1B, DDIT4, p53 and p73 expression were inversely correlated with hsa-miR-181a-2-3p and hsa-miR-663 expression.

Taken together, these results suggest that hsa-miR-181a-2-3p and hsa-miR-663 may serve as an oncogene in head and neck cancer. Furthermore, hsa-miR-181a-2-3p and hsa-miR-663 might be used as new biomarkers together with their common predicted targets in the prediction of prognosis of HNC in clinical practice. More functional and mechanistic studies are needed to validate the role of hsa-miR-181a-2-3p and hsa-miR-663 in the development, progression, and metastasis of HNC.

Abstrak tesis yang dikemukakan Kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

EKSPRESI DAN HUBUNGKAIT miR-181a DAN miR-663 DENGAN GEN SASARAN DALAM KANSER KEPALA DAN LEHER

Oleh

YAGHMA MASOOD

Februari 2018

Pengerusi: Cheah Yoke Kqueen, PhD
Fakulti: Perubutan dan Sain Kesihatan

Kanser kepala dan leher adalah kanser keenam yang paling biasa di seluruh dunia dan kanser kelima yang paling umum di Semenanjung Malaysia. Kadar survival selama lima tahun untuk pesakit kanser kepala dan leher hanya 40-50% kerana metastasis jauh, kawasan setempat yang berulang, dan tumor utama sekunder. miRNA telah terbukti mampu mengawal selia banyak proses selular, termasuk percambahan, pembezaan, angiogenesi, pembangunan sel, dan lain-lain. Terdapat bukti kukuh bahawa miRNAs boleh mewakili pelbagai sasaran untuk terapi antikanser. Ekspresi tidak normal gene manusia microRNA-181a-2-3p dan miR-663 telah terlibat dalam patogenesis pelbagai kanser. Walau bagaimanapun, peranan hsa-miR-181a-2-3p dan hsa-miR-663 dalam patogenesis kanser kepala dan leher dan kepentingan klinikalnya masih tidak jelas. Kajian ini adalah kesinambungan daripada kajian terdahulu yang dilakukan oleh kumpulan penyelidikan kami di mana ekspresi novel hsa-miR-181a-2-3p didapati dalam kanser kepala dan leher. Untuk menyemak dan membandingkan ekspresi hsa-miR-181a-2-3p, hsa-miR-663 telah dipilih, yang telah pun menyatakan ekspresi dalam kanser kepala dan leher. Oleh itu, matlamat kajian ini adalah untuk mencari sasaran molekul hsa-miR-181a -2-3p dan hsa-miR-663 dan menentukan ekspresi mereka dan sasaran ramalan mereka yang biasa dalam kanser kepala dan leher. Hipotesis kajian ini adalah hsa-miR-181a-2-3p dan hsa-miR-663 mungkin memainkan peranan penting dalam perkembangan kanser kepala dan leher dan mengawal selia beberapa sasaran umum yang membawa kepada pengaktifan laluan kanser dalam pembangunan kanser kepala dan leher.

Untuk menentukan sasaran hsa-miR-181a-23p dan hsa-miR-663, tiga algoritma yang berbeza iaitu Target Scan, miRanda-mirSVR dan RNA22 HAS telah digunakan. Dua algoritma iaitu TarBase dan miRTarBase digunakan untuk mengenalpasti sasaran-sasaran sah hsa-miR-181a-5p

(produk matang hsa-miR-181a) dan hsa-miR-663. Untuk mengecilkan senarai sasaran yang dikenalpasti daripada analisis *in silico,* gen-gen sasaran hsa-miR-181a-23p dan hsa-miR-663 telah disahkan menggunakan kajian-kajian terdahulu sebelum digunakan dalam kajian ini. Aplikasi web "Database for Annotation, Visualization and Integrated Discovery (DAVID)" telah digunakan untuk terjemahan fungsi biologi sasaran-sasaran sah hsa-miR-181a-5p dan hsa-miR-663. Tujuh puluh spesimen tisu dan 4 sampel tisu segar beku daripada pesakit HNC (26 peringkat I, 15 peringkat II, 11 peringkat II dan 22 peringkat 4 kes-kes HNC), dan 12 sampel bukan kanser telah dikumpul daripada populasi di Semenanjung Malaysia. Ekspresi miRNA serta sasaran jangkaan umum mereka telah ditentukan melalui q-PCR untuk barisan sel HNC, sampel HNC serta sampel bukan kanser.

Kajian bioinformatik kami telah menunjukkan bahawa hsa-miR-181a dan hsa-miR-663 mungkin mengawalselia sebahagian besar gen-gen sasaran yang memainkan peranan penting dalam kawalan proses-proses sel kritikal seperti takdir sel, kemandirian sel, metabolism serta kematian sel. Sehingga kini, 584 sasaran hsa-miR-181a telah disahkan dan 61 daripadanya merupakan gen kanser. Selain itu, kami juga telah mengenalpasti 101 sasaran hsa-miR-663 yang telah disahkan dan 15 daripadanya adalah gen kanser. Ketepatan jangkaan semua algoritma sasaran hsa-miR-181a-23p dan hsa-miR-663 adalah rendah. Berdasarkan DAVID dan laluan analisis "Kyoto Encyclopedia of Genes and Genomes (KEGG)", kebanyakan gen ini terlibat dalam genesis tumor kebanyakan kanser termasuklah HNC. Selain itu, laluan-laluan kanser utama yang dikawalselia oleh hsa-miR-181a dan hsa-miR-663 mungkin merupakan laluan-laluan signal PI3K/Akt, MAPK dan Wnt dalam kanser leher dan kepala. Berdasarkan gabungan analisis *in silico* dan kajian-kajian terdahulu, 9 sasaran jangkaan umum (ATM, BCL2, BCL2L2, CdKN1A, CDKN1B, DDIT4, p53, p73 dan PARP1) hsa-miR-181a-2-3p dan hsa-miR-663 telah dipilih untuk eksperimen penyelidikan seterusnya. Tambahan pula, keputusan kami menunjukkan HNC yang sudah teruk mempunyai level ekspresi hsa-miR-181a-2-3p dan hsa-miR-663 yang lebih tinggi dan signifikan berbanding HNC di peringkat awal, yang mungkin menunjukkan bahawa ia mungkin memainkan peranan yang penting dalam metastasis barah HNC yang sudah teruk. Kami juga mendapati bahawa BCL2 dan PARP1 juga telah meningkat seiring dengan peningkatan kawalan hsa-miR-181a-2-3p dan hsa-miR-663 dalam HNC berbanding tisu-tisu bukan kanser. Walau bagaimanapun, ekspresi ATM, CDKN1A, CDKN1B, DDIT4, p53 dan p73 mempunyai korrelasi yang berkadar songsang dengan ekspresi hsa-miR-181a-2-3p dan hsa-miR-663.

Apabila digabungkan, keputusan-keputusan ini mencadangkan bahawa hsa-miR-181a-2-3p dan hsa-miR-663 mungkin berfungsi sebagai gen kanser dalam kanser leher dan kepala. Selain itu, hsa-miR-181a-2-3p dan hsa-miR-663 serta sasaran-sasaran jangkaan umum mereka mungkin akan digunakan sebagai penanda biologi dalam menentukan nasib HNC dalam bidang klinikal. Kajian-kajian fungsi dan mekanisme perlu dilakukan lebih lagi

untuk mengesahkan fungsi hsa-miR-181a-2-3p dan hsa-miR-663 dalam penghasilan, kemajuan, dan metastasis HNC.

ACKNOWLEDGEMENT

I would like to express my thanks to all the people who have helped me complete the research described in this thesis. I would like to express my sincere gratitude to my supervisor Associate Professor Dr. Cheah Yoke Kqueen for his motivation, intelligent supervision, consistent support, and encouragement. I greatly appreciate all his contributions of time, advice, thought, and patience during the entire process of completing my PhD thesis. I could not have imagined having a better supervisor for my PhD study. I would also like to acknowledge to my co-supervisors Professor Dr. Pathmathan Rajadurai, Associate Professor Dr. Sethu Thakachy Subha and Dr. Norhafizah Muralib for their input in the research question development and later phase of the project. It has been a privilege to work with such highly respected researchers. I owe a big thanks to my brother-in-law, my proof-reader, Mr Asad Ahmad. Your comments have been very much appreciated during these final stages.

My deep appreciation also goes to my parents, Mr Syed Masood Ali and Late Mrs Naseem Bano. It was because of their support that I was able to realize my dream and make it to QueenMary London for my masters and now at Universiti Putra Malaysia for PhD. They have always listened to my thoughts and encouraged me. It is because of their love that this dissertation was even possible in the first place. I am so grateful for having such loving parents. I especially want to thank my loving husband, Dr. Mohd Masood who has been a constant source of support and encouragement. He has not only helped me in many practical ways such as reading my work and offering comments, but also offered unconditional love and encouragement. Without him, I could never have successfully finished my doctoral study. The work is also for Sarah Masood and Sofia Masood, who observed the final stages of this dissertation and always encouraged me with their sweet smiles. Sarah and Sofia were born during my PhD. Their births have provided me an additional joyful dimension to my life. Last and the most important, I am grateful to my sisters, Maryam Fozia and Bazghah Masood and my brothers Alamgir Hussain and Syed Anas Bin Masood for their love, joy, support and encouragement. I am grateful for their love and support that helped me even in the hardest part of my academic career. I hope I have made all of you proud.

I certify that a Thesis Examination Committee has met on 20 February 2018 to conduct the final examination of Yaghma Masood on her thesis entitled "Expression and Association of miR-181a and miR- 663 and their Target Genes in Head and Neck Cancer" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Doctor of Philosophy.

Members of the Thesis Examination Committee were as follows:

Rajesh a/l Ramasamy, PhD
Associate Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Syahrilnizam bin Abdullah, PhD
Associate Professor
Institute of Bioscience
Universiti Putra Malaysia
(Internal Examiner)

Noorjahan Banu binti Mohammed Alitheen, PhD
Associate Professor
Faculty of Biotechnology and Biomolecular Sciences
Universiti Putra Malaysia
(Internal Examiner)

Hui Kam Man, PhD
Senior Lecturer
National Cancer Centre Singapore
Singapore
(External Examiner)

NOR AINI AB. SHUKOR, PhD
Professor and Deputy Dean
School of Graduate Studies
Universiti Putra Malaysia

Date: 26 April 2018

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy.

The members of the Supervisory Committee were as follows:

Cheah Yoke Kqueen, PhD
Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Sethu Thakachy Subha, MBBS, MS ORL
Associate Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Norhafizah Mohtarrudin, MBBS, MPath
Associate Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Pathmanathan s/o Rajadurai, PhD
Professor
Department of Pathology
Sime Darby Medical Centre, Malaysia
(Member)

_____
ROBIAH BINTI YUNUS, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

Declaration by graduate student

I hereby confirm that:

- this thesis is the original work;
- quotations, illustrations and citations have been daily references;
- this thesis has not been submitted previously or concurrently for any other degree at any other institutions;
- intellectual property from the thesis and copyright of thesis are fully owned by Universiti Putra Malaysia, as according to the Universiti Putra Malaysia (Research) Rules 2012;
- written permission must be obtained from the supervisor and the office of Deputy Vice-Chancellor (Research and Innovation) before thesis is published (in the form of written, printed or in electronic form) including books, journals, modules, proceedings, popular writings, seminar papers, manuscripts, posters, reports, lecture notes, learning modules or any other materials as stated in the Universiti Putra Malaysia (Research) Rules 2012;
- there is no plagiarism or data falsification/fabrication in the thesis, and scholarly integrity is upheld as according to the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) and the Universiti Putra Malaysia (Research) Rules 2012. The thesis has undergone plagiarism detection soft

Signature: Yaghma Date: _____

Name and Matric No: Yaghma Masood, GS36051

Declaration by Members of Supervisory Committee

This is to confirm that:

- The research conducted and writing of this thesis was under our supervision;
- Supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

Signature:	_____	Signature:	_____
Name of Chairman of Supervisory Committee:	Cheah Yoke Kqueen	Name of Member of Supervisory Commitee	Sethu Thakachy Subha
Signature:	_____	Signature:	_____
Name of Member of Supervisory Commitee	Norhafizah Mohtarrudin	Name of Member of Supervisory Commitee	Pathmanathan s/o Rajadurai

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS/ANNOTATIONS

Abbreviations

ATM	Ataxia Telangiectasia Mutated
AMOs	Anti-mirnaoligonucleotides
ACTB	Cyclophilin, Actin Beta
ANOVA	One-Way Analysis of Variance
ASOs	Antisense Oligonucleotides
BLAST	Basic Local Alignment Search Tool
BCL2	B-Cell Lymphoma 2
BCL2L2	Bcl2 Like 2
CDKN1A	Cyclin Dependent Kinase Inhibitor 1A
CDKN1B	Cyclin Dependent Kinase Inhibitor 1B
Ct	Threshold Cycle
cDNA	Complementary DNA
CO2	Carbon Dioxide
CLASH	Cross-Linking, Ligation and Sequencing Hybrids
DDIT4	DNA Damage-Inducible Transcript 4
DNA	Deoxyribonucleic Acid
dsDNA	Double Stranded Deoxyribonucleic Acid
DAVID	Database for Annotation Visualization and Integrated Discovery
DMSO	Dimethyl Sulfoxide
DMEM	Dulbecco's Modified Eagle's Medium
EMT	Epithelial Mesenchymal Transition
FF	Fresh Frozen
FFPE	Formalin Fixed Paraffin Embedded
FBS	Fetal Bovine Serum
FASTA	Fast Adaptive Shrinkage Thresholding Algorithm
GAPDH	Glyceraldehyde- 3-Phosphate Dehydrogenase
GO	Gene Ontology
HNC	Head and Neck Cancer
HPV	Human Papilloma Virus
hsa-miRNA	Human microRNA
HNSCC	Head and Neck Squamous Cell Carcinoma
ISH	In Situ Hybridisation
JAK/STAT	Janus Kinase/Signal Transducer and Activator of Transcription
JNK	c-Jun NH2-terminal Kinase
KEGG	Kyoto Encyclopedia of Genes and Genomes Pathways
LNA	Locked Nucleic Acid
Ta	Annealing Temperature
MAPK	Mitogen Activated Protein Kinase
mRNA	Messenger Ribonucleic Acid
miRNA	MicroRNA
ncRNA	Non-Coding RNA
NCBI	National Centre for Biotechnology Information
NGS	Next Gene Sequencing
OC	Oral Cancer

ORF	Open Reading Frame
PTEN	Phosphatase and Tensin Homolog
PI3K/AKT	Phosphoinositide 3-kinase/Protein kinase B
pre-miRNA	Precursor miRNA
Pri-miRNA	Primary miRNA
PCR	Polymerase Chain Reaction
piRNA	Piwi-Interacting RNA
PAR-CLIP	Photoactivatable Ribonucleoside-Enhanced Crosslinking and Immunoprecipitation
PARP1	Poly(Adp-Ribose) Polymerase 1
p53	Tumor Protein p53
p73	Tumor Protein p73
q-PCR	Real Time Quantitative PCR
RNA	Ribonucleic Acid
RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
RISC	RNA-Induced Silencing Complex
RNAi	RNA-Mediated Interference
RNAse	Ribonuclease
SACC	Salivary Adenoid Cystic Carcinoma
snoRNA	Small Nucleolar RNA
SCC	Squamous Cell Carcinoma
SNP	Single Nucleotide Polymorphisms
SD	Standard Deviation
UTR	Untranslated Region
UDSP	Universal Degenerate Specific Primer
VEGF	Vascular Endothelial Growth Factor

Annotations

%	Percentage
Δ	Delta
°C	Degree Celsius
µl	Micro Liter
µm	Micrometer
cm	Centimeter
mg	Milligram
ml	Milliliter
mm	Millimeter
mM	MicroMolar
ng/µl	Nanogram/micro Liter
µg	Microgram
µM	MicroMolar

CHAPTER 1

INTRODUCTION

1.1 Introduction

Head and neck cancer (HNC) constitutes cancers that arise most often from the oral cavity, larynx, and oropharynx. It is the sixth most common malignancy worldwide, representing a major international health problem (Harris et al., 2012) and accounts for 650,000 new cases annually (Siegel, Naishadham, & Jemal, 2012). In South-Central Asia, HNC is the second most common cancer (Ferlay et al., 2010). It is the fifth most common cancer among the Peninsular Malaysian population. In 2006, nearly 3000 cases of head and neck cancers were reported in Peninsular Malaysia. Malaysia is a multiracial country, consisting of three major types of ethnicities; Malay, Chinese, and Indian. Prevalence of head and neck cancers in Malaysia varies according to these three major types of ethnicities; oral, laryngeal and pharyngeal cancers are more common in Indians, followed by Malays, and Chinese. On the other hand, nasopharyngeal cancer is most common among the Chinese followed by the Malays, and Indians (Razak, Saddki, Naing, & Abdullah, 2009).

Tobacco and alcohol consumption have been identified as important causes of head and neck cancer (Hashibe et al., 2007; Hashibe et al., 2009). Furthermore, studies have also reported that genetic factors, including family history and genetic variants, in multiple biological pathways, were involved in the development of HNC (Geisler & Olshan, 2001). Furthermore, in South-Central Asia, approximately 90% of HNC cases are attributable to the use of tobacco in various unrecorded forms, habitual chewing of Betel quid/ areca nut, and excessive alcohol drinking. It is the second leading cause of cancer death among males in South-Central Asia (Ferlay et al., 2010). In recent years, the demographics of the disease are moving to non-smoking younger men and women (Jakymiw et al., 2010; P. E. Petersen, 2009).

Despite considerable advances in multimodality therapy, including surgery, radiotherapy and chemotherapy, the major problem is that the overall five-year survival rate for patients with HNC is only 40-50% (J. Y. Chan & Wei, 2013; Takes et al., 2012). This has remained relatively unchanged over the past 3 to 4 decades because of distant metastasis, loco-regional recurrences and secondary primary tumours (Leemans, Braakhuis, & Brakenhoff, 2011). However, the exact mechanism of developing HNC has not been fully explored. Better understanding of the molecular mechanisms underlying invasion and metastasis is urgently needed to improve the diagnosis, approaches to therapy, and prevention of HNC (Kinoshita, Nohata, Fuse, et al., 2012).

Head and neck cancer is a heterogenous group of cancer. The heterogeneity of this cancer is increased by the growing rate of human papillomavirus (HPV)-associated tumour (Beck & Golemis, 2016). Studies have emphasised that HNC molecular heterogeneity are based on many factors like, methylation profiles, mutated genes, miRNA expression which may represent new targets for cancer therapies (Pezzuto et al., 2015) .

MicroRNAs (miRNAs) have been shown to play vital roles in various biological and pathological processes (Jackson & Standart, 2007). These functions include growth, invasion, angiogenesis, proliferation, and differentiation (Bartel, 2004; R. C. Lee, Feinbaum, & Ambros, 1993). Growing evidences suggest that miRNA play important roles in the initiation, development, metastasis and prognosis of human cancers including HNC (Guo et al., 2012; Jakymiw et al., 2010). miRNAs are small endogenous nonprotein-coding single stranded RNA molecules with an average length of 19–25 nucleotides (Esquela-Kerscher & Slack, 2006). They function by regulating the genes expression at the transcriptional or posttranscriptional level via binding 3' UTR of mRNA. The regulation of the genes is done either by suppressing the translation of protein coding genes or by degrading the mRNAs (Bartel, 2004; Kutter & Svoboda, 2008). A single miRNA can bind and regulate as many as 200 protein coding genes, often encoding proteins with related functions. On the other hand, many miRNAs could bind to a single gene promote (Nohata, Hanazawa, Kinoshita, Okamoto, & Seki, 2013). Some down regulated miRNAs could function as tumor suppressors by negatively regulating oncogenes whereas upregulated miRNAs could function as oncogenes by repressing tumor suppressors. This upregulation and downregulation of miRNAs have been shown to contribute to cancer development (Esquela-Kerscher & Slack, 2006).that a number of studies have reported the effect of miRNAs in the pathogenesis of cancers including HNC. Remarkably, miRNAs act as a valuable tool in therapeutics, diagnostics and prognostics in many types of cancer. There is strong evidence that miRNAs may also represent different targets for anticancer therapies. The aberrant expression of human miR-181a-2-3p and miR-663 has been implicated in the pathogenesis of various cancers. They either serve as an oncogene or a tumor suppressor in the pathogenesis of many cancers. A systematic search of the literature revealed that only one research was done on hsa-miR-181a-2-3p in head and neck cancer. Only two studies have shown expression of hsa-miR-663 in nasopharyngeal carcinoma. Limited work has been done on hsa-miR-181a-2-3p and hsa-miR-663 in the pathogenesis of HNC; and their clinical significance is still unclear. Moreover, this study is the continuation of previous work done by our research group where novel expression of hsa-miR-181a-2-3p was found in head and neck cancer. To check and compare the expression of hsa-miR-181a-2-3p, hsa-miR-663 was selected, which already has established expression in HNC.

1.1.1 Problem Statement

Head and neck cancer is the sixth most common malignancy worldwide and the fifth most common cancer in peninsular Malaysia. The over five-year survival rate for patients with HNC is only 40-50% because of distant metastasis, loco-regional recurrences and secondary primary tumours. MiRNAs have been shown to be able to regulate many cellular processes, including proliferation, differentiation, angiogenesis, cell development, etc. There is a strong evidence that miRNAs may represent different targets for anticancer therapies. The aberrant expression of human miR-181-a-2-3p and miR-663 has been implicated in the pathogenesis of various cancers. The role of hsa-miR-181a-2-3p and hsa-miR-663 in the pathogenesis of HNC is yet to be investigated upon. Therefore, it is important to address the following hypothesis and objectives.

1.1.2 Hypothesis

It was hypothesised that hsa-miR-181a-2-3p and hsa-miR-663 may play an important role in the progression of head and neck cancer and co-regulate few common targets which lead to the activation of cancer pathways in HNC development.

1.1.3 Aim

The aim of this study was to search for the molecular targets of hsa-miR-181a -2-3p and hsa-miR-663 and determine their expression and their common predicted targets in HNC.

1.1.4 Specific Objectives

The specific objectives of this study were to:
1) identify the predicted target genes of hsa-miR-181a-2-3p and hsa-miR-663 in HNC by using three different computational algorithms for miRNA target prediction;

2) identify the validated target genes of hsa-miR-181a-5p and hsa-miR-663, and their predicted cancer pathways (using DIANA) involved in the progression and development of HNC;

3) validate the role of hsa-miR-181a-2-3p and hsa-miR-663 and their selected common predicted targets in human HNC cell line and tissues; and

4) investigate the association between expression of miRNAs (hsa-miR-

181a-2-3p and hsa-miR-663), their selective common predicted targets, and clinopathological factors in HNC.

To address the above hypothesis and objectives, the HNC samples were obtained from Malaysian human population. The current study will provide a better understanding of the effect of hsa-miR-181a-2-3p and hsa-miR-663, and their selective common predicted targets in the progression and development of HNC. Hence, the study may contribute to a better accuracy in diagnosis, prognosis, and improving decision making by oncologists in the treatment of HNC patients.

REFERENCES

A. Elumalai, M. C. E. (2013). Review on application of bioinformatics. *Journal of science, 3*(1), 7.

Abbas, T., & Dutta, A. (2009). p21 in cancer: intricate networks and multiple activities. *Nat Rev Cancer, 9*(6), 400-414. doi:10.1038/nrc2657

Abbott, A. L., Alvarez-Saavedra, E., Miska, E. A., Lau, N. C., Bartel, D. P., Horvitz, H. R., & Ambros, V. (2005). The let-7 MicroRNA family members mir-48, mir-84, and mir-241 function together to regulate developmental timing in Caenorhabditis elegans. *Dev Cell, 9*(3), 403-414. doi:10.1016/j.devcel.2005.07.009

Adelstein, D. J., Saxton, J. P., Rybicki, L. A., Esclamado, R. M., Wood, B. G., Strome, M., . . . Carroll, M. A. (2006). Multiagent concurrent chemoradiotherapy for locoregionally advanced squamous cell head and neck cancer: mature results from a single institution. *J Clin Oncol, 24*(7), 1064-1071. doi:10.1200/JCO.2005.01.5867

Afonyushkin, T., Oskolkova, O. V., & Bochkov, V. N. (2012). Permissive role of miR-663 in induction of VEGF and activation of the ATF4 branch of unfolded protein response in endothelial cells by oxidized phospholipids. *Atherosclerosis, 225*(1), 50-55. doi:10.1016/j.atherosclerosis.2012.06.016

Agarwal, V., Bell, G. W., Nam, J. W., & Bartel, D. P. (2015). Predicting effective microRNA target sites in mammalian mRNAs. *Elife, 4*. doi:10.7554/eLife.05005

Agrawal, N., Frederick, M. J., Pickering, C. R., Bettegowda, C., Chang, K., Li, R. J., . . . Myers, J. N. (2011). Exome sequencing of head and neck squamous cell carcinoma reveals inactivating mutations in NOTCH1. *Science, 333*(6046), 1154-1157. doi:10.1126/science.1206923

Agrawal, R., Pandey, P., Jha, P., Dwivedi, V., Sarkar, C., & Kulshreshtha, R. (2014). Hypoxic signature of microRNAs in glioblastoma: insights from small RNA deep sequencing. *BMC Genomics, 15*, 686. doi:10.1186/1471-2164-15-686

Ai, L., Vo, Q. N., Zuo, C., Li, L., Ling, W., Suen, J. Y., . . . Fan, C. Y. (2004). Ataxia-telangiectasia-mutated (ATM) gene in head and neck squamous cell carcinoma: promoter hypermethylation with clinical correlation in 100 cases. *Cancer Epidemiol Biomarkers Prev, 13*(1), 150-156.

Alexiou, P., Maragkakis, M., Papadopoulos, G. L., Reczko, M., & Hatzigeorgiou, A. G. (2009). Lost in translation: an assessment and

perspective for computational microRNA target identification. *Bioinformatics, 25*(23), 3049-3055. doi:10.1093/bioinformatics/btp565

Altuvia, Y., Landgraf, P., Lithwick, G., Elefant, N., Pfeffer, S., Aravin, A., . . . Margalit, H. (2005). Clustering and conservation patterns of human microRNAs. *Nucleic Acids Res, 33*(8), 2697-2706. doi:10.1093/nar/gki567

Ambros, V. (2004). The functions of animal microRNAs. *Nature, 431*(7006), 350-355. doi:10.1038/nature02871

Ambros, V., Bartel, B., Bartel, D. P., Burge, C. B., Carrington, J. C., Chen, X., . . . Tuschl, T. (2003). A uniform system for microRNA annotation. *RNA, 9*(3), 277-279.

Ambs, S., Prueitt, R. L., Yi, M., Hudson, R. S., Howe, T. M., Petrocca, F., . . . Croce, C. M. (2008). Genomic profiling of microRNA and messenger RNA reveals deregulated microRNA expression in prostate cancer. *Cancer Res, 68*(15), 6162-6170. doi:68/15/6162 [pii]
10.1158/0008-5472.CAN-08-0144

Amundson, S. A., Myers, T. G., Scudiero, D., Kitada, S., Reed, J. C., & Fornace, A. J., Jr. (2000). An informatics approach identifying markers of chemosensitivity in human cancer cell lines. *Cancer Res, 60*(21), 6101-6110.

Ando, T., Yoshida, T., Enomoto, S., Asada, K., Tatematsu, M., Ichinose, M., . . . Ushijima, T. (2009). DNA methylation of microRNA genes in gastric mucosae of gastric cancer patients: its possible involvement in the formation of epigenetic field defect. *Int J Cancer, 124*(10), 2367-2374. doi:10.1002/ijc.24219

Asangani, I. A., Rasheed, S. A., Nikolova, D. A., Leupold, J. H., Colburn, N. H., Post, S., & Allgayer, H. (2008). MicroRNA-21 (miR-21) post-transcriptionally downregulates tumor suppressor Pdcd4 and stimulates invasion, intravasation and metastasis in colorectal cancer. *Oncogene, 27*(15), 2128-2136. doi:10.1038/sj.onc.1210856

Austen, B., Skowronska, A., Baker, C., Powell, J. E., Gardiner, A., Oscier, D., . . . Stankovic, T. (2007). Mutation status of the residual ATM allele is an important determinant of the cellular response to chemotherapy and survival in patients with chronic lymphocytic leukemia containing an 11q deletion. *J Clin Oncol, 25*(34), 5448-5457. doi:10.1200/JCO.2007.11.2649

Avissar, M., Christensen, B. C., Kelsey, K. T., & Marsit, C. J. (2009). MicroRNA expression ratio is predictive of head and neck squamous cell carcinoma. *Clin Cancer Res, 15*(8), 2850-2855. doi:10.1158/1078-0432.CCR-08-3131

Avissar, M., McClean, M. D., Kelsey, K. T., & Marsit, C. J. (2009). MicroRNA expression in head and neck cancer associates with alcohol

consumption and survival. *Carcinogenesis, 30*(12), 2059-2063. doi:10.1093/carcin/bgp277

Azuma-Mukai, A., Oguri, H., Mituyama, T., Qian, Z. R., Asai, K., Siomi, H., & Siomi, M. C. (2008). Characterization of endogenous human Argonautes and their miRNA partners in RNA silencing. *Proc Natl Acad Sci U S A, 105*(23), 7964-7969. doi:10.1073/pnas.0800334105

Bae, I. H., Park, M. J., Yoon, S. H., Kang, S. W., Lee, S. S., Choi, K. M., & Um, H. D. (2006). Bcl-w promotes gastric cancer cell invasion by inducing matrix metalloproteinase-2 expression via phosphoinositide 3-kinase, Akt, and Sp1. *Cancer Res, 66*(10), 4991-4995. doi:10.1158/0008-5472.CAN-05-4254

Bai, H., Cao, Z., Deng, C., Zhou, L., & Wang, C. (2012). miR-181a sensitizes resistant leukaemia HL-60/Ara-C cells to Ara-C by inducing apoptosis. *J Cancer Res Clin Oncol, 138*(4), 595-602. doi:10.1007/s00432-011-1137-3

Bancroft, C. C., Chen, Z., Yeh, J., Sunwoo, J. B., Yeh, N. T., Jackson, S., . . . Van Waes, C. (2002). Effects of pharmacologic antagonists of epidermal growth factor receptor, PI3K and MEK signal kinases on NF-kappaB and AP-1 activation and IL-8 and VEGF expression in human head and neck squamous cell carcinoma lines. *Int J Cancer, 99*(4), 538-548. doi:10.1002/ijc.10398

Bandres, E., Agirre, X., Bitarte, N., Ramirez, N., Zarate, R., Roman-Gomez, J., . . . Garcia-Foncillas, J. (2009). Epigenetic regulation of microRNA expression in colorectal cancer. *Int J Cancer, 125*(11), 2737-2743. doi:10.1002/ijc.24638

Bar, M., Wyman, S. K., Fritz, B. R., Qi, J., Garg, K. S., Parkin, R. K., . . . Tewari, M. (2008). MicroRNA discovery and profiling in human embryonic stem cells by deep sequencing of small RNA libraries. *Stem Cells, 26*(10), 2496-2505. doi:10.1634/stemcells.2008-0356

Bartel, D. P. (2004). MicroRNAs: genomics, biogenesis, mechanism, and function. *Cell, 116*(2), 281-297.

Bartkova, J., Bakkenist, C. J., Rajpert-De Meyts, E., Skakkebaek, N. E., Sehested, M., Lukas, J., . . . Bartek, J. (2005). ATM activation in normal human tissues and testicular cancer. *Cell Cycle, 4*(6), 838-845. doi:10.4161/cc.4.6.1742

Beck, T. N., & Golemis, E. A. (2016). Genomic insights into head and neck cancer. *Cancers Head Neck, 1*. doi:10.1186/s41199-016-0003-z

Bentwich, I., Avniel, A., Karov, Y., Aharonov, R., Gilad, S., Barad, O., . . . Bentwich, Z. (2005). Identification of hundreds of conserved and nonconserved human microRNAs. *Nat Genet, 37*(7), 766-770. doi:10.1038/ng1590

Bernardo, B. C., Charchar, F. J., Lin, R. C., & McMullen, J. R. (2012). A microRNA guide for clinicians and basic scientists: background and experimental techniques. *Heart Lung Circ, 21*(3), 131-142. doi:10.1016/j.hlc.2011.11.002

Berrino, F., Richiardi, L., Boffetta, P., Esteve, J., Belletti, I., Raymond, L., . . . Milan, J. E. M. W. G. (2003). Occupation and larynx and hypopharynx cancer: a job-exposure matrix approach in an international case-control study in France, Italy, Spain and Switzerland. *Cancer Causes Control, 14*(3), 213-223.

Besson, A., Hwang, H. C., Cicero, S., Donovan, S. L., Gurian-West, M., Johnson, D., . . . Roberts, J. M. (2007). Discovery of an oncogenic activity in p27Kip1 that causes stem cell expansion and a multiple tumor phenotype. *Genes Dev, 21*(14), 1731-1746. doi:10.1101/gad.1556607

Betel, D., Koppal, A., Agius, P., Sander, C., & Leslie, C. (2010). Comprehensive modeling of microRNA targets predicts functional non-conserved and non-canonical sites. *Genome Biol, 11*(8), R90. doi:10.1186/gb-2010-11-8-r90

Bhushan, R., Grunhagen, J., Becker, J., Robinson, P. N., Ott, C. E., & Knaus, P. (2013). miR-181a promotes osteoblastic differentiation through repression of TGF-beta signaling molecules. *Int J Biochem Cell Biol, 45*(3), 696-705. doi:10.1016/j.biocel.2012.12.008

Bhutia, S. K., Mallick, S. K., Maiti, S., & Maiti, T. K. (2009). Inhibitory effect of Abrus abrin-derived peptide fraction against Dalton's lymphoma ascites model. *Phytomedicine, 16*(4), 377-385. doi:10.1016/j.phymed.2008.07.001

Bi, C., Chung, T. H., Huang, G., Zhou, J., Yan, J., Ahmann, G. J., . . . Chng, W. J. (2015). Genome-wide pharmacologic unmasking identifies tumor suppressive microRNAs in multiple myeloma. *Oncotarget, 6*(28), 26508-26518. doi:10.18632/oncotarget.4769

Bisso, A., Faleschini, M., Zampa, F., Capaci, V., De Santa, J., Santarpia, L., . . . Del Sal, G. (2013). Oncogenic miR-181a/b affect the DNA damage response in aggressive breast cancer. *Cell Cycle, 12*(11), 1679-1687. doi:10.4161/cc.24757

Bloch, S. A., Lee, J. Y., Syburra, T., Rosendahl, U., Griffiths, M. J., Kemp, P. R., & Polkey, M. I. (2015). Increased expression of GDF-15 may mediate ICU-acquired weakness by down-regulating muscle microRNAs. *Thorax, 70*(3), 219-228. doi:10.1136/thoraxjnl-2014-206225

Boldrup, L., Coates, P. J., Wahlgren, M., Laurell, G., & Nylander, K. (2012). Subsite-based alterations in miR-21, miR-125b, and miR-203 in squamous cell carcinoma of the oral cavity and correlation to

important target proteins. *J Carcinog, 11*, 18. doi:10.4103/1477-3163.104007
JC-11-18 [pii]

Boominathan, L. (2010a). The guardians of the genome (p53, TA-p73, and TA-p63) are regulators of tumor suppressor miRNAs network. *Cancer Metastasis Rev, 29*(4), 613-639. doi:10.1007/s10555-010-9257-9

Boominathan, L. (2010b). The tumor suppressors p53, p63, and p73 are regulators of microRNA processing complex. *PLoS One, 5*(5), e10615. doi:10.1371/journal.pone.0010615

Borze, I., Guled, M., Musse, S., Raunio, A., Elonen, E., Saarinen-Pihkala, U., . . . Knuutila, S. (2011). MicroRNA microarrays on archive bone marrow core biopsies of leukemias--method validation. *Leuk Res, 35*(2), 188-195. doi:10.1016/j.leukres.2010.08.005

Bose, S., Yap, L. F., Fung, M., Starzcynski, J., Saleh, A., Morgan, S., . . . Murray, P. G. (2009). The ATM tumour suppressor gene is down-regulated in EBV-associated nasopharyngeal carcinoma. *J Pathol, 217*(3), 345-352. doi:10.1002/path.2487

Brandizzi D, C. J., Lanfranchi HE, Cabrini RL. (2005). Analysis of the epidemiological features of oral cancer in
the city of Buenos Aires. *Acta Odontol Latinoam, 18*, 6.

Brauer-Hartmann, D., Hartmann, J. U., Wurm, A. A., Gerloff, D., Katzerke, C., Verga Falzacappa, M. V., . . . Behre, G. (2015). PML/RARalpha-Regulated miR-181a/b Cluster Targets the Tumor Suppressor RASSF1A in Acute Promyelocytic Leukemia. *Cancer Res, 75*(16), 3411-3424. doi:10.1158/0008-5472.CAN-14-3521

Brockhausen, J., Tay, S. S., Grzelak, C. A., Bertolino, P., Bowen, D. G., d'Avigdor, W. M., . . . McCaughan, G. W. (2015). miR-181a mediates TGF-beta-induced hepatocyte EMT and is dysregulated in cirrhosis and hepatocellular cancer. *Liver Int, 35*(1), 240-253. doi:10.1111/liv.12517

Brouha, X. D., Tromp, D. M., Koole, R., Hordijk, G. J., Winnubst, J. A., & de Leeuw, J. R. (2007). Professional delay in head and neck cancer patients: analysis of the diagnostic pathway. *Oral Oncol, 43*(6), 551-556. doi:10.1016/j.oraloncology.2006.06.002

Buratti, E., De Conti, L., Stuani, C., Romano, M., Baralle, M., & Baralle, F. (2010). Nuclear factor TDP-43 can affect selected microRNA levels. *FEBS J, 277*(10), 2268-2281. doi:10.1111/j.1742-4658.2010.07643.x

Bustin, S. A., & Dorudi, S. (2004). Gene expression profiling for molecular staging and prognosis prediction in colorectal cancer. *Expert Rev Mol Diagn, 4*(5), 599-607. doi:10.1586/14737159.4.5.599

Calin, G. A., Dumitru, C. D., Shimizu, M., Bichi, R., Zupo, S., Noch, E., . . . Croce, C. M. (2002). Frequent deletions and down-regulation of micro-RNA genes miR15 and miR16 at 13q14 in chronic lymphocytic leukemia. *Proc Natl Acad Sci U S A, 99*(24), 15524-15529. doi:10.1073/pnas.242606799

Cao, J., Cai, J., Huang, D., Han, Q., Yang, Q., Li, T., . . . Wang, Z. (2013). miR-335 represents an invasion suppressor gene in ovarian cancer by targeting Bcl-w. *Oncol Rep, 30*(2), 701-706. doi:10.3892/or.2013.2482

Cao, J. X., Lu, Y., Qi, J. J., An, G. S., Mao, Z. B., Jia, H. T., . . . Ni, J. H. (2014). MiR-630 inhibits proliferation by targeting CDC7 kinase, but maintains the apoptotic balance by targeting multiple modulators in human lung cancer A549 cells. *Cell Death Dis, 5*, e1426. doi:10.1038/cddis.2014.386

Carvalho, A. L., Jeronimo, C., Kim, M. M., Henrique, R., Zhang, Z., Hoque, M. O., . . . Califano, J. A. (2008). Evaluation of promoter hypermethylation detection in body fluids as a screening/diagnosis tool for head and neck squamous cell carcinoma. *Clin Cancer Res, 14*(1), 97-107. doi:14/1/97 [pii]
10.1158/1078-0432.CCR-07-0722

Castellano, L., Giamas, G., Jacob, J., Coombes, R. C., Lucchesi, W., Thiruchelvam, P., . . . Stebbing, J. (2009). The estrogen receptor-alpha-induced microRNA signature regulates itself and its transcriptional response. *Proc Natl Acad Sci U S A, 106*(37), 15732-15737. doi:0906947106 [pii]
10.1073/pnas.0906947106

Castoldi, M., Schmidt, S., Benes, V., Hentze, M. W., & Muckenthaler, M. U. (2008). miChip: an array-based method for microRNA expression profiling using locked nucleic acid capture probes. *Nat Protoc, 3*(2), 321-329. doi:10.1038/nprot.2008.4

Castoldi, M., Schmidt, S., Benes, V., Noerholm, M., Kulozik, A. E., Hentze, M. W., & Muckenthaler, M. U. (2006). A sensitive array for microRNA expression profiling (miChip) based on locked nucleic acids (LNA). *RNA, 12*(5), 913-920. doi:10.1261/rna.2332406

Cerami, E., Gao, J., Dogrusoz, U., Gross, B. E., Sumer, S. O., Aksoy, B. A., . . . Schultz, N. (2012). The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. *Cancer Discov, 2*(5), 401-404. doi:10.1158/2159-8290.CD-12-0095

Cervigne, N. K., Reis, P. P., Machado, J., Sadikovic, B., Bradley, G., Galloni, N. N., . . . Kamel-Reid, S. (2009). Identification of a microRNA signature associated with progression of leukoplakia to oral carcinoma. *Hum Mol Genet, 18*(24), 4818-4829. doi:10.1093/hmg/ddp446

Chan, J. A., Krichevsky, A. M., & Kosik, K. S. (2005). MicroRNA-21 is an antiapoptotic factor in human glioblastoma cells. *Cancer Res, 65*(14), 6029-6033. doi:10.1158/0008-5472.CAN-05-0137

Chan, J. Y., & Wei, W. I. (2013). Current management strategy of hypopharyngeal carcinoma. *Auris Nasus Larynx, 40*(1), 2-6. doi:10.1016/j.anl.2011.11.009

Chang, K. W., Kao, S. Y., Wu, Y. H., Tsai, M. M., Tu, H. F., Liu, C. J., . . . Lin, S. C. (2013). Passenger strand miRNA miR-31* regulates the phenotypes of oral cancer cells by targeting RhoA. *Oral Oncol, 49*(1), 27-33. doi:S1368-8375(12)00231-X [pii]
10.1016/j.oraloncology.2012.07.003

Chang, S., Chen, B., Wang, X., Wu, K., & Sun, Y. (2017). Long non-coding RNA XIST regulates PTEN expression by sponging miR-181a and promotes hepatocellular carcinoma progression. *BMC Cancer, 17*(1), 248. doi:10.1186/s12885-017-3216-6

Chang, S. S., Jiang, W. W., Smith, I., Poeta, L. M., Begum, S., Glazer, C., . . . Califano, J. A. (2008). MicroRNA alterations in head and neck squamous cell carcinoma. *Int J Cancer, 123*(12), 2791-2797. doi:10.1002/ijc.23831

Chaturvedi, A. K., Anderson, W. F., Lortet-Tieulent, J., Curado, M. P., Ferlay, J., Franceschi, S., . . . Gillison, M. L. (2013). Worldwide trends in incidence rates for oral cavity and oropharyngeal cancers. *J Clin Oncol, 31*(36), 4550-4559. doi:10.1200/JCO.2013.50.3870

Cheah, Y. K., Cheng, R. W., Yeap, S. K., Khoo, C. H., & See, H. S. (2014). Analysis of TP53 gene expression and p53 level of human hypopharyngeal FaDu (HTB-43) head and neck cancer cell line after microRNA-181a inhibition. *Genet Mol Res, 13*(1), 1679-1683. doi:10.4238/2014.January.22.4

Chen, C., Lu, Z., Yang, J., Hao, W., Qin, Y., Wang, H., . . . Xie, R. (2016). MiR-17-5p promotes cancer cell proliferation and tumorigenesis in nasopharyngeal carcinoma by targeting p21. *Cancer Med, 5*(12), 3489-3499. doi:10.1002/cam4.863

Chen, C. Z., Li, L., Lodish, H. F., & Bartel, D. P. (2004). MicroRNAs modulate hematopoietic lineage differentiation. *Science, 303*(5654), 83-86. doi:10.1126/science.1091903

Chen, G., Zhu, W., Shi, D., Lv, L., Zhang, C., Liu, P., & Hu, W. (2010). MicroRNA-181a sensitizes human malignant glioma U87MG cells to radiation by targeting Bcl-2. *Oncol Rep, 23*(4), 997-1003.

Chen, P., Xu, W., Luo, Y., Zhang, Y., He, Y., Yang, S., & Yuan, Z. (2017). MicroRNA 543 suppresses breast cancer cell proliferation, blocks cell cycle and induces cell apoptosis via direct targeting of ERK/MAPK. *Onco Targets Ther, 10*, 1423-1431. doi:10.2147/OTT.S118366

Chen, S., Sun, Y. Y., Zhang, Z. X., Li, Y. H., Xu, Z. M., & Fu, W. N. (2017). Transcriptional suppression of microRNA-27a contributes to laryngeal cancer differentiation via GSK-3beta-involved Wnt/beta-catenin pathway. *Oncotarget, 8*(9), 14708-14718. doi:10.18632/oncotarget.14769

Chen, Y., Ke, G., Han, D., Liang, S., Yang, G., & Wu, X. (2014). MicroRNA-181a enhances the chemoresistance of human cervical squamous cell carcinoma to cisplatin by targeting PRKCD. *Exp Cell Res, 320*(1), 12-20. doi:10.1016/j.yexcr.2013.10.014

Cheng, L. S., Swan, G. E., & Carmelli, D. (2000). A genetic analysis of smoking behavior in family members of older adult males. *Addiction, 95*(3), 427-435.

Chi, Y., & Zhou, D. (2016). MicroRNAs in colorectal carcinoma--from pathogenesis to therapy. *J Exp Clin Cancer Res, 35*, 43. doi:10.1186/s13046-016-0320-4

Chiang, H. R., Schoenfeld, L. W., Ruby, J. G., Auyeung, V. C., Spies, N., Baek, D., . . . Bartel, D. P. (2010). Mammalian microRNAs: experimental evaluation of novel and previously annotated genes. *Genes Dev, 24*(10), 992-1009. doi:10.1101/gad.1884710

Chien, A. J., Haydu, L. E., Biechele, T. L., Kulikauskas, R. M., Rizos, H., Kefford, R. F., . . . Long, G. V. (2014). Targeted BRAF inhibition impacts survival in melanoma patients with high levels of Wnt/beta-catenin signaling. *PLoS One, 9*(4), e94748. doi:10.1371/journal.pone.0094748

Childs, G., Fazzari, M., Kung, G., Kawachi, N., Brandwein-Gensler, M., McLemore, M., . . . Schlecht, N. F. (2009). Low-level expression of microRNAs let-7d and miR-205 are prognostic markers of head and neck squamous cell carcinoma. *Am J Pathol, 174*(3), 736-745. doi:S0002-9440(10)60935-2 [pii]
10.2353/ajpath.2009.080731

Cho, J. G., Park, S., Lim, C. H., Kim, H. S., Song, S. Y., Roh, T. Y., . . . Park, S. G. (2016). ZNF224, Kruppel like zinc finger protein, induces cell growth and apoptosis-resistance by down-regulation of p21 and p53 via miR-663a. *Oncotarget, 7*(21), 31177-31190. doi:10.18632/oncotarget.8870

Chou, C. H., Chang, N. W., Shrestha, S., Hsu, S. D., Lin, Y. L., Lee, W. H., . . . Huang, H. D. (2016). miRTarBase 2016: updates to the experimentally validated miRNA-target interactions database. *Nucleic Acids Res, 44*(D1), D239-247. doi:10.1093/nar/gkv1258

Chow, C. W., Tabrizi, S. N., Tiedemann, K., & Waters, K. D. (2007). Squamous cell carcinomas in children and young adults: a new wave

of a very rare tumor? *J Pediatr Surg, 42*(12), 2035-2039. doi:10.1016/j.jpedsurg.2007.08.025

Christensen, B. C., Avissar-Whiting, M., Ouellet, L. G., Butler, R. A., Nelson, H. H., McClean, M. D., . . . Kelsey, K. T. (2010). Mature microRNA sequence polymorphism in MIR196A2 is associated with risk and prognosis of head and neck cancer. *Clin Cancer Res, 16*(14), 3713-3720. doi:1078-0432.CCR-10-0657 [pii]
10.1158/1078-0432.CCR-10-0657

Christensen, B. C., Moyer, B. J., Avissar, M., Ouellet, L. G., Plaza, S. L., McClean, M. D., . . . Kelsey, K. T. (2009). A let-7 microRNA-binding site polymorphism in the KRAS 3' UTR is associated with reduced survival in oral cancers. *Carcinogenesis, 30*(6), 1003-1007. doi:bgp099 [pii]
10.1093/carcin/bgp099

Chu, B., Wu, T., Miao, L., Mei, Y., & Wu, M. (2015). MiR-181a regulates lipid metabolism via IDH1. *Sci Rep, 5*, 8801. doi:10.1038/srep08801

Chung, C. H., & Gillison, M. L. (2009). Human papillomavirus in head and neck cancer: its role in pathogenesis and clinical implications. *Clin Cancer Res, 15*(22), 6758-6762. doi:10.1158/1078-0432.CCR-09-0784

Clevers, H. (2006). Wnt/beta-catenin signaling in development and disease. *Cell, 127*(3), 469-480. doi:10.1016/j.cell.2006.10.018

Condorelli, R., & Andre, F. (2017). Combining PI3K and PARP inhibitors for breast and ovarian cancer treatment. *Ann Oncol, 28*(6), 1167-1168. doi:10.1093/annonc/mdx218

Costello, J. F., Fruhwald, M. C., Smiraglia, D. J., Rush, L. J., Robertson, G. P., Gao, X., . . . Plass, C. (2000). Aberrant CpG-island methylation has non-random and tumour-type-specific patterns. *Nat Genet, 24*(2), 132-138. doi:10.1038/72785

Cottonham, C. L., Kaneko, S., & Xu, L. (2010). miR-21 and miR-31 converge on TIAM1 to regulate migration and invasion of colon carcinoma cells. *J Biol Chem, 285*(46), 35293-35302. doi:M110.160069 [pii]
10.1074/jbc.M110.160069

Croce, C. M. (2009). Causes and consequences of microRNA dysregulation in cancer. *Nat Rev Genet, 10*(10), 704-714. doi:10.1038/nrg2634

Cronin, M., Pho, M., Dutta, D., Stephans, J. C., Shak, S., Kiefer, M. C., . . . Baker, J. B. (2004). Measurement of gene expression in archival paraffin-embedded tissues: development and performance of a 92-gene reverse transcriptase-polymerase chain reaction assay. *Am J Pathol, 164*(1), 35-42. doi:10.1016/S0002-9440(10)63093-3

Cuesta, R., Martinez-Sanchez, A., & Gebauer, F. (2009). miR-181a regulates cap-dependent translation of p27(kip1) mRNA in myeloid cells. *Mol Cell Biol, 29*(10), 2841-2851. doi:10.1128/MCB.01971-08

Dahlhaus, M., Schult, C., Lange, S., Freund, M., & Junghanss, C. (2013). MicroRNA 181a influences the expression of HMGB1 and CD4 in acute Leukemias. *Anticancer Res, 33*(2), 445-452.

Datta, J., Kutay, H., Nasser, M. W., Nuovo, G. J., Wang, B., Majumder, S., . . . Jacob, S. T. (2008). Methylation mediated silencing of MicroRNA-1 gene and its role in hepatocellular carcinogenesis. *Cancer Res, 68*(13), 5049-5058. doi:68/13/5049 [pii]
10.1158/0008-5472.CAN-07-6655

Datta, J., Smith, A., Lang, J. C., Islam, M., Dutt, D., Teknos, T. N., & Pan, Q. (2012). microRNA-107 functions as a candidate tumor-suppressor gene in head and neck squamous cell carcinoma by downregulation of protein kinase Cvarepsilon. *Oncogene, 31*(36), 4045-4053. doi:onc2011565 [pii]
10.1038/onc.2011.565

de la Chapelle, A., & Jazdzewski, K. (2011). MicroRNAs in thyroid cancer. *J Clin Endocrinol Metab, 96*(11), 3326-3336. doi:jc.2011-1004 [pii]
10.1210/jc.2011-1004

Debernardi, S., Skoulakis, S., Molloy, G., Chaplin, T., Dixon-McIver, A., & Young, B. D. (2007). MicroRNA miR-181a correlates with morphological sub-class of acute myeloid leukaemia and the expression of its target genes in global genome-wide analysis. *Leukemia, 21*(5), 912-916. doi:10.1038/sj.leu.2404605

Denis, F., Garaud, P., Bardet, E., Alfonsi, M., Sire, C., Germain, T., . . . Calais, G. (2004). Final results of the 94-01 French Head and Neck Oncology and Radiotherapy Group randomized trial comparing radiotherapy alone with concomitant radiochemotherapy in advanced-stage oropharynx carcinoma. *J Clin Oncol, 22*(1), 69-76. doi:10.1200/JCO.2004.08.021

Dettmer, M., Perren, A., Moch, H., Komminoth, P., Nikiforov, Y. E., & Nikiforova, M. N. (2013). Comprehensive MicroRNA expression profiling identifies novel markers in follicular variant of papillary thyroid carcinoma. *Thyroid, 23*(11), 1383-1389. doi:10.1089/thy.2012.0632

DeYoung, M. P., Horak, P., Sofer, A., Sgroi, D., & Ellisen, L. W. (2008). Hypoxia regulates TSC1/2-mTOR signaling and tumor suppression through REDD1-mediated 14-3-3 shuttling. *Genes Dev, 22*(2), 239-251. doi:10.1101/gad.1617608

Di Leva, G., Garofalo, M., & Croce, C. M. (2014). MicroRNAs in cancer. *Annu Rev Pathol, 9*, 287-314. doi:10.1146/annurev-pathol-012513-104715

Di Nicolantonio, F., Martini, M., Molinari, F., Sartore-Bianchi, A., Arena, S., Saletti, P., . . . Bardelli, A. (2008). Wild-type BRAF is required for response to panitumumab or cetuximab in metastatic colorectal cancer. *J Clin Oncol, 26*(35), 5705-5712. doi:10.1200/JCO.2008.18.0786

Dillhoff, M., Liu, J., Frankel, W., Croce, C., & Bloomston, M. (2008). MicroRNA-21 is overexpressed in pancreatic cancer and a potential predictor of survival. *J Gastrointest Surg, 12*(12), 2171-2176. doi:10.1007/s11605-008-0584-x

Dong, N., Tang, X., & Xu, B. (2015). miRNA-181a inhibits the proliferation, migration, and epithelial-mesenchymal transition of lens epithelial cells. *Invest Ophthalmol Vis Sci, 56*(2), 993-1001. doi:10.1167/iovs.14-15860

Donnem, T., Fenton, C. G., Lonvik, K., Berg, T., Eklo, K., Andersen, S., . . . Busund, L. T. (2012). MicroRNA signatures in tumor tissue related to angiogenesis in non-small cell lung cancer. *PLoS One, 7*(1), e29671. doi:10.1371/journal.pone.0029671
PONE-D-11-12313 [pii]

Dweep, H., Sticht, C., Pandey, P., & Gretz, N. (2011). miRWalk--database: prediction of possible miRNA binding sites by "walking" the genes of three genomes. *J Biomed Inform, 44*(5), 839-847. doi:10.1016/j.jbi.2011.05.002

Eden, A., Gaudet, F., Waghmare, A., & Jaenisch, R. (2003). Chromosomal instability and tumors promoted by DNA hypomethylation. *Science, 300*(5618), 455. doi:10.1126/science.1083557

Ellisen, L. W., Ramsayer, K. D., Johannessen, C. M., Yang, A., Beppu, H., Minda, K., . . . Haber, D. A. (2002). REDD1, a developmentally regulated transcriptional target of p63 and p53, links p63 to regulation of reactive oxygen species. *Mol Cell, 10*(5), 995-1005.

Engelmann, D., Meier, C., Alla, V., & Putzer, B. M. (2015). A balancing act: orchestrating amino-truncated and full-length p73 variants as decisive factors in cancer progression. *Oncogene, 34*(33), 4287-4299. doi:10.1038/onc.2014.365

Esquela-Kerscher, A., & Slack, F. J. (2006). Oncomirs - microRNAs with a role in cancer. *Nat Rev Cancer, 6*(4), 259-269. doi:nrc1840 [pii]
10.1038/nrc1840

Esteller, M., Corn, P. G., Baylin, S. B., & Herman, J. G. (2001). A gene hypermethylation profile of human cancer. *Cancer Res, 61*(8), 3225-3229.

Fassan, M., Baffa, R., Palazzo, J. P., Lloyd, J., Crosariol, M., Liu, C. G., . . . Rosenberg, A. (2009). MicroRNA expression profiling of male breast cancer. *Breast Cancer Res, 11*(4), R58. doi:10.1186/bcr2348

Fedorenko, I. V., Paraiso, K. H., & Smalley, K. S. (2011). Acquired and intrinsic BRAF inhibitor resistance in BRAF V600E mutant melanoma. *Biochem Pharmacol, 82*(3), 201-209. doi:10.1016/j.bcp.2011.05.015

Fei, J., Li, Y., Zhu, X., & Luo, X. (2012). miR-181a post-transcriptionally downregulates oncogenic RalA and contributes to growth inhibition and apoptosis in chronic myelogenous leukemia (CML). *PLoS One, 7*(3), e32834. doi:10.1371/journal.pone.0032834

Feng, L., Xie, Y., Zhang, H., & Wu, Y. (2012). miR-107 targets cyclin-dependent kinase 6 expression, induces cell cycle G1 arrest and inhibits invasion in gastric cancer cells. *Med Oncol, 29*(2), 856-863. doi:10.1007/s12032-011-9823-1

Ferlay, J., Shin, H. R., Bray, F., Forman, D., Mathers, C., & Parkin, D. M. (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer, 127*(12), 2893-2917. doi:10.1002/ijc.25516

Fitzgerald, A. L., Osman, A. A., Xie, T. X., Patel, A., Skinner, H., Sandulache, V., & Myers, J. N. (2015). Reactive oxygen species and p21Waf1/Cip1 are both essential for p53-mediated senescence of head and neck cancer cells. *Cell Death Dis, 6*, e1678. doi:10.1038/cddis.2015.44

Flavin, R. J., Smyth, P. C., Finn, S. P., Laios, A., O'Toole, S. A., Barrett, C., . . . O'Leary, J. J. (2008). Altered eIF6 and Dicer expression is associated with clinicopathological features in ovarian serous carcinoma patients. *Mod Pathol, 21*(6), 676-684. doi:modpathol200833 [pii]
10.1038/modpathol.2008.33

Fontemaggi, G., Dell'Orso, S., Muti, P., Blandino, G., & Strano, S. (2010). Id2 gene is a transcriptional target of the protein complex mutant p53/E2F1. *Cell Cycle, 9*(12), 2464-2466. doi:10.4161/cc.9.12.11915

Forastiere, A. A., Goepfert, H., Maor, M., Pajak, T. F., Weber, R., Morrison, W., . . . Cooper, J. (2003). Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *N Engl J Med, 349*(22), 2091-2098. doi:10.1056/NEJMoa031317

Fragoso, R., Mao, T., Wang, S., Schaffert, S., Gong, X., Yue, S., . . . Chen, C. Z. (2012). Modulating the strength and threshold of NOTCH oncogenic signals by mir-181a-1/b-1. *PLoS Genet, 8*(8), e1002855. doi:10.1371/journal.pgen.1002855

Friedenson, B. (2007). The BRCA1/2 pathway prevents hematologic cancers in addition to breast and ovarian cancers. *BMC Cancer, 7*, 152. doi:10.1186/1471-2407-7-152

Friedlander, M. R., Chen, W., Adamidi, C., Maaskola, J., Einspanier, R., Knespel, S., & Rajewsky, N. (2008). Discovering microRNAs from

deep sequencing data using miRDeep. *Nat Biotechnol, 26*(4), 407-415. doi:10.1038/nbt1394

Friedman, R. C., Farh, K. K., Burge, C. B., & Bartel, D. P. (2009). Most mammalian mRNAs are conserved targets of microRNAs. *Genome Res, 19*(1), 92-105. doi:10.1101/gr.082701.108

Fritz, A. G. (2000). *International classification of diseases for oncology : ICD-O* (3rd ed.). Geneva: World Health Organization.

Fu, X., Wen, H., Jing, L., Yang, Y., Wang, W., Liang, X., . . . Tian, T. (2017). MicroRNA-155-5p promotes hepatocellular carcinoma progression by suppressing PTEN through the PI3K/Akt pathway. *Cancer Sci, 108*(4), 620-631. doi:10.1111/cas.13177

Furniss, C. S., Marsit, C. J., Houseman, E. A., Eddy, K., & Kelsey, K. T. (2008). Line region hypomethylation is associated with lifestyle and differs by human papillomavirus status in head and neck squamous cell carcinomas. *Cancer Epidemiol Biomarkers Prev, 17*(4), 966-971. doi:10.1158/1055-9965.EPI-07-2775

Futreal, P. A., Coin, L., Marshall, M., Down, T., Hubbard, T., Wooster, R., . . . Stratton, M. R. (2004). A census of human cancer genes. *Nat Rev Cancer, 4*(3), 177-183. doi:10.1038/nrc1299

Gabriely, G., Wurdinger, T., Kesari, S., Esau, C. C., Burchard, J., Linsley, P. S., & Krichevsky, A. M. (2008). MicroRNA 21 promotes glioma invasion by targeting matrix metalloproteinase regulators. *Mol Cell Biol, 28*(17), 5369-5380. doi:10.1128/MCB.00479-08

Gallagher, S., & Wiley, E. A. (2008). *Current protocols : essential laboratory techniques*. Chichester: Wiley.

Gallardo, E., Navarro, A., Vinolas, N., Marrades, R. M., Diaz, T., Gel, B., . . . Monzo, M. (2009). miR-34a as a prognostic marker of relapse in surgically resected non-small-cell lung cancer. *Carcinogenesis, 30*(11), 1903-1909. doi:bgp219 [pii]
10.1093/carcin/bgp219

Ganci, F., Sacconi, A., Bossel Ben-Moshe, N., Manciocco, V., Sperduti, I., Strigari, L., . . . Blandino, G. (2013). Expression of TP53 mutation-associated microRNAs predicts clinical outcome in head and neck squamous cell carcinoma patients. *Ann Oncol, 24*(12), 3082-3088. doi:10.1093/annonc/mdt380

Gao, L., Gu, W., Zheng, J., Ren, W., Chang, S., Wang, X., . . . Zhi, K. (2013). Clinicopathological and prognostic significance of p27 expression in oral squamous cell carcinoma: a meta-analysis. *Int J Biol Markers, 28*(4), e329-335. doi:10.5301/jbm.5000035

Gao, W., Shen, H., Liu, L., Xu, J., Xu, J., & Shu, Y. (2011). MiR-21 overexpression in human primary squamous cell lung carcinoma is

associated with poor patient prognosis. *J Cancer Res Clin Oncol, 137*(4), 557-566. doi:10.1007/s00432-010-0918-4

Gao, W., Yu, Y., Cao, H., Shen, H., Li, X., Pan, S., & Shu, Y. (2010). Deregulated expression of miR-21, miR-143 and miR-181a in non small cell lung cancer is related to clinicopathologic characteristics or patient prognosis. *Biomed Pharmacother, 64*(6), 399-408. doi:10.1016/j.biopha.2010.01.018

Garcia, D. M., Baek, D., Shin, C., Bell, G. W., Grimson, A., & Bartel, D. P. (2011). Weak seed-pairing stability and high target-site abundance decrease the proficiency of lsy-6 and other microRNAs. *Nat Struct Mol Biol, 18*(10), 1139-1146. doi:10.1038/nsmb.2115

Garofalo, M., Di Leva, G., Romano, G., Nuovo, G., Suh, S. S., Ngankeu, A., . . . Croce, C. M. (2009). miR-221&222 regulate TRAIL resistance and enhance tumorigenicity through PTEN and TIMP3 downregulation. *Cancer Cell, 16*(6), 498-509. doi:S1535-6108(09)00383-3 [pii]
10.1016/j.ccr.2009.10.014

Geisler, S. A., & Olshan, A. F. (2001). GSTM1, GSTT1, and the risk of squamous cell carcinoma of the head and neck: a mini-HuGE review. *Am J Epidemiol, 154*(2), 95-105.

Gibson, L., Holmgreen, S. P., Huang, D. C., Bernard, O., Copeland, N. G., Jenkins, N. A., . . . Cory, S. (1996). bcl-w, a novel member of the bcl-2 family, promotes cell survival. *Oncogene, 13*(4), 665-675.

Giovino, G. A., Mirza, S. A., Samet, J. M., Gupta, P. C., Jarvis, M. J., Bhala, N., . . . Group, G. C. (2012). Tobacco use in 3 billion individuals from 16 countries: an analysis of nationally representative cross-sectional household surveys. *Lancet, 380*(9842), 668-679. doi:10.1016/S0140-6736(12)61085-X

Godsey, B. (2013). Discovery of miR-mRNA interactions via simultaneous Bayesian inference of gene networks and clusters using sequence-based predictions and expression data. *J Integr Bioinform, 10*(1), 227. doi:10.2390/biecoll-jib-2013-227

Golia, B., Singh, H. R., & Timinszky, G. (2015). Poly-ADP-ribosylation signaling during DNA damage repair. *Front Biosci (Landmark Ed), 20*, 440-457.

Gonzalez, R., De la Rosa, A. J., Rufini, A., Rodriguez-Hernandez, M. A., Navarro-Villaran, E., Marchal, T., . . . Muntane, J. (2017). Role of p63 and p73 isoforms on the cell death in patients with hepatocellular carcinoma submitted to orthotopic liver transplantation. *PLoS One, 12*(3), e0174326. doi:10.1371/journal.pone.0174326

Gorenchtein, M., Poh, C. F., Saini, R., & Garnis, C. (2012). MicroRNAs in an oral cancer context - from basic biology to clinical utility. *J Dent Res, 91*(5), 440-446. doi:0022034511431261 [pii]

10.1177/0022034511431261

Gorgoulis, V. G., Vassiliou, L. V., Karakaidos, P., Zacharatos, P., Kotsinas, A., Liloglou, T., . . . Halazonetis, T. D. (2005). Activation of the DNA damage checkpoint and genomic instability in human precancerous lesions. *Nature, 434*(7035), 907-913. doi:10.1038/nature03485

Goy, J., Hall, S. F., Feldman-Stewart, D., & Groome, P. A. (2009). Diagnostic delay and disease stage in head and neck cancer: a systematic review. *Laryngoscope, 119*(5), 889-898. doi:10.1002/lary.20185

Green, A. R., Barros, F. F., Abdel-Fatah, T. M., Moseley, P., Nolan, C. C., Durham, A. C., . . . Ellis, I. O. (2014). HER2/HER3 heterodimers and p21 expression are capable of predicting adjuvant trastuzumab response in HER2+ breast cancer. *Breast Cancer Res Treat, 145*(1), 33-44. doi:10.1007/s10549-014-2925-7

Green, A. R., Caracappa, D., Benhasouna, A. A., Alshareeda, A., Nolan, C. C., Macmillan, R. D., . . . Rakha, E. A. (2015). Biological and clinical significance of PARP1 protein expression in breast cancer. *Breast Cancer Res Treat, 149*(2), 353-362. doi:10.1007/s10549-014-3230-1

Grimson, A., Farh, K. K., Johnston, W. K., Garrett-Engele, P., Lim, L. P., & Bartel, D. P. (2007). MicroRNA targeting specificity in mammals: determinants beyond seed pairing. *Mol Cell, 27*(1), 91-105. doi:10.1016/j.molcel.2007.06.017

Guha, N., Boffetta, P., Wunsch Filho, V., Eluf Neto, J., Shangina, O., Zaridze, D., . . . Brennan, P. (2007). Oral health and risk of squamous cell carcinoma of the head and neck and esophagus: results of two multicentric case-control studies. *Am J Epidemiol, 166*(10), 1159-1173. doi:10.1093/aje/kwm193

Guo, J., Miao, Y., Xiao, B., Huan, R., Jiang, Z., Meng, D., & Wang, Y. (2009). Differential expression of microRNA species in human gastric cancer versus non-tumorous tissues. *J Gastroenterol Hepatol, 24*(4), 652-657. doi:JGH5666 [pii]
10.1111/j.1440-1746.2008.05666.x

Guo, L. M., Pu, Y., Han, Z., Liu, T., Li, Y. X., Liu, M., . . . Tang, H. (2009). MicroRNA-9 inhibits ovarian cancer cell growth through regulation of NF-kappaB1. *FEBS J, 276*(19), 5537-5546. doi:EJB7237 [pii]
10.1111/j.1742-4658.2009.07237.x

Guo, X., Liao, Q., Chen, P., Li, X., Xiong, W., Ma, J., . . . Li, G. (2012). The microRNA-processing enzymes: Drosha and Dicer can predict prognosis of nasopharyngeal carcinoma. *J Cancer Res Clin Oncol, 138*(1), 49-56. doi:10.1007/s00432-011-1058-1

Gupta, A., Bhatt, M. L., & Misra, M. K. (2010). Assessment of free radical-mediated damage in head and neck squamous cell carcinoma

patients and after treatment with radiotherapy. *Indian J Biochem Biophys, 47*(2), 96-99.

Gutschner, T., & Diederichs, S. (2012). The hallmarks of cancer: a long non-coding RNA point of view. *RNA Biol, 9*(6), 703-719. doi:10.4161/rna.20481

Hackenberg, M., Sturm, M., Langenberger, D., Falcon-Perez, J. M., & Aransay, A. M. (2009). miRanalyzer: a microRNA detection and analysis tool for next-generation sequencing experiments. *Nucleic Acids Res, 37*(Web Server issue), W68-76. doi:10.1093/nar/gkp347

Haidar, M. A., Kantarjian, H., Manshouri, T., Chang, C. Y., O'Brien, S., Freireich, E., . . . Albitar, M. (2000). ATM gene deletion in patients with adult acute lymphoblastic leukemia. *Cancer, 88*(5), 1057-1062.

Hallajian, Z., Mahjoubi, F., & Nafissi, N. (2017). Simultaneous ATM/BRCA1/RAD51 expression variations associated with prognostic factors in Iranian sporadic breast cancer patients. *Breast Cancer*. doi:10.1007/s12282-016-0750-z

Hammond, S. M. (2006). MicroRNA therapeutics: a new niche for antisense nucleic acids. *Trends Mol Med, 12*(3), 99-101. doi:10.1016/j.molmed.2006.01.004

Haram, K. M., Peltier, H. J., Lu, B., Bhasin, M., Otu, H. H., Choy, B., . . . Arredouani, M. S. (2008). Gene expression profile of mouse prostate tumors reveals dysregulations in major biological processes and identifies potential murine targets for preclinical development of human prostate cancer therapy. *Prostate, 68*(14), 1517-1530. doi:10.1002/pros.20803

Harris, T., Jimenez, L., Kawachi, N., Fan, J. B., Chen, J., Belbin, T., . . . Childs, G. (2012). Low-level expression of miR-375 correlates with poor outcome and metastasis while altering the invasive properties of head and neck squamous cell carcinomas. *Am J Pathol, 180*(3), 917-928. doi:S0002-9440(11)01094-7 [pii]
10.1016/j.ajpath.2011.12.004

Hartmann, A., Blaszyk, H., McGovern, R. M., Schroeder, J. J., Cunningham, J., De Vries, E. M., . . . Sommer, S. S. (1995). p53 gene mutations inside and outside of exons 5-8: the patterns differ in breast and other cancers. *Oncogene, 10*(4), 681-688.

Hashibe, M., Brennan, P., Benhamou, S., Castellsague, X., Chen, C., Curado, M. P., . . . Boffetta, P. (2007). Alcohol drinking in never users of tobacco, cigarette smoking in never drinkers, and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *J Natl Cancer Inst, 99*(10), 777-789. doi:10.1093/jnci/djk179

Hashibe, M., Brennan, P., Chuang, S. C., Boccia, S., Castellsague, X., Chen, C., . . . Boffetta, P. (2009). Interaction between tobacco and alcohol use and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *Cancer Epidemiol Biomarkers Prev, 18*(2), 541-550. doi:10.1158/1055-9965.EPI-08-0347

Havelange, V., Stauffer, N., Heaphy, C. C., Volinia, S., Andreeff, M., Marcucci, G., . . . Garzon, R. (2011). Functional implications of microRNAs in acute myeloid leukemia by integrating microRNA and messenger RNA expression profiling. *Cancer, 117*(20), 4696-4706. doi:10.1002/cncr.26096

He, M., Liu, Y., Deng, X., Qi, S., Sun, X., Liu, G., . . . Zhao, M. (2013). Down-regulation of miR-200b-3p by low p73 contributes to the androgen-independence of prostate cancer cells. *Prostate, 73*(10), 1048-1056. doi:10.1002/pros.22652

He, Q., Zhou, X., Li, S., Jin, Y., Chen, Z., Chen, D., . . . Wang, A. (2013). MicroRNA-181a suppresses salivary adenoid cystic carcinoma metastasis by targeting MAPK-Snai2 pathway. *Biochim Biophys Acta, 1830*(11), 5258-5266. doi:10.1016/j.bbagen.2013.07.028

He, S., Zeng, S., Zhou, Z. W., He, Z. X., & Zhou, S. F. (2015). Hsa-microRNA-181a is a regulator of a number of cancer genes and a biomarker for endometrial carcinoma in patients: a bioinformatic and clinical study and the therapeutic implication. *Drug Des Devel Ther, 9*, 1103-1175. doi:10.2147/DDDT.S73551

Heid, C. A., Stevens, J., Livak, K. J., & Williams, P. M. (1996). Real time quantitative PCR. *Genome Res, 6*(10), 986-994.

Hensel, J. A., Chanda, D., Kumar, S., Sawant, A., Grizzle, W. E., Siegal, G. P., & Ponnazhagan, S. (2011). LL-37 as a therapeutic target for late stage prostate cancer. *Prostate, 71*(6), 659-670. doi:10.1002/pros.21282

Hildebrandt, M. A., Gu, J., Lin, J., Ye, Y., Tan, W., Tamboli, P., . . . Wu, X. (2010). Hsa-miR-9 methylation status is associated with cancer development and metastatic recurrence in patients with clear cell renal cell carcinoma. *Oncogene, 29*(42), 5724-5728. doi:onc2010305 [pii]
10.1038/onc.2010.305

Hollis, M., Nair, K., Vyas, A., Chaturvedi, L. S., Gambhir, S., & Vyas, D. (2015). MicroRNAs potential utility in colon cancer: Early detection, prognosis, and chemosensitivity. *World J Gastroenterol, 21*(27), 8284-8292. doi:10.3748/wjg.v21.i27.8284

Hoofnagle, J. H., Doo, E., Liang, T. J., Fleischer, R., & Lok, A. S. (2007). Management of hepatitis B: summary of a clinical research workshop. *Hepatology, 45*(4), 1056-1075. doi:10.1002/hep.21627

Hsia, S. M., Yu, C. C., Shih, Y. H., Yuanchien Chen, M., Wang, T. H., Huang, Y. T., & Shieh, T. M. (2016). Isoliquiritigenin as a cause of DNA damage and inhibitor of ataxia-telangiectasia mutated expression leading to G2/M phase arrest and apoptosis in oral squamous cell carcinoma. *Head Neck, 38 Suppl 1*, E360-371. doi:10.1002/hed.24001

Hsu, P. Y., Deatherage, D. E., Rodriguez, B. A., Liyanarachchi, S., Weng, Y. I., Zuo, T., . . . Huang, T. H. (2009). Xenoestrogen-induced epigenetic repression of microRNA-9-3 in breast epithelial cells. *Cancer Res, 69*(14), 5936-5945. doi:0008-5472.CAN-08-4914 [pii]
10.1158/0008-5472.CAN-08-4914

Hu, H., Li, S., Cui, X., Lv, X., Jiao, Y., Yu, F., . . . Lin, L. (2013). The overexpression of hypomethylated miR-663 induces chemotherapy resistance in human breast cancer cells by targeting heparin sulfate proteoglycan 2 (HSPG2). *J Biol Chem, 288*(16), 10973-10985. doi:10.1074/jbc.M112.434340

Hu, X., Schwarz, J. K., Lewis, J. S., Jr., Huettner, P. C., Rader, J. S., Deasy, J. O., . . . Wang, X. (2010). A microRNA expression signature for cervical cancer prognosis. *Cancer Res, 70*(4), 1441-1448. doi:0008-5472.CAN-09-3289 [pii]
10.1158/0008-5472.CAN-09-3289

Huang, D. W., Sherman, B. T., Tan, Q., Collins, J. R., Alvord, W. G., Roayaei, J., . . . Lempicki, R. A. (2007). The DAVID Gene Functional Classification Tool: a novel biological module-centric algorithm to functionally analyze large gene lists. *Genome Biol, 8*(9), R183. doi:10.1186/gb-2007-8-9-r183

Huang, S., Wu, S., Ding, J., Lin, J., Wei, L., Gu, J., & He, X. (2010). MicroRNA-181a modulates gene expression of zinc finger family members by directly targeting their coding regions. *Nucleic Acids Res, 38*(20), 7211-7218. doi:10.1093/nar/gkq564

Huang, W., Li, J., Guo, X., Zhao, Y., & Yuan, X. (2016). miR-663a inhibits hepatocellular carcinoma cell proliferation and invasion by targeting HMGA2. *Biomed Pharmacother, 81*, 431-438. doi:10.1016/j.biopha.2016.04.034

Huang, X., Schwind, S., Santhanam, R., Eisfeld, A. K., Chiang, C. L., Lankenau, M., . . . Marcucci, G. (2016). Targeting the RAS/MAPK pathway with miR-181a in acute myeloid leukemia. *Oncotarget, 7*(37), 59273-59286. doi:10.18632/oncotarget.11150

Huang, Y., Chuang, A., Hao, H., Talbot, C., Sen, T., Trink, B., . . . Ratovitski, E. (2011). Phospho-DeltaNp63alpha is a key regulator of the cisplatin-induced microRNAome in cancer cells. *Cell Death Differ, 18*(7), 1220-1230. doi:10.1038/cdd.2010.188

Huang, Z., Huang, S., Wang, Q., Liang, L., Ni, S., Wang, L., . . . Du, X. (2011). MicroRNA-95 promotes cell proliferation and targets sorting Nexin 1 in human colorectal carcinoma. *Cancer Res, 71*(7), 2582-2589. doi:0008-5472.CAN-10-3032 [pii]
10.1158/0008-5472.CAN-10-3032

Hui, A. B., Bruce, J. P., Alajez, N. M., Shi, W., Yue, S., Perez-Ordonez, B., . . . Liu, F. F. (2011). Significance of dysregulated metadherin and microRNA-375 in head and neck cancer. *Clin Cancer Res, 17*(24), 7539-7550. doi:1078-0432.CCR-11-2102 [pii]
10.1158/1078-0432.CCR-11-2102

Hui, A. B., Lenarduzzi, M., Krushel, T., Waldron, L., Pintilie, M., Shi, W., . . . Liu, F. F. (2010). Comprehensive MicroRNA profiling for head and neck squamous cell carcinomas. *Clin Cancer Res, 16*(4), 1129-1139. doi:1078-0432.CCR-09-2166 [pii]
10.1158/1078-0432.CCR-09-2166

Hui, A. B., Shi, W., Boutros, P. C., Miller, N., Pintilie, M., Fyles, T., . . . Liu, F. F. (2009). Robust global micro-RNA profiling with formalin-fixed paraffin-embedded breast cancer tissues. *Lab Invest, 89*(5), 597-606. doi:10.1038/labinvest.2009.12

Humphreys, D. T., Westman, B. J., Martin, D. I., & Preiss, T. (2005). MicroRNAs control translation initiation by inhibiting eukaryotic initiation factor 4E/cap and poly(A) tail function. *Proc Natl Acad Sci U S A, 102*(47), 16961-16966. doi:10.1073/pnas.0506482102

Hwang-Verslues, W. W., Chang, P. H., Wei, P. C., Yang, C. Y., Huang, C. K., Kuo, W. H., . . . Lee, W. H. (2011). miR-495 is upregulated by E12/E47 in breast cancer stem cells, and promotes oncogenesis and hypoxia resistance via downregulation of E-cadherin and REDD1. *Oncogene, 30*(21), 2463-2474. doi:10.1038/onc.2010.618

Ibrahim, Y. H., Garcia-Garcia, C., Serra, V., He, L., Torres-Lockhart, K., Prat, A., . . . Baselga, J. (2012). PI3K inhibition impairs BRCA1/2 expression and sensitizes BRCA-proficient triple-negative breast cancer to PARP inhibition. *Cancer Discov, 2*(11), 1036-1047. doi:10.1158/2159-8290.CD-11-0348

Jackson, R. J., & Standart, N. (2007). How do microRNAs regulate gene expression? *Sci STKE, 2007*(367), re1. doi:10.1126/stke.3672007re1

Jakymiw, A., Patel, R. S., Deming, N., Bhattacharyya, I., Shah, P., Lamont, R. J., . . . Chan, E. K. (2010). Overexpression of dicer as a result of reduced let-7 MicroRNA levels contributes to increased cell proliferation of oral cancer cells. *Genes Chromosomes Cancer, 49*(6), 549-559. doi:10.1002/gcc.20765

Jazdzewski, K., Boguslawska, J., Jendrzejewski, J., Liyanarachchi, S., Pachucki, J., Wardyn, K. A., . . . de la Chapelle, A. (2011). Thyroid

hormone receptor beta (THRB) is a major target gene for microRNAs deregulated in papillary thyroid carcinoma (PTC). *J Clin Endocrinol Metab, 96*(3), E546-553. doi:10.1210/jc.2010-1594

Jemal, A., Siegel, R., Ward, E., Hao, Y., Xu, J., & Thun, M. J. (2009). Cancer statistics, 2009. *CA Cancer J Clin, 59*(4), 225-249. doi:10.3322/caac.20006

Jemal, A., Siegel, R., Xu, J., & Ward, E. (2010). Cancer statistics, 2010. *CA Cancer J Clin, 60*(5), 277-300. doi:10.3322/caac.20073

Ji, D., Chen, Z., Li, M., Zhan, T., Yao, Y., Zhang, Z., . . . Gu, J. (2014). MicroRNA-181a promotes tumor growth and liver metastasis in colorectal cancer by targeting the tumor suppressor WIF-1. *Mol Cancer, 13*, 86. doi:10.1186/1476-4598-13-86

Ji, J., Yamashita, T., Budhu, A., Forgues, M., Jia, H. L., Li, C., . . . Wang, X. W. (2009). Identification of microRNA-181 by genome-wide screening as a critical player in EpCAM-positive hepatic cancer stem cells. *Hepatology, 50*(2), 472-480. doi:10.1002/hep.22989

Jia, W., Chang, B., Sun, L., Zhu, H., Pang, L., Tao, L., . . . Zhao, X. (2014). REDD1 and p-AKT over-expression may predict poor prognosis in ovarian cancer. *Int J Clin Exp Pathol, 7*(9), 5940-5949.

Jiang, C., Fang, X., Zhang, H., Wang, X., Li, M., Jiang, W., . . . Bian, Z. (2017). Triptolide inhibits the growth of osteosarcoma by regulating microRNA-181a via targeting PTEN gene in vivo and vitro. *Tumour Biol, 39*(4), 1010428317697556. doi:10.1177/1010428317697556

Jianwei, Z., Fan, L., Xiancheng, L., Enzhong, B., Shuai, L., & Can, L. (2013). MicroRNA 181a improves proliferation and invasion, suppresses apoptosis of osteosarcoma cell. *Tumour Biol, 34*(6), 3331-3337. doi:10.1007/s13277-013-0902-0

Jiao, L., Deng, Z., Xu, C., Yu, Y., Li, Y., Yang, C., . . . Sun, Y. (2014). miR-663 induces castration-resistant prostate cancer transformation and predicts clinical recurrence. *J Cell Physiol, 229*(7), 834-844. doi:10.1002/jcp.24510

Jiao, L. R., Frampton, A. E., Jacob, J., Pellegrino, L., Krell, J., Giamas, G., . . . Castellano, L. (2012). MicroRNAs targeting oncogenes are down-regulated in pancreatic malignant transformation from benign tumors. *PLoS One, 7*(2), e32068. doi:10.1371/journal.pone.0032068
PONE-D-11-09708 [pii]

Jiao, X., Zhao, L., Ma, M., Bai, X., He, M., Yan, Y., . . . Wei, M. (2013). MiR-181a enhances drug sensitivity in mitoxantone-resistant breast cancer cells by targeting breast cancer resistance protein (BCRP/ABCG2). *Breast Cancer Res Treat, 139*(3), 717-730. doi:10.1007/s10549-013-2607-x

Jin, H. O., Seo, S. K., Woo, S. H., Kim, E. S., Lee, H. C., Yoo, D. H., . . . Park, I. C. (2009). Activating transcription factor 4 and CCAAT/enhancer-binding protein-beta negatively regulate the mammalian target of rapamycin via Redd1 expression in response to oxidative and endoplasmic reticulum stress. *Free Radic Biol Med, 46*(8), 1158-1167. doi:10.1016/j.freeradbiomed.2009.01.015

Jin, H. O., Seo, S. K., Woo, S. H., Kim, Y. S., Hong, S. E., Yi, J. Y., . . . Park, I. C. (2011). Redd1 inhibits the invasiveness of non-small cell lung cancer cells. *Biochem Biophys Res Commun, 407*(3), 507-511. doi:10.1016/j.bbrc.2011.03.047

Jin, L., Hu, W. L., Jiang, C. C., Wang, J. X., Han, C. C., Chu, P., . . . Wu, M. (2011). MicroRNA-149*, a p53-responsive microRNA, functions as an oncogenic regulator in human melanoma. *Proc Natl Acad Sci U S A, 108*(38), 15840-15845. doi:1019312108 [pii]
10.1073/pnas.1019312108

Johnson, C. D., Esquela-Kerscher, A., Stefani, G., Byrom, M., Kelnar, K., Ovcharenko, D., . . . Slack, F. J. (2007). The let-7 microRNA represses cell proliferation pathways in human cells. *Cancer Res, 67*(16), 7713-7722. doi:10.1158/0008-5472.CAN-07-1083

Johnson, N. (2001). Tobacco use and oral cancer: a global perspective. *J Dent Educ, 65*(4), 328-339.

Josson, S., Sung, S. Y., Lao, K., Chung, L. W., & Johnstone, P. A. (2008). Radiation modulation of microRNA in prostate cancer cell lines. *Prostate, 68*(15), 1599-1606. doi:10.1002/pros.20827

Kaczkowski, B., Morevati, M., Rossing, M., Cilius, F., & Norrild, B. (2012). A Decade of Global mRNA and miRNA Profiling of HPV-Positive Cell Lines and Clinical Specimens. *Open Virol J, 6*, 216-231. doi:10.2174/1874357901206010216

Kaelin, W. G., Jr. (1999). The p53 gene family. *Oncogene, 18*(53), 7701-7705. doi:10.1038/sj.onc.1202955

Kano, M., Seki, N., Kikkawa, N., Fujimura, L., Hoshino, I., Akutsu, Y., . . . Matsubara, H. (2010). miR-145, miR-133a and miR-133b: Tumor-suppressive miRNAs target FSCN1 in esophageal squamous cell carcinoma. *Int J Cancer, 127*(12), 2804-2814. doi:10.1002/ijc.25284

Kastan, M. B., & Lim, D. S. (2000). The many substrates and functions of ATM. *Nat Rev Mol Cell Biol, 1*(3), 179-186. doi:10.1038/35043058

Kastrati, I., Canestrari, E., & Frasor, J. (2015). PHLDA1 expression is controlled by an estrogen receptor-NFkappaB-miR-181 regulatory loop and is essential for formation of ER+ mammospheres. *Oncogene, 34*(18), 2309-2316. doi:10.1038/onc.2014.180

Kawasaki, T., Yokoi, S., Tsuda, H., Izumi, H., Kozaki, K., Aida, S., . . . Inazawa, J. (2007). BCL2L2 is a probable target for novel 14q11.2 amplification detected in a non-small cell lung cancer cell line. *Cancer Sci, 98*(7), 1070-1077. doi:10.1111/j.1349-7006.2007.00491.x

Kazenwadel, J., Michael, M. Z., & Harvey, N. L. (2010). Prox1 expression is negatively regulated by miR-181 in endothelial cells. *Blood, 116*(13), 2395-2401. doi:10.1182/blood-2009-12-256297

Ke, G., Liang, L., Yang, J. M., Huang, X., Han, D., Huang, S., . . . Wu, X. (2013). MiR-181a confers resistance of cervical cancer to radiation therapy through targeting the pro-apoptotic PRKCD gene. *Oncogene, 32*(25), 3019-3027. doi:10.1038/onc.2012.323

Khan, H. A., Zhao, Y., Wang, L., Li, Q., Du, Y. A., Dan, Y., & Huo, L. J. (2015). Identification of miRNAs during mouse postnatal ovarian development and superovulation. *J Ovarian Res, 8*, 44. doi:10.1186/s13048-015-0170-2

Kikkawa, N., Hanazawa, T., Fujimura, L., Nohata, N., Suzuki, H., Chazono, H., . . . Seki, N. (2010). miR-489 is a tumour-suppressive miRNA target PTPN11 in hypopharyngeal squamous cell carcinoma (HSCC). *Br J Cancer, 103*(6), 877-884. doi:6605811 [pii]
10.1038/sj.bjc.6605811

Kim, J. S., Park, M. G., Lee, S. A., Park, S. Y., Kim, H. J., Yu, S. K., . . . Kim, D. K. (2014). Downregulation of adenomatous polyposis coli by microRNA-663 promotes odontogenic differentiation through activation of Wnt/beta-catenin signaling. *Biochem Biophys Res Commun, 446*(4), 894-900. doi:10.1016/j.bbrc.2014.03.027

Kim, M. S., Lee, J., & Sidransky, D. (2010). DNA methylation markers in colorectal cancer. *Cancer Metastasis Rev, 29*(1), 181-206. doi:10.1007/s10555-010-9207-6

Kinoshita, T., Hanazawa, T., Nohata, N., Kikkawa, N., Enokida, H., Yoshino, H., . . . Seki, N. (2012). Tumor suppressive microRNA-218 inhibits cancer cell migration and invasion through targeting laminin-332 in head and neck squamous cell carcinoma. *Oncotarget, 3*(11), 1386-1400. doi:709 [pii]

Kinoshita, T., Nohata, N., Fuse, M., Hanazawa, T., Kikkawa, N., Fujimura, L., . . . Seki, N. (2012). Tumor suppressive microRNA-133a regulates novel targets: moesin contributes to cancer cell proliferation and invasion in head and neck squamous cell carcinoma. *Biochem Biophys Res Commun, 418*(2), 378-383. doi:S0006-291X(12)00053-8 [pii]
10.1016/j.bbrc.2012.01.030

Kinoshita, T., Nohata, N., Watanabe-Takano, H., Yoshino, H., Hidaka, H., Fujimura, L., . . . Seki, N. (2012). Actin-related protein 2/3 complex

subunit 5 (ARPC5) contributes to cell migration and invasion and is directly regulated by tumor-suppressive microRNA-133a in head and neck squamous cell carcinoma. *Int J Oncol, 40*(6), 1770-1778. doi:10.3892/ijo.2012.1390

Kloosterman, W. P., Wienholds, E., de Bruijn, E., Kauppinen, S., & Plasterk, R. H. (2006). In situ detection of miRNAs in animal embryos using LNA-modified oligonucleotide probes. *Nat Methods, 3*(1), 27-29. doi:10.1038/nmeth843

Kloosterman, W. P., Wienholds, E., Ketting, R. F., & Plasterk, R. H. (2004). Substrate requirements for let-7 function in the developing zebrafish embryo. *Nucleic Acids Res, 32*(21), 6284-6291. doi:10.1093/nar/gkh968

Kojima, S., Chiyomaru, T., Kawakami, K., Yoshino, H., Enokida, H., Nohata, N., . . . Seki, N. (2012). Tumour suppressors miR-1 and miR-133a target the oncogenic function of purine nucleoside phosphorylase (PNP) in prostate cancer. *Br J Cancer, 106*(2), 405-413. doi:bjc2011462 [pii]
10.1038/bjc.2011.462

Kong, L. Y., Xue, M., Zhang, Q. C., & Su, C. F. (2017). In vivo and in vitro effects of microRNA-27a on proliferation, migration and invasion of breast cancer cells through targeting of SFRP1 gene via Wnt/beta-catenin signaling pathway. *Oncotarget, 8*(9), 15507-15519. doi:10.18632/oncotarget.14662

Koo, J. S., & Jung, W. (2010). Alteration of REDD1-mediated mammalian target of rapamycin pathway and hypoxia-inducible factor-1alpha regulation in human breast cancer. *Pathobiology, 77*(6), 289-300. doi:10.1159/000320936

Koonin, E. V. (2000). How many genes can make a cell: the minimal-gene-set concept. *Annu Rev Genomics Hum Genet, 1*, 99-116. doi:10.1146/annurev.genom.1.1.99

Korhan, P., Erdal, E., & Atabey, N. (2014). MiR-181a-5p is downregulated in hepatocellular carcinoma and suppresses motility, invasion and branching-morphogenesis by directly targeting c-Met. *Biochem Biophys Res Commun, 450*(4), 1304-1312. doi:10.1016/j.bbrc.2014.06.142

Koscianska, E., & Krzyzosiak, W. J. (2014). Current understanding of the role of microRNAs in spinocerebellar ataxias. *Cerebellum Ataxias, 1*, 7. doi:10.1186/2053-8871-1-7

Kowarsch, A., Preusse, M., Marr, C., & Theis, F. J. (2011). miTALOS: analyzing the tissue-specific regulation of signaling pathways by human and mouse microRNAs. *RNA, 17*(5), 809-819. doi:10.1261/rna.2474511

Kozaki, K., Imoto, I., Mogi, S., Omura, K., & Inazawa, J. (2008). Exploration of tumor-suppressive microRNAs silenced by DNA hypermethylation in oral cancer. *Cancer Res, 68*(7), 2094-2105. doi:10.1158/0008-5472.CAN-07-5194

Krek, A., Grun, D., Poy, M. N., Wolf, R., Rosenberg, L., Epstein, E. J., . . . Rajewsky, N. (2005). Combinatorial microRNA target predictions. *Nat Genet, 37*(5), 495-500. doi:10.1038/ng1536

Kumar, B., Yadav, A., Lang, J., Teknos, T. N., & Kumar, P. (2012). Dysregulation of microRNA-34a expression in head and neck squamous cell carcinoma promotes tumor growth and tumor angiogenesis. *PLoS One, 7*(5), e37601. doi:10.1371/journal.pone.0037601

Kumar, S., Mohan, A., & Guleria, R. (2006). Biomarkers in cancer screening, research and detection: present and future: a review. *Biomarkers, 11*(5), 385-405. doi:10.1080/13547500600775011

Kuroda, K., Fukuda, T., Krstic-Demonacos, M., Demonacos, C., Okumura, K., Isogai, H., . . . Isogai, E. (2017). miR-663a regulates growth of colon cancer cells, after administration of antimicrobial peptides, by targeting CXCR4-p21 pathway. *BMC Cancer, 17*(1), 33. doi:10.1186/s12885-016-3003-9

Kutter, C., & Svoboda, P. (2008). miRNA, siRNA, piRNA: Knowns of the unknown. *RNA Biol, 5*(4), 181-188.

Lane, D. P., & Lain, S. (2002). Therapeutic exploitation of the p53 pathway. *Trends Mol Med, 8*(4 Suppl), S38-42.

Langevin, S. M., Stone, R. A., Bunker, C. H., Grandis, J. R., Sobol, R. W., & Taioli, E. (2010). MicroRNA-137 promoter methylation in oral rinses from patients with squamous cell carcinoma of the head and neck is associated with gender and body mass index. *Carcinogenesis, 31*(5), 864-870. doi:bgq051 [pii]
10.1093/carcin/bgq051

Langevin, S. M., Stone, R. A., Bunker, C. H., Lyons-Weiler, M. A., LaFramboise, W. A., Kelly, L., . . . Taioli, E. (2011). MicroRNA-137 promoter methylation is associated with poorer overall survival in patients with squamous cell carcinoma of the head and neck. *Cancer, 117*(7), 1454-1462. doi:10.1002/cncr.25689

Lao, K., Xu, N. L., Yeung, V., Chen, C., Livak, K. J., & Straus, N. A. (2006). Multiplexing RT-PCR for the detection of multiple miRNA species in small samples. *Biochem Biophys Res Commun, 343*(1), 85-89. doi:10.1016/j.bbrc.2006.02.106

Latonen, L., & Laiho, M. (2005). Cellular UV damage responses--functions of tumor suppressor p53. *Biochim Biophys Acta, 1755*(2), 71-89. doi:10.1016/j.bbcan.2005.04.003

Lawrie, C. H., Gal, S., Dunlop, H. M., Pushkaran, B., Liggins, A. P., Pulford, K., . . . Harris, A. L. (2008). Detection of elevated levels of tumour-associated microRNAs in serum of patients with diffuse large B-cell lymphoma. *Br J Haematol, 141*(5), 672-675. doi:10.1111/j.1365-2141.2008.07077.x

Lee, B., Lee, H. J., Cho, H. Y., Suh, D. H., Kim, K., No, J. H., . . . Kim, Y. B. (2015). Ataxia-Telangiectasia and RAD3-Related and Ataxia-Telangiectasia-Mutated Proteins in Epithelial Ovarian Carcinoma: Their Expression and Clinical Significance. *Anticancer Res, 35*(7), 3909-3916.

Lee, R. C., Feinbaum, R. L., & Ambros, V. (1993). The C. elegans heterochronic gene lin-4 encodes small RNAs with antisense complementarity to lin-14. *Cell, 75*(5), 843-854.

Lee, Y., Ahn, C., Han, J., Choi, H., Kim, J., Yim, J., . . . Kim, V. N. (2003). The nuclear RNase III Drosha initiates microRNA processing. *Nature, 425*(6956), 415-419. doi:10.1038/nature01957
nature01957 [pii]

Leemans, C. R., Braakhuis, B. J., & Brakenhoff, R. H. (2011). The molecular biology of head and neck cancer. *Nat Rev Cancer, 11*(1), 9-22. doi:10.1038/nrc2982

Leong, C. O., Vidnovic, N., DeYoung, M. P., Sgroi, D., & Ellisen, L. W. (2007). The p63/p73 network mediates chemosensitivity to cisplatin in a biologically defined subset of primary breast cancers. *J Clin Invest, 117*(5), 1370-1380. doi:10.1172/JCI30866

Levine, B., & Abrams, J. (2008). p53: The Janus of autophagy? *Nat Cell Biol, 10*(6), 637-639. doi:10.1038/ncb0608-637

Levine, B., Sinha, S. C., & Kroemer, G. (2008). Bcl-2 family members: Dual regulators of apoptosis and autophagy. *Autophagy, 4*(5), 600-606. doi:10.4161/auto.6260

Lewis, B. P., Burge, C. B., & Bartel, D. P. (2005). Conserved seed pairing, often flanked by adenosines, indicates that thousands of human genes are microRNA targets. *Cell, 120*(1), 15-20. doi:10.1016/j.cell.2004.12.035

Lewis, F., Maughan, N. J., Smith, V., Hillan, K., & Quirke, P. (2001). Unlocking the archive--gene expression in paraffin-embedded tissue. *J Pathol, 195*(1), 66-71. doi:10.1002/1096-9896(200109)195:1<66::AID-PATH921>3.0.CO;2-F

Li, C., Lyu, J., & Meng, Q. H. (2017). MiR-93 Promotes Tumorigenesis and Metastasis of Non-Small Cell Lung Cancer Cells by Activating the PI3K/Akt Pathway via Inhibition of LKB1/PTEN/CDKN1A. *J Cancer, 8*(5), 870-879. doi:10.7150/jca.17958

Li, D., Chen, P., Li, X. Y., Zhang, L. Y., Xiong, W., Zhou, M., . . . Li, G. Y. (2011). Grade-specific expression profiles of miRNAs/mRNAs and docking study in human grade I-III astrocytomas. *OMICS, 15*(10), 673-682. doi:10.1089/omi.2011.0064

Li, G., Yu, M., Lee, W. W., Tsang, M., Krishnan, E., Weyand, C. M., & Goronzy, J. J. (2012). Decline in miR-181a expression with age impairs T cell receptor sensitivity by increasing DUSP6 activity. *Nat Med, 18*(10), 1518-1524. doi:10.1038/nm.2963

Li, G. Y., Zhou, Y., Ying, R. S., Shi, L., Cheng, Y. Q., Ren, J. P., . . . Yao, Z. Q. (2015). Hepatitis C virus-induced reduction in miR-181a impairs CD4(+) T-cell responses through overexpression of DUSP6. *Hepatology, 61*(4), 1163-1173. doi:10.1002/hep.27634

Li, H., Hui, L., & Xu, W. (2012). miR-181a sensitizes a multidrug-resistant leukemia cell line K562/A02 to daunorubicin by targeting BCL-2. *Acta Biochim Biophys Sin (Shanghai), 44*(3), 269-277. doi:10.1093/abbs/gmr128

Li, J., Smyth, P., Flavin, R., Cahill, S., Denning, K., Aherne, S., . . . Sheils, O. (2007). Comparison of miRNA expression patterns using total RNA extracted from matched samples of formalin-fixed paraffin-embedded (FFPE) cells and snap frozen cells. *BMC Biotechnol, 7*, 36. doi:10.1186/1472-6750-7-36

Li, J. H., Liu, S., Zhou, H., Qu, L. H., & Yang, J. H. (2014). starBase v2.0: decoding miRNA-ceRNA, miRNA-ncRNA and protein-RNA interaction networks from large-scale CLIP-Seq data. *Nucleic Acids Res, 42*(Database issue), D92-97. doi:10.1093/nar/gkt1248

Li, L., Xu, Q. H., Dong, Y. H., Li, G. X., Yang, L., Wang, L. W., & Li, H. Y. (2016). MiR-181a upregulation is associated with epithelial-to-mesenchymal transition (EMT) and multidrug resistance (MDR) of ovarian cancer cells. *Eur Rev Med Pharmacol Sci, 20*(10), 2004-2010.

Li, N., Fu, H., Tie, Y., Hu, Z., Kong, W., Wu, Y., & Zheng, X. (2009). miR-34a inhibits migration and invasion by down-regulation of c-Met expression in human hepatocellular carcinoma cells. *Cancer Lett, 275*(1), 44-53. doi:S0304-3835(08)00804-5 [pii]
10.1016/j.canlet.2008.09.035

Li, P., Zhu, N., Yi, B., Wang, N., Chen, M., You, X., . . . Sun, J. (2013). MicroRNA-663 regulates human vascular smooth muscle cell phenotypic switch and vascular neointimal formation. *Circ Res, 113*(10), 1117-1127. doi:10.1161/CIRCRESAHA.113.301306

Li, S., Wang, C., Yu, X., Wu, H., Hu, J., Wang, S., & Ye, Z. (2017). miR-3619-5p inhibits prostate cancer cell growth by activating CDKN1A expression. *Oncol Rep, 37*(1), 241-248. doi:10.3892/or.2016.5250

Li, S., Wu, L., & Zhang, Z. (2006). Constructing biological networks through combined literature mining and microarray analysis: a LMMA approach. *Bioinformatics, 22*(17), 2143-2150. doi:10.1093/bioinformatics/btl363

Li, W. G., Yuan, Y. Z., Qiao, M. M., & Zhang, Y. P. (2012). High dose glargine alters the expression profiles of microRNAs in pancreatic cancer cells. *World J Gastroenterol, 18*(21), 2630-2639. doi:10.3748/wjg.v18.i21.2630

Li, Y., Liang, C., Ma, H., Zhao, Q., Lu, Y., Xiang, Z., . . . Yu, Z. (2014). miR-221/222 promotes S-phase entry and cellular migration in control of basal-like breast cancer. *Molecules, 19*(6), 7122-7137. doi:10.3390/molecules19067122

Li, Y., Yan, L., Zhang, W., Wang, H., Chen, W., Hu, N., & Ou, H. (2014). miR-21 inhibitor suppresses proliferation and migration of nasopharyngeal carcinoma cells through down-regulation of BCL2 expression. *Int J Clin Exp Pathol, 7*(6), 3478-3487.

Li, Z., Huang, H., Li, Y., Jiang, X., Chen, P., Arnovitz, S., . . . Chen, J. (2012). Up-regulation of a HOXA-PBX3 homeobox-gene signature following down-regulation of miR-181 is associated with adverse prognosis in patients with cytogenetically abnormal AML. *Blood, 119*(10), 2314-2324. doi:10.1182/blood-2011-10-386235

Li, Z., Wang, H., Xu, Z., Sun, Y., & Han, J. (2016). Expression and mechanism of microRNA-181A on incidence and survival in late liver metastases of colorectal cancer. *Oncol Rep, 35*(3), 1403-1408. doi:10.3892/or.2016.4546

Lian, R., Lu, B., Jiao, L., Li, S., Wang, H., Miao, W., & Yu, W. (2016). MiR-132 plays an oncogenic role in laryngeal squamous cell carcinoma by targeting FOXO1 and activating the PI3K/AKT pathway. *Eur J Pharmacol, 792*, 1-6. doi:10.1016/j.ejphar.2016.10.015

Liang, S., Zhang, N., Deng, Y., Chen, L., Zhang, Y., Zheng, Z., . . . Xun, T. (2016). Increased Serum Level of MicroRNA-663 Is Correlated with Poor Prognosis of Patients with Nasopharyngeal Carcinoma. *Dis Markers, 2016*, 7648215. doi:10.1155/2016/7648215

Liao, Y., Shen, L., Zhao, H., Liu, Q., Fu, J., Guo, Y., . . . Cheng, L. (2017). LncRNA CASC2 Interacts With miR-181a to Modulate Glioma Growth and Resistance to TMZ Through PTEN Pathway. *J Cell Biochem, 118*(7), 1889-1899. doi:10.1002/jcb.25910

Licitra, L., Perrone, F., Bossi, P., Suardi, S., Mariani, L., Artusi, R., . . . Pilotti, S. (2006). High-risk human papillomavirus affects prognosis in patients with surgically treated oropharyngeal squamous cell carcinoma. *J Clin Oncol, 24*(36), 5630-5636. doi:10.1200/JCO.2005.04.6136

Lin, F., Li, Y., Yan, S., Liu, S., Qian, W., Shen, D., . . . Mao, W. (2015). MicroRNA-181a inhibits tumor proliferation, invasiveness, and metastasis and is downregulated in gastric cancer. *Oncol Res, 22*(2), 75-84. doi:10.3727/096504014X14024160459203

Lin, M. S., Chen, W. C., Huang, J. X., Gao, H. J., & Sheng, H. H. (2014). Aberrant expression of microRNAs in serum may identify individuals with pancreatic cancer. *Int J Clin Exp Med, 7*(12), 5226-5234.

Lin, Y., Nie, Y., Zhao, J., Chen, X., Ye, M., Li, Y., . . . Li, Y. (2012). Genetic polymorphism at miR-181a binding site contributes to gastric cancer susceptibility. *Carcinogenesis, 33*(12), 2377-2383. doi:10.1093/carcin/bgs292

Ling, H., Fabbri, M., & Calin, G. A. (2013). MicroRNAs and other non-coding RNAs as targets for anticancer drug development. *Nat Rev Drug Discov, 12*(11), 847-865. doi:10.1038/nrd4140

Liu, A., Tetzlaff, M. T., Vanbelle, P., Elder, D., Feldman, M., Tobias, J. W., . . . Xu, X. (2009). MicroRNA expression profiling outperforms mRNA expression profiling in formalin-fixed paraffin-embedded tissues. *Int J Clin Exp Pathol, 2*(6), 519-527.

Liu, C., Kelnar, K., Liu, B., Chen, X., Calhoun-Davis, T., Li, H., . . . Tang, D. G. (2011). The microRNA miR-34a inhibits prostate cancer stem cells and metastasis by directly repressing CD44. *Nat Med, 17*(2), 211-215. doi:nm.2284 [pii]
10.1038/nm.2284

Liu, C. J., Tsai, M. M., Hung, P. S., Kao, S. Y., Liu, T. Y., Wu, K. J., . . . Chang, K. W. (2010). miR-31 ablates expression of the HIF regulatory factor FIH to activate the HIF pathway in head and neck carcinoma. *Cancer Res, 70*(4), 1635-1644. doi:0008-5472.CAN-09-2291 [pii]
10.1158/0008-5472.CAN-09-2291

Liu, J., Valencia-Sanchez, M. A., Hannon, G. J., & Parker, R. (2005). MicroRNA-dependent localization of targeted mRNAs to mammalian P-bodies. *Nat Cell Biol, 7*(7), 719-723. doi:10.1038/ncb1274

Liu, J., Xu, D., Wang, Q., Zheng, D., Jiang, X., & Xu, L. (2014). LPS induced miR-181a promotes pancreatic cancer cell migration via targeting PTEN and MAP2K4. *Dig Dis Sci, 59*(7), 1452-1460. doi:10.1007/s10620-014-3049-y

Liu, L., Wang, Y., Fan, H., Zhao, X., Liu, D., Hu, Y., . . . Hou, Y. (2012). MicroRNA-181a regulates local immune balance by inhibiting proliferation and immunosuppressive properties of mesenchymal stem cells. *Stem Cells, 30*(8), 1756-1770. doi:10.1002/stem.1156

Liu, M., Wang, J., Huang, H., Hou, J., Zhang, B., & Wang, A. (2013). miR-181a-Twist1 pathway in the chemoresistance of tongue squamous cell

carcinoma. *Biochem Biophys Res Commun, 441*(2), 364-370. doi:10.1016/j.bbrc.2013.10.051

Liu, M., Zhang, X., Hu, C. F., Xu, Q., Zhu, H. X., & Xu, N. Z. (2014). MicroRNA-mRNA functional pairs for cisplatin resistance in ovarian cancer cells. *Chin J Cancer, 33*(6), 285-294. doi:10.5732/cjc.013.10136

Liu, S., Gao, G., Yan, D., Chen, X., Yao, X., Guo, S., . . . Zhao, Y. (2017). Effects of miR-145-5p through NRAS on the cell proliferation, apoptosis, migration, and invasion in melanoma by inhibiting MAPK and PI3K/AKT pathways. *Cancer Med, 6*(4), 819-833. doi:10.1002/cam4.1030

Liu, W. H., Yeh, S. H., Lu, C. C., Yu, S. L., Chen, H. Y., Lin, C. Y., . . . Chen, P. J. (2009). MicroRNA-18a prevents estrogen receptor-alpha expression, promoting proliferation of hepatocellular carcinoma cells. *Gastroenterology, 136*(2), 683-693. doi:S0016-5085(08)01864-7 [pii]
10.1053/j.gastro.2008.10.029

Liu, X., Liao, W., Peng, H., Luo, X., Luo, Z., Jiang, H., & Xu, L. (2016). miR-181a promotes G1/S transition and cell proliferation in pediatric acute myeloid leukemia by targeting ATM. *J Cancer Res Clin Oncol, 142*(1), 77-87. doi:10.1007/s00432-015-1995-1

Liu, Y., Zhao, Z., Yang, F., Gao, Y., Song, J., & Wan, Y. (2013). microRNA-181a is involved in insulin-like growth factor-1-mediated regulation of the transcription factor CREB1. *J Neurochem, 126*(6), 771-780. doi:10.1111/jnc.12370

Liu, Z., Li, G., Wei, S., Niu, J., El-Naggar, A. K., Sturgis, E. M., & Wei, Q. (2010). Genetic variants in selected pre-microRNA genes and the risk of squamous cell carcinoma of the head and neck. *Cancer, 116*(20), 4753-4760. doi:10.1002/cncr.25323

Liu, Z. L., Wang, H., Liu, J., & Wang, Z. X. (2013). MicroRNA-21 (miR-21) expression promotes growth, metastasis, and chemo- or radioresistance in non-small cell lung cancer cells by targeting PTEN. *Mol Cell Biochem, 372*(1-2), 35-45. doi:10.1007/s11010-012-1443-3

Liu, Z. Y., Zhang, G. L., Wang, M. M., Xiong, Y. N., & Cui, H. Q. (2011). MicroRNA-663 targets TGFB1 and regulates lung cancer proliferation. *Asian Pac J Cancer Prev, 12*(11), 2819-2823.

Livak, K. J., & Schmittgen, T. D. (2001). Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) Method. *Methods, 25*(4), 402-408. doi:10.1006/meth.2001.1262

Lo, W. L., Yu, C. C., Chiou, G. Y., Chen, Y. W., Huang, P. I., Chien, C. S., . . . Chiou, S. H. (2011). MicroRNA-200c attenuates tumour growth and metastasis of presumptive head and neck squamous cell carcinoma stem cells. *J Pathol, 223*(4), 482-495. doi:10.1002/path.2826

Lo, W. Y., Wang, H. J., Chiu, C. W., & Chen, S. F. (2012). miR-27b-regulated TCTP as a novel plasma biomarker for oral cancer: from quantitative proteomics to post-transcriptional study. *J Proteomics, 77*, 154-166. doi:S1874-3919(12)00569-6 [pii]
10.1016/j.jprot.2012.07.039

Logan, C. Y., & Nusse, R. (2004). The Wnt signaling pathway in development and disease. *Annu Rev Cell Dev Biol, 20*, 781-810. doi:10.1146/annurev.cellbio.20.010403.113126

Lokker, M. E., Offerman, M. P., van der Velden, L. A., de Boer, M. F., Pruyn, J. F., & Teunissen, S. C. (2013). Symptoms of patients with incurable head and neck cancer: prevalence and impact on daily functioning. *Head Neck, 35*(6), 868-876. doi:10.1002/hed.23053

Long, J. S., Schoonen, P. M., Graczyk, D., O'Prey, J., & Ryan, K. M. (2015). p73 engages A2B receptor signalling to prime cancer cells to chemotherapy-induced death. *Oncogene, 34*(40), 5152-5162. doi:10.1038/onc.2014.436

Lu, J., Getz, G., Miska, E. A., Alvarez-Saavedra, E., Lamb, J., Peck, D., . . . Golub, T. R. (2005). MicroRNA expression profiles classify human cancers. *Nature, 435*(7043), 834-838. doi:10.1038/nature03702

Lu, J., He, M. L., Wang, L., Chen, Y., Liu, X., Dong, Q., . . . Li, X. P. (2011). MiR-26a inhibits cell growth and tumorigenesis of nasopharyngeal carcinoma through repression of EZH2. *Cancer Res, 71*(1), 225-233. doi:10.1158/0008-5472.CAN-10-1850

Lu, M., Chen, W. H., Wang, C. Y., Mao, C. Q., & Wang, J. (2017). Reciprocal regulation of miR-1254 and c-Myc in oral squamous cell carcinoma suppresses EMT-mediated metastasis and tumor-initiating properties through MAPK signaling. *Biochem Biophys Res Commun, 484*(4), 801-807. doi:10.1016/j.bbrc.2017.01.170

Lu, X., Chen, L., Chen, Y., Shao, Q., & Qin, W. (2015). Bafilomycin A1 inhibits the growth and metastatic potential of the BEL-7402 liver cancer and HO-8910 ovarian cancer cell lines and induces alterations in their microRNA expression. *Exp Ther Med, 10*(5), 1829-1834. doi:10.3892/etm.2015.2758

Lu, Z., Jiao, D., Qiao, J., Yang, S., Yan, M., Cui, S., & Liu, Z. (2015). Restin suppressed epithelial-mesenchymal transition and tumor metastasis in breast cancer cells through upregulating mir-200a/b expression via association with p73. *Mol Cancer, 14*, 102. doi:10.1186/s12943-015-0370-9

Luga, V., Zhang, L., Viloria-Petit, A. M., Ogunjimi, A. A., Inanlou, M. R., Chiu, E., . . . Wrana, J. L. (2012). Exosomes mediate stromal mobilization of autocrine Wnt-PCP signaling in breast cancer cell migration. *Cell, 151*(7), 1542-1556. doi:10.1016/j.cell.2012.11.024

Lui, V. W., Hedberg, M. L., Li, H., Vangara, B. S., Pendleton, K., Zeng, Y., . . . Grandis, J. R. (2013). Frequent mutation of the PI3K pathway in head and neck cancer defines predictive biomarkers. *Cancer Discov, 3*(7), 761-769. doi:10.1158/2159-8290.CD-13-0103

Luis, T. C., Ichii, M., Brugman, M. H., Kincade, P., & Staal, F. J. (2012). Wnt signaling strength regulates normal hematopoiesis and its deregulation is involved in leukemia development. *Leukemia, 26*(3), 414-421. doi:10.1038/leu.2011.387

Luo, J., Manning, B. D., & Cantley, L. C. (2003). Targeting the PI3K-Akt pathway in human cancer: rationale and promise. *Cancer Cell, 4*(4), 257-262.

Luo, Y., Tong, L., Meng, H., Zhu, W., Guo, L., Wei, T., & Zhang, J. (2017). MiR-335 regulates the chemo-radioresistance of small cell lung cancer cells by targeting PARP-1. *Gene, 600*, 9-15. doi:10.1016/j.gene.2016.11.031

Luo, Z., Dai, Y., Zhang, L., Jiang, C., Li, Z., Yang, J., . . . Li, G. (2013). miR-18a promotes malignant progression by impairing microRNA biogenesis in nasopharyngeal carcinoma. *Carcinogenesis, 34*(2), 415-425. doi:bgs329 [pii]
10.1093/carcin/bgs329

Lytle, J. R., Yario, T. A., & Steitz, J. A. (2007). Target mRNAs are repressed as efficiently by microRNA-binding sites in the 5' UTR as in the 3' UTR. *Proc Natl Acad Sci U S A, 104*(23), 9667-9672. doi:10.1073/pnas.0703820104

Lyu, X., Fang, W., Cai, L., Zheng, H., Ye, Y., Zhang, L., . . . Li, X. (2014). TGFbetaR2 is a major target of miR-93 in nasopharyngeal carcinoma aggressiveness. *Mol Cancer, 13*, 51. doi:10.1186/1476-4598-13-51

Lyu, X., Li, J., Yun, X., Huang, R., Deng, X., Wang, Y., . . . Xiao, G. (2017). miR-181a-5p, an inducer of Wnt-signaling, facilitates cell proliferation in acute lymphoblastic leukemia. *Oncol Rep, 37*(3), 1469-1476. doi:10.3892/or.2017.5425

Ma, J., Yao, Y., Wang, P., Liu, Y., Zhao, L., Li, Z., . . . Xue, Y. (2014). MiR-181a regulates blood-tumor barrier permeability by targeting Kruppel-like factor 6. *J Cereb Blood Flow Metab, 34*(11), 1826-1836. doi:10.1038/jcbfm.2014.152

Ma, L., Young, J., Prabhala, H., Pan, E., Mestdagh, P., Muth, D., . . . Weinberg, R. A. (2010). miR-9, a MYC/MYCN-activated microRNA, regulates E-cadherin and cancer metastasis. *Nat Cell Biol, 12*(3), 247-256. doi:10.1038/ncb2024

Manikantan, K., Sayed, S. I., Syrigos, K. N., Rhys-Evans, P., Nutting, C. M., Harrington, K. J., & Kazi, R. (2009). Challenges for the future modifications of the TNM staging system for head and neck cancer:

case for a new computational model? *Cancer Treat Rev, 35*(7), 639-644. doi:10.1016/j.ctrv.2009.04.010

Mansour, W. Y., Bogdanova, N. V., Kasten-Pisula, U., Rieckmann, T., Kocher, S., Borgmann, K., . . . Dahm-Daphi, J. (2013). Aberrant overexpression of miR-421 downregulates ATM and leads to a pronounced DSB repair defect and clinical hypersensitivity in SKX squamous cell carcinoma. *Radiother Oncol, 106*(1), 147-154. doi:10.1016/j.radonc.2012.10.020

Mao, X., Du, S., Yang, Z., Zhang, L., Peng, X., Jiang, N., & Zhou, H. (2017). Inhibitors of PARP-1 exert inhibitory effects on the biological characteristics of hepatocellular carcinoma cells in vitro. *Mol Med Rep*. doi:10.3892/mmr.2017.6568

Marques, F. Z., Campain, A. E., Tomaszewski, M., Zukowska-Szczechowska, E., Yang, Y. H., Charchar, F. J., & Morris, B. J. (2011). Gene expression profiling reveals renin mRNA overexpression in human hypertensive kidneys and a role for microRNAs. *Hypertension, 58*(6), 1093-1098. doi:10.1161/HYPERTENSIONAHA.111.180729

Marques, L. A., Eluf-Neto, J., Figueiredo, R. A., Gois-Filho, J. F., Kowalski, L. P., Carvalho, M. B., . . . Wunsch-Filho, V. (2008). Oral health, hygiene practices and oral cancer. *Rev Saude Publica, 42*(3), 471-479.

Martello, G., Rosato, A., Ferrari, F., Manfrin, A., Cordenonsi, M., Dupont, S., . . . Piccolo, S. (2010). A MicroRNA targeting dicer for metastasis control. *Cell, 141*(7), 1195-1207. doi:S0092-8674(10)00553-2 [pii]
10.1016/j.cell.2010.05.017

Maselli, V., Di Bernardo, D., & Banfi, S. (2008). CoGemiR: a comparative genomics microRNA database. *BMC Genomics, 9*, 457. doi:10.1186/1471-2164-9-457

Mazzotta, A., Partipilo, G., De Summa, S., Giotta, F., Simone, G., & Mangia, A. (2016). Nuclear PARP1 expression and its prognostic significance in breast cancer patients. *Tumour Biol, 37*(5), 6143-6153. doi:10.1007/s13277-015-4465-0

McCullough, M. J., & Farah, C. S. (2008). The role of alcohol in oral carcinogenesis with particular reference to alcohol-containing mouthwashes. *Aust Dent J, 53*(4), 302-305. doi:10.1111/j.1834-7819.2008.00070.x

McDermott, A. M., Miller, N., Wall, D., Martyn, L. M., Ball, G., Sweeney, K. J., & Kerin, M. J. (2014). Identification and validation of oncologic miRNA biomarkers for luminal A-like breast cancer. *PLoS One, 9*(1), e87032. doi:10.1371/journal.pone.0087032

Meister J, S. M. (2010). miR-126 and miR-126*: new players in cancer. *Sci World J, 10*, 11.

Melino, G., De Laurenzi, V., & Vousden, K. H. (2002). p73: Friend or foe in tumorigenesis. *Nat Rev Cancer, 2*(8), 605-615. doi:10.1038/nrc861

Meng, F., Glaser, S. S., Francis, H., DeMorrow, S., Han, Y., Passarini, J. D., . . . Alpini, G. (2012). Functional analysis of microRNAs in human hepatocellular cancer stem cells. *J Cell Mol Med, 16*(1), 160-173. doi:10.1111/j.1582-4934.2011.01282.x

Meuer, S. C., Wittwer, C., & Nakagawara, K. (2001). *Rapid cycle real-time PCR : methods and applications*. New York ; London: Springer.

Meyer, M. S., Applebaum, K. M., Furniss, C. S., Peters, E. S., Luckett, B. G., Smith, J. F., . . . Kelsey, K. T. (2008). Human papillomavirus-16 modifies the association between fruit consumption and head and neck squamous cell carcinoma. *Cancer Epidemiol Biomarkers Prev, 17*(12), 3419-3426. doi:10.1158/1055-9965.EPI-08-0560

Mi, Y., Zhang, D., Jiang, W., Weng, J., Zhou, C., Huang, K., . . . Wen, Y. (2017). miR-181a-5p promotes the progression of gastric cancer via RASSF6-mediated MAPK signalling activation. *Cancer Lett, 389*, 11-22. doi:10.1016/j.canlet.2016.12.033

Miko, E., Czimmerer, Z., Csanky, E., Boros, G., Buslig, J., Dezso, B., & Scholtz, B. (2009). Differentially expressed microRNAs in small cell lung cancer. *Exp Lung Res, 35*(8), 646-664. doi:10.3109/01902140902822312 [pii]
10.3109/01902140902822312

Miller, T. E., Ghoshal, K., Ramaswamy, B., Roy, S., Datta, J., Shapiro, C. L., . . . Majumder, S. (2008). MicroRNA-221/222 confers tamoxifen resistance in breast cancer by targeting p27Kip1. *J Biol Chem, 283*(44), 29897-29903. doi:10.1074/jbc.M804612200

Minor, J., Wang, X., Zhang, F., Song, J., Jimeno, A., Wang, X. J., . . . Lu, S. L. (2012). Methylation of microRNA-9 is a specific and sensitive biomarker for oral and oropharyngeal squamous cell carcinomas. *Oral Oncol, 48*(1), 73-78. doi:S1368-8375(11)00885-2 [pii]
10.1016/j.oraloncology.2011.11.006

Mintz, P. J., Saetrom, P., Reebye, V., Lundbaek, M. B., Lao, K., Rossi, J. J., . . . Habib, N. A. (2012). MicroRNA-181a* Targets Nanog in a Subpopulation of CD34(+) Cells Isolated From Peripheral Blood. *Mol Ther Nucleic Acids, 1*, e34. doi:10.1038/mtna.2012.29

Miranda, K. C., Huynh, T., Tay, Y., Ang, Y. S., Tam, W. L., Thomson, A. M., . . . Rigoutsos, I. (2006). A pattern-based method for the identification of MicroRNA binding sites and their corresponding heteroduplexes. *Cell, 126*(6), 1203-1217. doi:10.1016/j.cell.2006.07.031

Miska, E. A. (2005). How microRNAs control cell division, differentiation and death. *Curr Opin Genet Dev, 15*(5), 563-568. doi:10.1016/j.gde.2005.08.005

Mody, H., Hung, S. W., Pathak, R., Griffin, J., Cruz-Monserrate, Z., & Govindarajan, R. (2017). miR-202 Diminishes TGFbeta Receptors and Attenuates TGFbeta1-induced EMT in Pancreatic Cancer. *Mol Cancer Res*. doi:10.1158/1541-7786.MCR-16-0327

Mody, H. R., Hung, S. W., AlSaggar, M., Griffin, J., & Govindarajan, R. (2016). Inhibition of S-Adenosylmethionine-Dependent Methyltransferase Attenuates TGFbeta1-Induced EMT and Metastasis in Pancreatic Cancer: Putative Roles of miR-663a and miR-4787-5p. *Mol Cancer Res, 14*(11), 1124-1135. doi:10.1158/1541-7786.MCR-16-0083

Motoyama, K., Inoue, H., Nakamura, Y., Uetake, H., Sugihara, K., & Mori, M. (2008). Clinical significance of high mobility group A2 in human gastric cancer and its relationship to let-7 microRNA family. *Clin Cancer Res, 14*(8), 2334-2340. doi:10.1158/1078-0432.CCR-07-4667

Motoyama, K., Inoue, H., Takatsuno, Y., Tanaka, F., Mimori, K., Uetake, H., . . . Mori, M. (2009). Over- and under-expressed microRNAs in human colorectal cancer. *Int J Oncol, 34*(4), 1069-1075.

Muwonge, R., Ramadas, K., Sankila, R., Thara, S., Thomas, G., Vinoda, J., & Sankaranarayanan, R. (2008). Role of tobacco smoking, chewing and alcohol drinking in the risk of oral cancer in Trivandrum, India: a nested case-control design using incident cancer cases. *Oral Oncol, 44*(5), 446-454. doi:10.1016/j.oraloncology.2007.06.002

Nakada, C., Matsuura, K., Tsukamoto, Y., Tanigawa, M., Yoshimoto, T., Narimatsu, T., . . . Moriyama, M. (2008). Genome-wide microRNA expression profiling in renal cell carcinoma: significant down-regulation of miR-141 and miR-200c. *J Pathol, 216*(4), 418-427. doi:10.1002/path.2437

Nam, E. J., Yoon, H., Kim, S. W., Kim, H., Kim, Y. T., Kim, J. H., . . . Kim, S. (2008). MicroRNA expression profiles in serous ovarian carcinoma. *Clin Cancer Res, 14*(9), 2690-2695. doi:14/9/2690 [pii]
10.1158/1078-0432.CCR-07-1731

Nana-Sinkam, S. P., & Croce, C. M. (2013). Clinical applications for microRNAs in cancer. *Clin Pharmacol Ther, 93*(1), 98-104. doi:10.1038/clpt.2012.192

Nasser, M. W., Datta, J., Nuovo, G., Kutay, H., Motiwala, T., Majumder, S., . . . Ghoshal, K. (2008). Down-regulation of micro-RNA-1 (miR-1) in lung cancer. Suppression of tumorigenic property of lung cancer cells and their sensitization to doxorubicin-induced apoptosis by miR-1. *J Biol Chem, 283*(48), 33394-33405. doi:M804788200 [pii]
10.1074/jbc.M804788200

Negrini, M., Nicoloso, M. S., & Calin, G. A. (2009). MicroRNAs and cancer--new paradigms in molecular oncology. *Curr Opin Cell Biol, 21*(3), 470-479. doi:10.1016/j.ceb.2009.03.002

Nemes, J. A., Nemes, Z., & Marton, I. J. (2005). p21WAF1/CIP1 expression is a marker of poor prognosis in oral squamous cell carcinoma. *J Oral Pathol Med, 34*(5), 274-279. doi:10.1111/j.1600-0714.2005.00310.x

Ng, W. L., Yan, D., Zhang, X., Mo, Y. Y., & Wang, Y. (2010). Over-expression of miR-100 is responsible for the low-expression of ATM in the human glioma cell line: M059J. *DNA Repair (Amst), 9*(11), 1170-1175. doi:10.1016/j.dnarep.2010.08.007

Nishimura, J., Handa, R., Yamamoto, H., Tanaka, F., Shibata, K., Mimori, K., . . . Mori, M. (2012). microRNA-181a is associated with poor prognosis of colorectal cancer. *Oncol Rep, 28*(6), 2221-2226. doi:10.3892/or.2012.2059

Niu, J., Xue, A., Chi, Y., Xue, J., Wang, W., Zhao, Z., . . . Wu, Z. H. (2016). Induction of miRNA-181a by genotoxic treatments promotes chemotherapeutic resistance and metastasis in breast cancer. *Oncogene, 35*(10), 1302-1313. doi:10.1038/onc.2015.189

Niwa, R., & Slack, F. J. (2007). The evolution of animal microRNA function. *Curr Opin Genet Dev, 17*(2), 145-150. doi:10.1016/j.gde.2007.02.004

Noh, H., Hong, S., Dong, Z., Pan, Z. K., Jing, Q., & Huang, S. (2011). Impaired MicroRNA Processing Facilitates Breast Cancer Cell Invasion by Upregulating Urokinase-Type Plasminogen Activator Expression. *Genes Cancer, 2*(2), 140-150. doi:10.1177/1947601911408888

Nohata, N., Hanazawa, T., Kikkawa, N., Mutallip, M., Fujimura, L., Yoshino, H., . . . Seki, N. (2011). Caveolin-1 mediates tumor cell migration and invasion and its regulation by miR-133a in head and neck squamous cell carcinoma. *Int J Oncol, 38*(1), 209-217.

Nohata, N., Hanazawa, T., Kikkawa, N., Mutallip, M., Sakurai, D., Fujimura, L., . . . Seki, N. (2011). Tumor suppressive microRNA-375 regulates oncogene AEG-1/MTDH in head and neck squamous cell carcinoma (HNSCC). *J Hum Genet, 56*(8), 595-601. doi:jhg201166 [pii]
10.1038/jhg.2011.66

Nohata, N., Hanazawa, T., Kikkawa, N., Sakurai, D., Sasaki, K., Chiyomaru, T., . . . Seki, N. (2011). Identification of novel molecular targets regulated by tumor suppressive miR-1/miR-133a in maxillary sinus squamous cell carcinoma. *Int J Oncol, 39*(5), 1099-1107. doi:10.3892/ijo.2011.1096

Nohata, N., Hanazawa, T., Kinoshita, T., Okamoto, Y., & Seki, N. (2013). MicroRNAs function as tumor suppressors or oncogenes: aberrant

expression of microRNAs in head and neck squamous cell carcinoma. *Auris Nasus Larynx, 40*(2), 143-149. doi:S0385-8146(12)00184-8 [pii]
10.1016/j.anl.2012.07.001

Nohata, N., Sone, Y., Hanazawa, T., Fuse, M., Kikkawa, N., Yoshino, H., . . . Seki, N. (2011). miR-1 as a tumor suppressive microRNA targeting TAGLN2 in head and neck squamous cell carcinoma. *Oncotarget, 2*(1-2), 29-42. doi:213 [pii]

Nurul-Syakima Ab Mutalib, L. L.-H., Shiran Mohd Sidik, Sabariah Abdul Rahman, Avatar Singh Mohan Singh and Cheah Yoke-Kqueen. (2012). miR-181a regulates multiple pathways in hypopharyngeal squamous cell carcinoma. *African Journal of Biotechnology, 11*(22), 8.

Nurul-Syakima, A. M., Yoke-Kqueen, C., Sabariah, A. R., Shiran, M. S., Singh, A., & Learn-Han, L. (2011). Differential microRNA expression and identification of putative miRNA targets and pathways in head and neck cancers. *Int J Mol Med, 28*(3), 327-336. doi:10.3892/ijmm.2011.714

Ogawa, T., Saiki, Y., Shiga, K., Chen, N., Fukushige, S., Sunamura, M., . . . Horii, A. (2012). miR-34a is downregulated in cis-diamminedichloroplatinum treated sinonasal squamous cell carcinoma patients with poor prognosis. *Cancer Sci, 103*(9), 1737-1743. doi:10.1111/j.1349-7006.2012.02338.x

Ogmundsdottir, H. M., Bjornsson, J., & Holbrook, W. P. (2009). Role of TP53 in the progression of pre-malignant and malignant oral mucosal lesions. A follow-up study of 144 patients. *J Oral Pathol Med, 38*(7), 565-571. doi:10.1111/j.1600-0714.2009.00766.x

Ohta, K., Hoshino, H., Wang, J., Ono, S., Iida, Y., Hata, K., . . . Hoon, D. S. (2015). MicroRNA-93 activates c-Met/PI3K/Akt pathway activity in hepatocellular carcinoma by directly inhibiting PTEN and CDKN1A. *Oncotarget, 6*(5), 3211-3224. doi:10.18632/oncotarget.3085

Otsubo, T., Akiyama, Y., Hashimoto, Y., Shimada, S., Goto, K., & Yuasa, Y. (2011). MicroRNA-126 inhibits SOX2 expression and contributes to gastric carcinogenesis. *PLoS One, 6*(1), e16617. doi:10.1371/journal.pone.0016617

Ouyang, Y. B., Lu, Y., Yue, S., & Giffard, R. G. (2012). miR-181 targets multiple Bcl-2 family members and influences apoptosis and mitochondrial function in astrocytes. *Mitochondrion, 12*(2), 213-219. doi:10.1016/j.mito.2011.09.001

Ouyang, Y. B., Lu, Y., Yue, S., Xu, L. J., Xiong, X. X., White, R. E., . . . Giffard, R. G. (2012). miR-181 regulates GRP78 and influences outcome from cerebral ischemia in vitro and in vivo. *Neurobiol Dis, 45*(1), 555-563. doi:10.1016/j.nbd.2011.09.012

Ozen, M., Creighton, C. J., Ozdemir, M., & Ittmann, M. (2008). Widespread deregulation of microRNA expression in human prostate cancer. *Oncogene, 27*(12), 1788-1793. doi:10.1038/sj.onc.1210809

Pallasch, C. P., Patz, M., Park, Y. J., Hagist, S., Eggle, D., Claus, R., . . . Wendtner, C. M. (2009). miRNA deregulation by epigenetic silencing disrupts suppression of the oncogene PLAG1 in chronic lymphocytic leukemia. *Blood, 114*(15), 3255-3264. doi:10.1182/blood-2009-06-229898

Pan, J., Hu, H., Zhou, Z., Sun, L., Peng, L., Yu, L., . . . Ran, Y. (2010). Tumor-suppressive mir-663 gene induces mitotic catastrophe growth arrest in human gastric cancer cells. *Oncol Rep, 24*(1), 105-112.

Panda, H., Chuang, T. D., Luo, X., & Chegini, N. (2012). Endometrial miR-181a and miR-98 expression is altered during transition from normal into cancerous state and target PGR, PGRMC1, CYP19A1, DDX3X, and TIMP3. *J Clin Endocrinol Metab, 97*(7), E1316-1326. doi:10.1210/jc.2012-1018

Papadopoulos, G. L., Alexiou, P., Maragkakis, M., Reczko, M., & Hatzigeorgiou, A. G. (2009). DIANA-mirPath: Integrating human and mouse microRNAs in pathways. *Bioinformatics, 25*(15), 1991-1993. doi:10.1093/bioinformatics/btp299

Parikh, A., Lee, C., Joseph, P., Marchini, S., Baccarini, A., Kolev, V., . . . DiFeo, A. (2014). microRNA-181a has a critical role in ovarian cancer progression through the regulation of the epithelial-mesenchymal transition. *Nat Commun, 5*, 2977. doi:10.1038/ncomms3977

Parma, P., Radi, O., Vidal, V., Chaboissier, M. C., Dellambra, E., Valentini, S., . . . Camerino, G. (2006). R-spondin1 is essential in sex determination, skin differentiation and malignancy. *Nat Genet, 38*(11), 1304-1309. doi:10.1038/ng1907

Peltonen, J. K., Vahakangas, K. H., Helppi, H. M., Bloigu, R., Paakko, P., & Turpeenniemi-Hujanen, T. (2011). Specific TP53 mutations predict aggressive phenotype in head and neck squamous cell carcinoma: a retrospective archival study. *Head Neck Oncol, 3*, 20. doi:10.1186/1758-3284-3-20

Peters, E. S., Luckett, B. G., Applebaum, K. M., Marsit, C. J., McClean, M. D., & Kelsey, K. T. (2008). Dairy products, leanness, and head and neck squamous cell carcinoma. *Head Neck, 30*(9), 1193-1205. doi:10.1002/hed.20846

Petersen, C. P., Bordeleau, M. E., Pelletier, J., & Sharp, P. A. (2006). Short RNAs repress translation after initiation in mammalian cells. *Mol Cell, 21*(4), 533-542. doi:10.1016/j.molcel.2006.01.031

Petersen, P. E. (2009). Oral cancer prevention and control--the approach of the World Health Organization. *Oral Oncol, 45*(4-5), 454-460. doi:10.1016/j.oraloncology.2008.05.023

Petti, S. (2009). Lifestyle risk factors for oral cancer. *Oral Oncol, 45*(4-5), 340-350. doi:10.1016/j.oraloncology.2008.05.018

Petti, S., Masood, M., Messano, G. A., & Scully, C. (2013). Alcohol is not a risk factor for oral cancer in nonsmoking, betel quid non-chewing individuals. A meta-analysis update. *Ann Ig, 25*(1), 3-14. doi:10.7416/ai.2013.1901

Petti, S., Masood, M., & Scully, C. (2013). The magnitude of tobacco smoking-betel quid chewing-alcohol drinking interaction effect on oral cancer in South-East Asia. A meta-analysis of observational studies. *PLoS One, 8*(11), e78999. doi:10.1371/journal.pone.0078999

Pezzuto, F., Buonaguro, L., Caponigro, F., Ionna, F., Starita, N., Annunziata, C., . . . Tornesello, M. L. (2015). Update on Head and Neck Cancer: Current Knowledge on Epidemiology, Risk Factors, Molecular Features and Novel Therapies. *Oncology, 89*(3), 125-136. doi:10.1159/000381717

Pichiorri, F., Suh, S. S., Ladetto, M., Kuehl, M., Palumbo, T., Drandi, D., . . . Croce, C. M. (2008). MicroRNAs regulate critical genes associated with multiple myeloma pathogenesis. *Proc Natl Acad Sci U S A, 105*(35), 12885-12890. doi:10.1073/pnas.0806202105

Pichler, M., Winter, E., Ress, A. L., Bauernhofer, T., Gerger, A., Kiesslich, T., . . . Hoefler, G. (2014). miR-181a is associated with poor clinical outcome in patients with colorectal cancer treated with EGFR inhibitor. *J Clin Pathol, 67*(3), 198-203. doi:10.1136/jclinpath-2013-201904

Pillaire, M. J., Selves, J., Gordien, K., Gourraud, P. A., Gentil, C., Danjoux, M., . . . Cazaux, C. (2010). A 'DNA replication' signature of progression and negative outcome in colorectal cancer. *Oncogene, 29*(6), 876-887. doi:10.1038/onc.2009.378

Pineau, P., Volinia, S., McJunkin, K., Marchio, A., Battiston, C., Terris, B., . . . Dejean, A. (2010). miR-221 overexpression contributes to liver tumorigenesis. *Proc Natl Acad Sci U S A, 107*(1), 264-269. doi:10.1073/pnas.0907904107

Pinto, J. A., Rolfo, C., Raez, L. E., Prado, A., Araujo, J. M., Bravo, L., . . . Gomez, H. L. (2017). In silico evaluation of DNA Damage Inducible Transcript 4 gene (DDIT4) as prognostic biomarker in several malignancies. *Sci Rep, 7*(1), 1526. doi:10.1038/s41598-017-01207-3

Pio, G., Malerba, D., D'Elia, D., & Ceci, M. (2014). Integrating microRNA target predictions for the discovery of gene regulatory networks: a semi-supervised ensemble learning approach. *BMC Bioinformatics, 15 Suppl 1*, S4. doi:10.1186/1471-2105-15-S1-S4

Poeta, M. L., Manola, J., Goldwasser, M. A., Forastiere, A., Benoit, N., Califano, J. A., . . . Koch, W. M. (2007). TP53 mutations and survival in squamous-cell carcinoma of the head and neck. *N Engl J Med, 357*(25), 2552-2561. doi:10.1056/NEJMoa073770

Polakis, P. (2007). The many ways of Wnt in cancer. *Curr Opin Genet Dev, 17*(1), 45-51. doi:10.1016/j.gde.2006.12.007

Qian, B., Katsaros, D., Lu, L., Preti, M., Durando, A., Arisio, R., . . . Yu, H. (2009). High miR-21 expression in breast cancer associated with poor disease-free survival in early stage disease and high TGF-beta1. *Breast Cancer Res Treat, 117*(1), 131-140. doi:10.1007/s10549-008-0219-7

Qiao, B., He, B. X., Cai, J. H., Tao, Q., & King-Yin Lam, A. (2017). MicroRNA-27a-3p Modulates the Wnt/beta-Catenin Signaling Pathway to Promote Epithelial-Mesenchymal Transition in Oral Squamous Carcinoma Stem Cells by Targeting SFRP1. *Sci Rep, 7*, 44688. doi:10.1038/srep44688

Qin, W., Shi, Y., Zhao, B., Yao, C., Jin, L., Ma, J., & Jin, Y. (2010). miR-24 regulates apoptosis by targeting the open reading frame (ORF) region of FAF1 in cancer cells. *PLoS One, 5*(2), e9429. doi:10.1371/journal.pone.0009429

Qu, C., Liang, Z., Huang, J., Zhao, R., Su, C., Wang, S., . . . Yang, H. (2012). MiR-205 determines the radioresistance of human nasopharyngeal carcinoma by directly targeting PTEN. *Cell Cycle, 11*(4), 785-796. doi:10.4161/cc.11.4.19228

Rahmani, A., Alzohairy, M., Babiker, A. Y., Rizvi, M. A., & Elkarimahmad, H. G. (2012). Clinicopathological significance of PTEN and bcl2 expressions in oral squamous cell carcinoma. *Int J Clin Exp Pathol, 5*(9), 965-971.

Rajnai, H., Heyning, F. H., Koens, L., Sebestyen, A., Andrikovics, H., Hogendoorn, P. C., . . . Szepesi, A. (2014). The density of CD8+ T-cell infiltration and expression of BCL2 predicts outcome of primary diffuse large B-cell lymphoma of bone. *Virchows Arch, 464*(2), 229-239. doi:10.1007/s00428-013-1519-9

Ramdas, L., Giri, U., Ashorn, C. L., Coombes, K. R., El-Naggar, A., Ang, K. K., & Story, M. D. (2009). miRNA expression profiles in head and neck squamous cell carcinoma and adjacent normal tissue. *Head Neck, 31*(5), 642-654. doi:10.1002/hed.21017

Razak, A. A., Saddki, N., Naing, N. N., & Abdullah, N. (2009). Oral cancer presentation among Malay patients in hospital Universiti Sains Malaysia, Kelantan. *Asian Pac J Cancer Prev, 10*(6), 1131-1136.

Reed, J. C. (2008). Bcl-2-family proteins and hematologic malignancies: history and future prospects. *Blood, 111*(7), 3322-3330. doi:10.1182/blood-2007-09-078162

Reid, G., Kao, S. C., Pavlakis, N., Brahmbhatt, H., MacDiarmid, J., Clarke, S., . . . van Zandwijk, N. (2016). Clinical development of TargomiRs, a miRNA mimic-based treatment for patients with recurrent thoracic cancer. *Epigenomics, 8*(8), 1079-1085. doi:10.2217/epi-2016-0035

Reis, P. P., Tomenson, M., Cervigne, N. K., Machado, J., Jurisica, I., Pintilie, M., . . . Kamel-Reid, S. (2010). Programmed cell death 4 loss increases tumor cell invasion and is regulated by miR-21 in oral squamous cell carcinoma. *Mol Cancer, 9*, 238. doi:1476-4598-9-238 [pii]
10.1186/1476-4598-9-238

Rheinwald, J. G., & Beckett, M. A. (1981). Tumorigenic keratinocyte lines requiring anchorage and fibroblast support cultured from human squamous cell carcinomas. *Cancer Res, 41*(5), 1657-1663.

Richman, S. D., Seymour, M. T., Chambers, P., Elliott, F., Daly, C. L., Meade, A. M., . . . Quirke, P. (2009). KRAS and BRAF mutations in advanced colorectal cancer are associated with poor prognosis but do not preclude benefit from oxaliplatin or irinotecan: results from the MRC FOCUS trial. *J Clin Oncol, 27*(35), 5931-5937. doi:10.1200/JCO.2009.22.4295

Rippo, M. R., Olivieri, F., Monsurro, V., Prattichizzo, F., Albertini, M. C., & Procopio, A. D. (2014). MitomiRs in human inflamm-aging: a hypothesis involving miR-181a, miR-34a and miR-146a. *Exp Gerontol, 56*, 154-163. doi:10.1016/j.exger.2014.03.002

Ritchie, W., Flamant, S., & Rasko, J. E. (2009). Predicting microRNA targets and functions: traps for the unwary. *Nat Methods, 6*(6), 397-398. doi:10.1038/nmeth0609-397

Ryan, B. M., Robles, A. I., & Harris, C. C. (2010). Genetic variation in microRNA networks: the implications for cancer research. *Nat Rev Cancer, 10*(6), 389-402. doi:10.1038/nrc2867

Rychlik, W., Spencer, W. J., & Rhoads, R. E. (1990). Optimization of the annealing temperature for DNA amplification in vitro. *Nucleic Acids Res, 18*(21), 6409-6412.

Saba, R., Storchel, P. H., Aksoy-Aksel, A., Kepura, F., Lippi, G., Plant, T. D., & Schratt, G. M. (2012). Dopamine-regulated microRNA MiR-181a controls GluA2 surface expression in hippocampal neurons. *Mol Cell Biol, 32*(3), 619-632. doi:10.1128/MCB.05896-11

Sand, M., Skrygan, M., Sand, D., Georgas, D., Gambichler, T., Hahn, S. A., . . . Bechara, F. G. (2013). Comparative microarray analysis of microRNA expression profiles in primary cutaneous malignant

melanoma, cutaneous malignant melanoma metastases, and benign melanocytic nevi. *Cell Tissue Res, 351*(1), 85-98. doi:10.1007/s00441-012-1514-5

Santos-Beneit, A. M., & Mollinedo, F. (2000). Expression of genes involved in initiation, regulation, and execution of apoptosis in human neutrophils and during neutrophil differentiation of HL-60 cells. *J Leukoc Biol, 67*(5), 712-724.

Sasahira, T., Kurihara, M., Bhawal, U. K., Ueda, N., Shimomoto, T., Yamamoto, K., . . . Kuniyasu, H. (2012). Downregulation of miR-126 induces angiogenesis and lymphangiogenesis by activation of VEGF-A in oral cancer. *Br J Cancer, 107*(4), 700-706. doi:bjc2012330 [pii]
10.1038/bjc.2012.330

Schaefer, A., Jung, M., Mollenkopf, H. J., Wagner, I., Stephan, C., Jentzmik, F., . . . Jung, K. (2010). Diagnostic and prognostic implications of microRNA profiling in prostate carcinoma. *Int J Cancer, 126*(5), 1166-1176. doi:10.1002/ijc.24827

Schaefer, A., Stephan, C., Busch, J., Yousef, G. M., & Jung, K. (2010). Diagnostic, prognostic and therapeutic implications of microRNAs in urologic tumors. *Nat Rev Urol, 7*(5), 286-297. doi:10.1038/nrurol.2010.45

Schetter, A. J., & Harris, C. C. (2012). Tumor suppressor p53 (TP53) at the crossroads of the exposome and the cancer genome. *Proc Natl Acad Sci U S A, 109*(21), 7955-7956. doi:10.1073/pnas.1205457109

Schneider, A., Younis, R. H., & Gutkind, J. S. (2008). Hypoxia-induced energy stress inhibits the mTOR pathway by activating an AMPK/REDD1 signaling axis in head and neck squamous cell carcinoma. *Neoplasia, 10*(11), 1295-1302.

Scott, S. E., Grunfeld, E. A., & McGurk, M. (2005). The idiosyncratic relationship between diagnostic delay and stage of oral squamous cell carcinoma. *Oral Oncol, 41*(4), 396-403. doi:10.1016/j.oraloncology.2004.10.010

Scoumanne, A., Harms, K. L., & Chen, X. (2005). Structural basis for gene activation by p53 family members. *Cancer Biol Ther, 4*(11), 1178-1185.

Selbach, M., Schwanhausser, B., Thierfelder, N., Fang, Z., Khanin, R., & Rajewsky, N. (2008). Widespread changes in protein synthesis induced by microRNAs. *Nature, 455*(7209), 58-63. doi:nature07228 [pii]
10.1038/nature07228

Selcuklu, S. D., Donoghue, M. T., & Spillane, C. (2009). miR-21 as a key regulator of oncogenic processes. *Biochem Soc Trans, 37*(Pt 4), 918-925. doi:10.1042/BST0370918

Sevinc, E. D., Cecener, G., Ak, S., Tunca, B., Egeli, U., Gokgoz, S., . . . Tasdelen, I. (2016). Expression and clinical significance of miRNAs that may be associated with the FHIT gene in breast cancer. *Gene, 590*(2), 278-284. doi:10.1016/j.gene.2016.05.033

Shangina, O., Brennan, P., Szeszenia-Dabrowska, N., Mates, D., Fabianova, E., Fletcher, T., . . . Zaridze, D. (2006). Occupational exposure and laryngeal and hypopharyngeal cancer risk in central and eastern Europe. *Am J Epidemiol, 164*(4), 367-375. doi:10.1093/aje/kwj208

Sharma, S., Kelly, T. K., & Jones, P. A. (2010). Epigenetics in cancer. *Carcinogenesis, 31*(1), 27-36. doi:bgp220 [pii]
10.1093/carcin/bgp220

She, X., Yu, Z., Cui, Y., Lei, Q., Wang, Z., Xu, G., . . . Wu, M. (2014). miR-181 subunits enhance the chemosensitivity of temozolomide by Rap1B-mediated cytoskeleton remodeling in glioblastoma cells. *Med Oncol, 31*(4), 892. doi:10.1007/s12032-014-0892-9

Sheaff, R. J., Groudine, M., Gordon, M., Roberts, J. M., & Clurman, B. E. (1997). Cyclin E-CDK2 is a regulator of p27Kip1. *Genes Dev, 11*(11), 1464-1478.

Sherr, C. J., & Roberts, J. M. (1999). CDK inhibitors: positive and negative regulators of G1-phase progression. *Genes Dev, 13*(12), 1501-1512.

Shi, L., Cheng, Z., Zhang, J., Li, R., Zhao, P., Fu, Z., & You, Y. (2008). hsa-mir-181a and hsa-mir-181b function as tumor suppressors in human glioma cells. *Brain Res, 1236*, 185-193. doi:10.1016/j.brainres.2008.07.085

Shi, Y., Chen, C., Zhang, X., Liu, Q., Xu, J. L., Zhang, H. R., . . . Bian, X. W. (2014). Primate-specific miR-663 functions as a tumor suppressor by targeting PIK3CD and predicts the prognosis of human glioblastoma. *Clin Cancer Res, 20*(7), 1803-1813. doi:10.1158/1078-0432.CCR-13-2284

Shield, K. D., Rylett, M., Gmel, G., Gmel, G., Kehoe-Chan, T. A., & Rehm, J. (2013). Global alcohol exposure estimates by country, territory and region for 2005--a contribution to the Comparative Risk Assessment for the 2010 Global Burden of Disease Study. *Addiction, 108*(5), 912-922. doi:10.1111/add.12112

Shimono, Y., Zabala, M., Cho, R. W., Lobo, N., Dalerba, P., Qian, D., . . . Clarke, M. F. (2009). Downregulation of miRNA-200c links breast cancer stem cells with normal stem cells. *Cell, 138*(3), 592-603. doi:S0092-8674(09)00850-2 [pii]
10.1016/j.cell.2009.07.011

Shin, K. H., Bae, S. D., Hong, H. S., Kim, R. H., Kang, M. K., & Park, N. H. (2011). miR-181a shows tumor suppressive effect against oral squamous cell carcinoma cells by downregulating K-ras. *Biochem*

Biophys Res Commun, 404(4), 896-902. doi:10.1016/j.bbrc.2010.12.055

Shirdel, E. A., Xie, W., Mak, T. W., & Jurisica, I. (2011). NAViGaTing the micronome--using multiple microRNA prediction databases to identify signalling pathway-associated microRNAs. *PLoS One, 6*(2), e17429. doi:10.1371/journal.pone.0017429

Shomron, N. (2010). MicroRNAs and pharmacogenomics. *Pharmacogenomics, 11*(5), 629-632. doi:10.2217/pgs.10.26

Si, M. L., Zhu, S., Wu, H., Lu, Z., Wu, F., & Mo, Y. Y. (2007). miR-21-mediated tumor growth. *Oncogene, 26*(19), 2799-2803. doi:10.1038/sj.onc.1210083

Siebolts, U., Varnholt, H., Drebber, U., Dienes, H. P., Wickenhauser, C., & Odenthal, M. (2009). Tissues from routine pathology archives are suitable for microRNA analyses by quantitative PCR. *J Clin Pathol, 62*(1), 84-88. doi:10.1136/jcp.2008.058339

Siegel, R., Naishadham, D., & Jemal, A. (2012). Cancer statistics, 2012. *CA Cancer J Clin, 62*(1), 10-29. doi:10.3322/caac.20138

Singer, G., Oldt, R., 3rd, Cohen, Y., Wang, B. G., Sidransky, D., Kurman, R. J., & Shih Ie, M. (2003). Mutations in BRAF and KRAS characterize the development of low-grade ovarian serous carcinoma. *J Natl Cancer Inst, 95*(6), 484-486.

Singh, S. K., Banerjee, S., Acosta, E. P., Lillard, J. W., & Singh, R. (2017). Resveratrol induces cell cycle arrest and apoptosis with docetaxel in prostate cancer cells via a p53/ p21WAF1/CIP1 and p27KIP1 pathway. *Oncotarget, 8*(10), 17216-17228. doi:10.18632/oncotarget.15303

Sinha, N., Panda, P. K., Naik, P. P., Das, D. N., Mukhopadhyay, S., Maiti, T. K., . . . Bhutia, S. K. (2017). Abrus agglutinin promotes irreparable DNA damage by triggering ROS generation followed by ATM-p73 mediated apoptosis in oral squamous cell carcinoma. *Mol Carcinog*. doi:10.1002/mc.22679

Siriwardena, B. S., Rasnayaka, R. M., Masood, Y., Masood, M., Kumarasiri, P. V., & Tilakaratne, W. M. (2016). Predictive model of oral cancer metastasis for different cancer sites and age groups. *J Investig Clin Dent, 7*(2), 127-131. doi:10.1111/jicd.12145

Skinner, H. D., Sandulache, V. C., Ow, T. J., Meyn, R. E., Yordy, J. S., Beadle, B. M., . . . Myers, J. N. (2012). TP53 disruptive mutations lead to head and neck cancer treatment failure through inhibition of radiation-induced senescence. *Clin Cancer Res, 18*(1), 290-300. doi:10.1158/1078-0432.CCR-11-2260

Slaby, O., Redova, M., Poprach, A., Nekvindova, J., Iliev, R., Radova, L., . . . Vyzula, R. (2012). Identification of MicroRNAs associated with early relapse after nephrectomy in renal cell carcinoma patients. *Genes Chromosomes Cancer, 51*(7), 707-716. doi:10.1002/gcc.21957

Smrt, R. D., Szulwach, K. E., Pfeiffer, R. L., Li, X., Guo, W., Pathania, M., . . . Zhao, X. (2010). MicroRNA miR-137 regulates neuronal maturation by targeting ubiquitin ligase mind bomb-1. *Stem Cells, 28*(6), 1060-1070. doi:10.1002/stem.431

Sofer, A., Lei, K., Johannessen, C. M., & Ellisen, L. W. (2005). Regulation of mTOR and cell growth in response to energy stress by REDD1. *Mol Cell Biol, 25*(14), 5834-5845. doi:10.1128/MCB.25.14.5834-5845.2005

Song, K. H., Ko, S. H., Ahn, Y. B., Yoo, S. J., Chin, H. M., Kaneto, H., . . . Son, H. Y. (2004). In vitro transdifferentiation of adult pancreatic acinar cells into insulin-expressing cells. *Biochem Biophys Res Commun, 316*(4), 1094-1100. doi:10.1016/j.bbrc.2004.02.153

Sorahan, T., & Williams, S. P. (2006). Respiratory cancer in nickel carbonyl refinery workers. *Occup Environ Med, 63*(12), 856; author reply 856.

Stewart, B. W., Wild, C., International Agency for Research on Cancer, & World Health Organization. (2014). *World cancer report 2014*. Lyon, France
Geneva, Switzerland: International Agency for Research on Cancer
WHO Press.

Strano, S., Dell'Orso, S., Di Agostino, S., Fontemaggi, G., Sacchi, A., & Blandino, G. (2007). Mutant p53: an oncogenic transcription factor. *Oncogene, 26*(15), 2212-2219. doi:10.1038/sj.onc.1210296

Streppel, M. M., Pai, S., Campbell, N. R., Hu, C., Yabuuchi, S., Canto, M. I., . . . Maitra, A. (2013). MicroRNA 223 is upregulated in the multistep progression of Barrett's esophagus and modulates sensitivity to chemotherapy by targeting PARP1. *Clin Cancer Res, 19*(15), 4067-4078. doi:10.1158/1078-0432.CCR-13-0601

Strotbek, M., Schmid, S., Sanchez-Gonzalez, I., Boerries, M., Busch, H., & Olayioye, M. A. (2017). miR-181 elevates Akt signaling by co-targeting PHLPP2 and INPP4B phosphatases in luminal breast cancer. *Int J Cancer, 140*(10), 2310-2320. doi:10.1002/ijc.30661

Su, R., Lin, H. S., Zhang, X. H., Yin, X. L., Ning, H. M., Liu, B., . . . Zhang, J. W. (2015). MiR-181 family: regulators of myeloid differentiation and acute myeloid leukemia as well as potential therapeutic targets. *Oncogene, 34*(25), 3226-3239. doi:10.1038/onc.2014.274

Su, S. F., Chang, Y. W., Andreu-Vieyra, C., Fang, J. Y., Yang, Z., Han, B., . . . Liang, G. (2013). miR-30d, miR-181a and miR-199a-5p cooperatively suppress the endoplasmic reticulum chaperone and signaling

regulator GRP78 in cancer. *Oncogene, 32*(39), 4694-4701. doi:10.1038/onc.2012.483

Sun, C., Li, N., Yang, Z., Zhou, B., He, Y., Weng, D., . . . Chen, G. (2013). miR-9 regulation of BRCA1 and ovarian cancer sensitivity to cisplatin and PARP inhibition. *J Natl Cancer Inst, 105*(22), 1750-1758. doi:10.1093/jnci/djt302

Sun, C., Ma, P., Wang, Y., Liu, W., Chen, Q., Pan, Y., . . . Shu, Y. (2017). KLF15 Inhibits Cell Proliferation in Gastric Cancer Cells via Up-Regulating CDKN1A/p21 and CDKN1C/p57 Expression. *Dig Dis Sci, 62*(6), 1518-1526. doi:10.1007/s10620-017-4558-2

Sun, X., Wei, L., Chen, Q., & Terek, R. M. (2015). MicroRNA regulates vascular endothelial growth factor expression in chondrosarcoma cells. *Clin Orthop Relat Res, 473*(3), 907-913. doi:10.1007/s11999-014-3842-0

Szanyi, I., Bauer, M., Gerlinger, I., Jarai, T., Gobel, G., Lujber, L., . . . Kiss, I. (2011). Changes in expression of oncogenes and TP53 tumour suppressor gene as biomarkers in head and neck cancers. *Eur Arch Otorhinolaryngol, 268*(7), 1041-1046. doi:10.1007/s00405-010-1425-6

Takamizawa, J., Konishi, H., Yanagisawa, K., Tomida, S., Osada, H., Endoh, H., . . . Takahashi, T. (2004). Reduced expression of the let-7 microRNAs in human lung cancers in association with shortened postoperative survival. *Cancer Res, 64*(11), 3753-3756. doi:10.1158/0008-5472.CAN-04-0637

Takes, R. P., Strojan, P., Silver, C. E., Bradley, P. J., Haigentz, M., Jr., Wolf, G. T., . . . Neck Scientific, G. (2012). Current trends in initial management of hypopharyngeal cancer: the declining use of open surgery. *Head Neck, 34*(2), 270-281. doi:10.1002/hed.21613

Tan, J. Y., Habib, N. A., Chuah, Y. W., Yau, Y. H., Geifman-Shochat, S., & Chen, W. N. (2015). Identification of Cellular Targets of MicroRNA-181a in HepG2 Cells: A New Approach for Functional Analysis of MicroRNAs. *PLoS One, 10*(4), e0123167. doi:10.1371/journal.pone.0123167

Tanic, M., Yanowski, K., Gomez-Lopez, G., Rodriguez-Pinilla, M. S., Marquez-Rodas, I., Osorio, A., . . . Benitez, J. (2015). MicroRNA expression signatures for the prediction of BRCA1/2 mutation-associated hereditary breast cancer in paraffin-embedded formalin-fixed breast tumors. *Int J Cancer, 136*(3), 593-602. doi:10.1002/ijc.29021

Tao, J. e. a. (2012). microRNA-18a, a member of the oncogenic miR-17-92 cluster, targets Dicer and suppresses cell proliferation in bladder cancer

T24 cells. *Mol. Med. Report, 5*, 6.

Tekirdag, K. A., Korkmaz, G., Ozturk, D. G., Agami, R., & Gozuacik, D. (2013). MIR181A regulates starvation- and rapamycin-induced autophagy through targeting of ATG5. *Autophagy, 9*(3), 374-385. doi:10.4161/auto.23117

Tezal, M., Sullivan, M. A., Hyland, A., Marshall, J. R., Stoler, D., Reid, M. E., . . . Scannapieco, F. A. (2009). Chronic periodontitis and the incidence of head and neck squamous cell carcinoma. *Cancer Epidemiol Biomarkers Prev, 18*(9), 2406-2412. doi:10.1158/1055-9965.EPI-09-0334

Thomas, G. R., Nadiminti, H., & Regalado, J. (2005). Molecular predictors of clinical outcome in patients with head and neck squamous cell carcinoma. *Int J Exp Pathol, 86*(6), 347-363. doi:10.1111/j.0959-9673.2005.00447.x

Tie, J., Pan, Y., Zhao, L., Wu, K., Liu, J., Sun, S., . . . Fan, D. (2010). MiR-218 inhibits invasion and metastasis of gastric cancer by targeting the Robo1 receptor. *PLoS Genet, 6*(3), e1000879. doi:10.1371/journal.pgen.1000879

Tili, E., Michaille, J. J., Alder, H., Volinia, S., Delmas, D., Latruffe, N., & Croce, C. M. (2010). Resveratrol modulates the levels of microRNAs targeting genes encoding tumor-suppressors and effectors of TGFbeta signaling pathway in SW480 cells. *Biochem Pharmacol, 80*(12), 2057-2065. doi:10.1016/j.bcp.2010.07.003

Tran, N., O'Brien, C. J., Clark, J., & Rose, B. (2010). Potential role of micro-RNAs in head and neck tumorigenesis. *Head Neck, 32*(8), 1099-1111. doi:10.1002/hed.21356

Tu, H. F., Liu, C. J., Chang, C. L., Wang, P. W., Kao, S. Y., Yang, C. C., . . . Chang, K. W. (2012). The association between genetic polymorphism and the processing efficiency of miR-149 affects the prognosis of patients with head and neck squamous cell carcinoma. *PLoS One, 7*(12), e51606. doi:10.1371/journal.pone.0051606
PONE-D-12-19877 [pii]

Turner, B. M. (2002). Cellular memory and the histone code. *Cell, 111*(3), 285-291.

Uesugi, A., Kozaki, K., Tsuruta, T., Furuta, M., Morita, K., Imoto, I., . . . Inazawa, J. (2011). The tumor suppressive microRNA miR-218 targets the mTOR component Rictor and inhibits AKT phosphorylation in oral cancer. *Cancer Res, 71*(17), 5765-5778. doi:0008-5472.CAN-11-0368 [pii]
10.1158/0008-5472.CAN-11-0368

Ujpal, M., Matos, O., Bibok, G., Somogyi, A., Szabo, G., & Suba, Z. (2004). Diabetes and oral tumors in Hungary: epidemiological correlations. *Diabetes Care, 27*(3), 770-774.

van Haaften, G., & Agami, R. (2010). Tumorigenicity of the miR-17-92 cluster distilled. *Genes Dev, 24*(1), 1-4. doi:10.1101/gad.1887110

VanderWeele, D. J., Paner, G. P., Fleming, G. F., & Szmulewitz, R. Z. (2015). Sustained Complete Response to Cytotoxic Therapy and the PARP Inhibitor Veliparib in Metastatic Castration-Resistant Prostate Cancer - A Case Report. *Front Oncol, 5*, 169. doi:10.3389/fonc.2015.00169

Verduci, L., Azzalin, G., Gioiosa, S., Carissimi, C., Laudadio, I., Fulci, V., & Macino, G. (2015). microRNA-181a enhances cell proliferation in acute lymphoblastic leukemia by targeting EGR1. *Leuk Res, 39*(4), 479-485. doi:10.1016/j.leukres.2015.01.010

Vinci, S., Gelmini, S., Pratesi, N., Conti, S., Malentacchi, F., Simi, L., . . . Orlando, C. (2011). Genetic variants in miR-146a, miR-149, miR-196a2, miR-499 and their influence on relative expression in lung cancers. *Clin Chem Lab Med, 49*(12), 2073-2080. doi:10.1515/CCLM.2011.708
/j/cclm.2011.49.issue-12/cclm.2011.708/cclm.2011.708.xml [pii]

Vislovukh, A., Kratassiouk, G., Porto, E., Gralievska, N., Beldiman, C., Pinna, G., . . . Groisman, I. (2013). Proto-oncogenic isoform A2 of eukaryotic translation elongation factor eEF1 is a target of miR-663 and miR-744. *Br J Cancer, 108*(11), 2304-2311. doi:10.1038/bjc.2013.243

Visone, R., Russo, L., Pallante, P., De Martino, I., Ferraro, A., Leone, V., . . . Fusco, A. (2007). MicroRNAs (miR)-221 and miR-222, both overexpressed in human thyroid papillary carcinomas, regulate p27Kip1 protein levels and cell cycle. *Endocr Relat Cancer, 14*(3), 791-798. doi:10.1677/ERC-07-0129

Vlachos, I. S., & Hatzigeorgiou, A. G. (2013). Online resources for miRNA analysis. *Clin Biochem, 46*(10-11), 879-900. doi:10.1016/j.clinbiochem.2013.03.006

Vlachos, I. S., Paraskevopoulou, M. D., Karagkouni, D., Georgakilas, G., Vergoulis, T., Kanellos, I., . . . Hatzigeorgiou, A. G. (2015). DIANA-TarBase v7.0: indexing more than half a million experimentally supported miRNA:mRNA interactions. *Nucleic Acids Res, 43*(Database issue), D153-159. doi:10.1093/nar/gku1215

Vogelstein, B., Papadopoulos, N., Velculescu, V. E., Zhou, S., Diaz, L. A., Jr., & Kinzler, K. W. (2013). Cancer genome landscapes. *Science, 339*(6127), 1546-1558. doi:10.1126/science.1235122

Volinia, S., Calin, G. A., Liu, C. G., Ambs, S., Cimmino, A., Petrocca, F., . . . Croce, C. M. (2006). A microRNA expression signature of human solid tumors defines cancer gene targets. *Proc Natl Acad Sci U S A, 103*(7), 2257-2261. doi:10.1073/pnas.0510565103

Vrba, L., Jensen, T. J., Garbe, J. C., Heimark, R. L., Cress, A. E., Dickinson, S., . . . Futscher, B. W. (2010). Role for DNA methylation in the regulation of miR-200c and miR-141 expression in normal and cancer cells. *PLoS One, 5*(1), e8697. doi:10.1371/journal.pone.0008697

Wahlestedt, C., Salmi, P., Good, L., Kela, J., Johnsson, T., Hokfelt, T., . . . Wengel, J. (2000). Potent and nontoxic antisense oligonucleotides containing locked nucleic acids. *Proc Natl Acad Sci U S A, 97*(10), 5633-5638.

Walter, B. A., Valera, V. A., Pinto, P. A., & Merino, M. J. (2013). Comprehensive microRNA Profiling of Prostate Cancer. *J Cancer, 4*(5), 350-357. doi:10.7150/jca.6394
jcav04p0350 [pii]

Wang, H., Chen, H., Zhou, H., Yu, W., & Lu, Z. (2017). Cyclin-dependent kinase inhibitor 3 promotes cancer cell proliferation and tumorigenesis in nasopharyngeal carcinoma by targeting P27. *Oncol Res*. doi:10.3727/096504017X14835311718295

Wang, J., Dong, Y., Wang, X., Ma, H., Sheng, Z., Li, G., . . . Zhou, X. (2010). Expression of EphA1 in gastric carcinomas is associated with metastasis and survival. *Oncol Rep, 24*(6), 1577-1584.

Wang, J., Du, Y., Liu, X., Cho, W. C., & Yang, Y. (2015). MicroRNAs as Regulator of Signaling Networks in Metastatic Colon Cancer. *Biomed Res Int, 2015*, 823620. doi:10.1155/2015/823620

Wang, L. L., Guo, H. H., Zhan, Y., Feng, C. L., Huang, S., Han, Y. X., . . . Jiang, J. D. (2017). Specific up-regulation of p21 by a small active RNA sequence suppresses human colorectal cancer growth. *Oncotarget, 8*(15), 25055-25065. doi:10.18632/oncotarget.15918

Wang, S. T., Ho, H. J., Lin, J. T., Shieh, J. J., & Wu, C. Y. (2017). Simvastatin-induced cell cycle arrest through inhibition of STAT3/SKP2 axis and activation of AMPK to promote p27 and p21 accumulation in hepatocellular carcinoma cells. *Cell Death Dis, 8*(2), e2626. doi:10.1038/cddis.2016.472

Wang, V., & Wu, W. (2009). MicroRNA-based therapeutics for cancer. *BioDrugs, 23*(1), 15-23. doi:10.2165/00063030-200923010-00002

Wang, W. C., Lin, F. M., Chang, W. C., Lin, K. Y., Huang, H. D., & Lin, N. S. (2009). miRExpress: analyzing high-throughput sequencing data for profiling microRNA expression. *BMC Bioinformatics, 10*, 328. doi:10.1186/1471-2105-10-328

Wang, X., Gocek, E., Liu, C. G., & Studzinski, G. P. (2009). MicroRNAs181 regulate the expression of p27Kip1 in human myeloid leukemia cells induced to differentiate by 1,25-dihydroxyvitamin D3. *Cell Cycle, 8*(5), 736-741. doi:7870 [pii]

Wang, Y., Yu, Y., Tsuyada, A., Ren, X., Wu, X., Stubblefield, K., . . . Wang, S. E. (2011). Transforming growth factor-beta regulates the sphere-initiating stem cell-like feature in breast cancer through miRNA-181 and ATM. *Oncogene, 30*(12), 1470-1480. doi:10.1038/onc.2010.531

Wang, Z., Zhang, H., Zhang, P., Dong, W., & He, L. (2016). MicroRNA-663 suppresses cell invasion and migration by targeting transforming growth factor beta 1 in papillary thyroid carcinoma. *Tumour Biol, 37*(6), 7633-7644. doi:10.1007/s13277-015-4653-y

Wark, A. W., Lee, H. J., & Corn, R. M. (2008). Multiplexed detection methods for profiling microRNA expression in biological samples. *Angew Chem Int Ed Engl, 47*(4), 644-652. doi:10.1002/anie.200702450

Watahiki, A., Wang, Y., Morris, J., Dennis, K., O'Dwyer, H. M., Gleave, M., & Gout, P. W. (2011). MicroRNAs associated with metastatic prostate cancer. *PLoS One, 6*(9), e24950. doi:10.1371/journal.pone.0024950
PONE-D-11-04350 [pii]

Weidhaas, J. B., Babar, I., Nallur, S. M., Trang, P., Roush, S., Boehm, M., . . . Slack, F. J. (2007). MicroRNAs as potential agents to alter resistance to cytotoxic anticancer therapy. *Cancer Res, 67*(23), 11111-11116. doi:10.1158/0008-5472.CAN-07-2858

Wellner, U., Schubert, J., Burk, U. C., Schmalhofer, O., Zhu, F., Sonntag, A., . . . Brabletz, T. (2009). The EMT-activator ZEB1 promotes tumorigenicity by repressing stemness-inhibiting microRNAs. *Nat Cell Biol, 11*(12), 1487-1495. doi:ncb1998 [pii]
10.1038/ncb1998

Weng, J., Zhang, H., Wang, C., Liang, J., Chen, G., Li, W., . . . Hou, J. (2017). miR-373-3p Targets DKK1 to Promote EMT-Induced Metastasis via the Wnt/beta-Catenin Pathway in Tongue Squamous Cell Carcinoma. *Biomed Res Int, 2017*, 6010926. doi:10.1155/2017/6010926

Whitney, M. L., Jefferson, L. S., & Kimball, S. R. (2009). ATF4 is necessary and sufficient for ER stress-induced upregulation of REDD1 expression. *Biochem Biophys Res Commun, 379*(2), 451-455. doi:10.1016/j.bbrc.2008.12.079

Wienholds, E., Kloosterman, W. P., Miska, E., Alvarez-Saavedra, E., Berezikov, E., de Bruijn, E., . . . Plasterk, R. H. (2005). MicroRNA expression in zebrafish embryonic development. *Science, 309*(5732), 310-311. doi:10.1126/science.1114519

Wiklund, E. D., Bramsen, J. B., Hulf, T., Dyrskjot, L., Ramanathan, R., Hansen, T. B., . . . Clark, S. J. (2011). Coordinated epigenetic repression of the miR-200 family and miR-205 in invasive bladder cancer. *Int J Cancer, 128*(6), 1327-1334. doi:10.1002/ijc.25461

Wiklund, E. D., Gao, S., Hulf, T., Sibbritt, T., Nair, S., Costea, D. E., . . . Kjems, J. (2011). MicroRNA alterations and associated aberrant DNA methylation patterns across multiple sample types in oral squamous cell carcinoma. *PLoS One, 6*(11), e27840. doi:10.1371/journal.pone.0027840
PONE-D-11-13192 [pii]

Wilson, J. W., Nostro, M. C., Balzi, M., Faraoni, P., Cianchi, F., Becciolini, A., & Potten, C. S. (2000). Bcl-w expression in colorectal adenocarcinoma. *Br J Cancer, 82*(1), 178-185. doi:10.1054/bjoc.1999.0897

Witkos, T. M., Koscianska, E., & Krzyzosiak, W. J. (2011). Practical Aspects of microRNA Target Prediction. *Curr Mol Med, 11*(2), 93-109.

Wong, T. S., Liu, X. B., Wong, B. Y., Ng, R. W., Yuen, A. P., & Wei, W. I. (2008). Mature miR-184 as Potential Oncogenic microRNA of Squamous Cell Carcinoma of Tongue. *Clin Cancer Res, 14*(9), 2588-2592. doi:10.1158/1078-0432.CCR-07-0666

Wu, C., Gong, Y., Yuan, J., Zhang, W., Zhao, G., Li, H., . . . Ge, J. (2012). microRNA-181a represses ox-LDL-stimulated inflammatory response in dendritic cell by targeting c-Fos. *J Lipid Res, 53*(11), 2355-2363. doi:10.1194/jlr.M028878

Wu, C. W., Dong, Y. J., Liang, Q. Y., He, X. Q., Ng, S. S., Chan, F. K., . . . Yu, J. (2013). MicroRNA-18a attenuates DNA damage repair through suppressing the expression of ataxia telangiectasia mutated in colorectal cancer. *PLoS One, 8*(2), e57036. doi:10.1371/journal.pone.0057036

Wu, X., & Watson, M. (2009). CORNA: testing gene lists for regulation by microRNAs. *Bioinformatics, 25*(6), 832-833. doi:10.1093/bioinformatics/btp059

Xi, Y., Nakajima, G., Gavin, E., Morris, C. G., Kudo, K., Hayashi, K., & Ju, J. (2007). Systematic analysis of microRNA expression of RNA extracted from fresh frozen and formalin-fixed paraffin-embedded samples. *RNA, 13*(10), 1668-1674. doi:10.1261/rna.642907

Xie, W., Li, M., Xu, N., Lv, Q., Huang, N., He, J., & Zhang, Y. (2013). MiR-181a regulates inflammation responses in monocytes and macrophages. *PLoS One, 8*(3), e58639. doi:10.1371/journal.pone.0058639

Xie, X., Clausen, O. P., & Boysen, M. (2002). Prognostic significance of p21WAF1/CIP1 expression in tongue squamous cell carcinomas. *Arch Otolaryngol Head Neck Surg, 128*(8), 897-902.

Xu, H., Zhu, J., Hu, C., Song, H., & Li, Y. (2016). Inhibition of microRNA-181a may suppress proliferation and invasion and promote apoptosis

of cervical cancer cells through the PTEN/Akt/FOXO1 pathway. *J Physiol Biochem, 72*(4), 721-732. doi:10.1007/s13105-016-0511-7

Xu, J. Y., Yang, L. L., Ma, C., Huang, Y. L., Zhu, G. X., & Chen, Q. L. (2013). MiR-25-3p attenuates the proliferation of tongue squamous cell carcinoma cell line Tca8113. *Asian Pac J Trop Med, 6*(9), 743-747. doi:10.1016/S1995-7645(13)60130-3

Xu, X. M., Qian, J. C., Deng, Z. L., Cai, Z., Tang, T., Wang, P., . . . Cai, J. P. (2012). Expression of miR-21, miR-31, miR-96 and miR-135b is correlated with the clinical parameters of colorectal cancer. *Oncol Lett, 4*(2), 339-345. doi:10.3892/ol.2012.714

Xu, Y., Ma, H., Yu, H., Liu, Z., Wang, L. E., Tan, D., . . . Wei, Q. (2013). The miR-184 binding-site rs8126 T>C polymorphism in TNFAIP2 is associated with risk of gastric cancer. *PLoS One, 8*(5), e64973. doi:10.1371/journal.pone.0064973
PONE-D-12-21538 [pii]

Yamamichi, N., Shimomura, R., Inada, K., Sakurai, K., Haraguchi, T., Ozaki, Y., . . . Iba, H. (2009). Locked nucleic acid in situ hybridization analysis of miR-21 expression during colorectal cancer development. *Clin Cancer Res, 15*(12), 4009-4016. doi:10.1158/1078-0432.CCR-08-3257

Yan, B., Fu, Q., Lai, L., Tao, X., Fei, Y., Shen, J., . . . Wang, Q. (2012). Downregulation of microRNA 99a in oral squamous cell carcinomas contributes to the growth and survival of oral cancer cells. *Mol Med Rep, 6*(3), 675-681. doi:10.3892/mmr.2012.971

Yan, D., Ng, W. L., Zhang, X., Wang, P., Zhang, Z., Mo, Y. Y., . . . Wang, Y. (2010). Targeting DNA-PKcs and ATM with miR-101 sensitizes tumors to radiation. *PLoS One, 5*(7), e11397. doi:10.1371/journal.pone.0011397

Yan, L. X., Huang, X. F., Shao, Q., Huang, M. Y., Deng, L., Wu, Q. L., . . . Shao, J. Y. (2008). MicroRNA miR-21 overexpression in human breast cancer is associated with advanced clinical stage, lymph node metastasis and patient poor prognosis. *RNA, 14*(11), 2348-2360. doi:10.1261/rna.1034808

Yan, Z. X., Zheng, Z., Xue, W., Zhao, M. Z., Fei, X. C., Wu, L. L., . . . Zhao, W. L. (2015). MicroRNA181a Is Overexpressed in T-Cell Leukemia/Lymphoma and Related to Chemoresistance. *Biomed Res Int, 2015*, 197241. doi:10.1155/2015/197241

Yan-Fang, T., Jian, N., Jun, L., Na, W., Pei-Fang, X., Wen-Li, Z., . . . Jian, P. (2013). The promoter of miR-663 is hypermethylated in Chinese pediatric acute myeloid leukemia (AML). *BMC Med Genet, 14*, 74. doi:10.1186/1471-2350-14-74

Yang, C. C., Hung, P. S., Wang, P. W., Liu, C. J., Chu, T. H., Cheng, H. W., & Lin, S. C. (2011). miR-181 as a putative biomarker for lymph-node metastasis of oral squamous cell carcinoma. *J Oral Pathol Med, 40*(5), 397-404. doi:10.1111/j.1600-0714.2010.01003.x

Yang, C. J., Shen, W. G., Liu, C. J., Chen, Y. W., Lu, H. H., Tsai, M. M., & Lin, S. C. (2011). miR-221 and miR-222 expression increased the growth and tumorigenesis of oral carcinoma cells. *J Oral Pathol Med, 40*(7), 560-566. doi:10.1111/j.1600-0714.2010.01005.x

Yang, S. H., Sharrocks, A. D., & Whitmarsh, A. J. (2013). MAP kinase signalling cascades and transcriptional regulation. *Gene, 513*(1), 1-13. doi:10.1016/j.gene.2012.10.033

Yang, Y., Wang, L. L., Wang, H. X., Guo, Z. K., Gao, X. F., Cen, J., . . . Yu, L. (2013). The epigenetically-regulated miR-663 targets H-ras in K-562 cells. *FEBS J, 280*(20), 5109-5117. doi:10.1111/febs.12485

Yang, Y. L., Yen, C. T., Pai, C. H., Chen, H. Y., Yu, S. L., Lin, C. Y., . . . Lin, S. W. (2015). A Double Negative Loop Comprising ETV6/RUNX1 and MIR181A1 Contributes to Differentiation Block in t(12;21)-Positive Acute Lymphoblastic Leukemia. *PLoS One, 10*(11), e0142863. doi:10.1371/journal.pone.0142863

Yao, Y., Suo, A. L., Li, Z. F., Liu, L. Y., Tian, T., Ni, L., . . . Huang, C. (2009). MicroRNA profiling of human gastric cancer. *Mol Med Rep, 2*(6), 963-970. doi:10.3892/mmr_00000199

Yasui, K., Mihara, S., Zhao, C., Okamoto, H., Saito-Ohara, F., Tomida, A., . . . Inazawa, J. (2004). Alteration in copy numbers of genes as a mechanism for acquired drug resistance. *Cancer Res, 64*(4), 1403-1410.

Yasukawa, M., Fujihara, H., Fujimori, H., Kawaguchi, K., Yamada, H., Nakayama, R., . . . Masutani, M. (2016). Synergetic Effects of PARP Inhibitor AZD2281 and Cisplatin in Oral Squamous Cell Carcinoma in Vitro and in Vivo. *Int J Mol Sci, 17*(3), 272. doi:10.3390/ijms17030272

Yates, L. A., Norbury, C. J., & Gilbert, R. J. (2013). The long and short of microRNA. *Cell, 153*(3), 516-519. doi:10.1016/j.cell.2013.04.003

Yi, C., Wang, Q., Wang, L., Huang, Y., Li, L., Liu, L., . . . Yun, J. P. (2012). MiR-663, a microRNA targeting p21(WAF1/CIP1), promotes the proliferation and tumorigenesis of nasopharyngeal carcinoma. *Oncogene, 31*(41), 4421-4433. doi:10.1038/onc.2011.629

Yip, K. W., & Reed, J. C. (2008). Bcl-2 family proteins and cancer. *Oncogene, 27*(50), 6398-6406. doi:10.1038/onc.2008.307

Yoshino, H., Chiyomaru, T., Enokida, H., Kawakami, K., Tatarano, S., Nishiyama, K., . . . Nakagawa, M. (2011). The tumour-suppressive

function of miR-1 and miR-133a targeting TAGLN2 in bladder cancer. *Br J Cancer, 104*(5), 808-818. doi:bjc201123 [pii]
10.1038/bjc.2011.23

Youlden, D. R., Youl, P. H., Peter Soyer, H., Fritschi, L., & Baade, P. D. (2014). Multiple primary cancers associated with Merkel cell carcinoma in Queensland, Australia, 1982-2011. *J Invest Dermatol, 134*(12), 2883-2889. doi:10.1038/jid.2014.266

Yu, C. C., Chen, Y. W., Chiou, G. Y., Tsai, L. L., Huang, P. I., Chang, C. Y., . . . Lo, W. L. (2011). MicroRNA let-7a represses chemoresistance and tumourigenicity in head and neck cancer via stem-like properties ablation. *Oral Oncol, 47*(3), 202-210. doi:S1368-8375(10)00372-6 [pii]
10.1016/j.oraloncology.2010.12.001

Zang, W., Wang, Y., Wang, T., Du, Y., Chen, X., Li, M., & Zhao, G. (2015). miR-663 attenuates tumor growth and invasiveness by targeting eEF1A2 in pancreatic cancer. *Mol Cancer, 14*, 37. doi:10.1186/s12943-015-0315-3

Zhai, X. F., Fang, F. F., Liu, Q., Meng, Y. B., Guo, Y. Y., & Chen, Z. (2013). MiR-181a contributes to bufalin-induced apoptosis in PC-3 prostate cancer cells. *BMC Complement Altern Med, 13*, 325. doi:10.1186/1472-6882-13-325

Zhang, J., Han, L., Ge, Y., Zhou, X., Zhang, A., Zhang, C., . . . Kang, C. (2010). miR-221/222 promote malignant progression of glioma through activation of the Akt pathway. *Int J Oncol, 36*(4), 913-920.

Zhang, L., Deng, T., Li, X., Liu, H., Zhou, H., Ma, J., . . . Li, G. (2010). microRNA-141 is involved in a nasopharyngeal carcinoma-related genes network. *Carcinogenesis, 31*(4), 559-566. doi:bgp335 [pii]
10.1093/carcin/bgp335

Zhang, L. Y., Ho-Fun Lee, V., Wong, A. M., Kwong, D. L., Zhu, Y. H., Dong, S. S., . . . Fu, L. (2013). MicroRNA-144 promotes cell proliferation, migration and invasion in nasopharyngeal carcinoma through repression of PTEN. *Carcinogenesis, 34*(2), 454-463. doi:10.1093/carcin/bgs346

Zhang, M., Jin, M., Yu, Y., Zhang, S., Wu, Y., Liu, H., . . . Chen, K. (2012). Associations of miRNA polymorphisms and female physiological characteristics with breast cancer risk in Chinese population. *Eur J Cancer Care (Engl), 21*(2), 274-280. doi:10.1111/j.1365-2354.2011.01308.x

Zhang, X., Li, X., Tan, F., Yu, N., & Pei, H. (2017). STAT1 Inhibits miR-181a Expression to Suppress Colorectal Cancer Cell Proliferation through PTEN/Akt. *J Cell Biochem*. doi:10.1002/jcb.26000

Zhang, X., Nie, Y., Du, Y., Cao, J., Shen, B., & Li, Y. (2012). MicroRNA-181a promotes gastric cancer by negatively regulating tumor suppressor

KLF6. *Tumour Biol, 33*(5), 1589-1597. doi:10.1007/s13277-012-0414-3

Zhang, X., Nie, Y., Li, X., Wu, G., Huang, Q., Cao, J., . . . Wei, B. (2014). MicroRNA-181a functions as an oncomir in gastric cancer by targeting the tumour suppressor gene ATM. *Pathol Oncol Res, 20*(2), 381-389. doi:10.1007/s12253-013-9707-0

Zhang, Y., Guo, J., Li, D., Xiao, B., Miao, Y., Jiang, Z., & Zhuo, H. (2010). Down-regulation of miR-31 expression in gastric cancer tissues and its clinical significance. *Med Oncol, 27*(3), 685-689. doi:10.1007/s12032-009-9269-x

Zhang, Y., Zhou, X., Xu, X., Zhang, M., Wang, X., Bai, X., . . . He, P. (2015). Waltonitone induces apoptosis through mir-663-induced Bcl-2 downregulation in non-small cell lung cancer. *Tumour Biol, 36*(2), 871-876. doi:10.1007/s13277-014-2704-4

Zhao, J., Gong, A. Y., Zhou, R., Liu, J., Eischeid, A. N., & Chen, X. M. (2012). Downregulation of PCAF by miR-181a/b provides feedback regulation to TNF-alpha-induced transcription of proinflammatory genes in liver epithelial cells. *J Immunol, 188*(3), 1266-1274. doi:10.4049/jimmunol.1101976

Zhen, Y., Liu, Z., Yang, H., Yu, X., Wu, Q., Hua, S., . . . Fang, W. (2013). Tumor suppressor PDCD4 modulates miR-184-mediated direct suppression of C-MYC and BCL2 blocking cell growth and survival in nasopharyngeal carcinoma. *Cell Death Dis, 4*, e872. doi:10.1038/cddis.2013.376

Zheng, J., Xue, H., Wang, T., Jiang, Y., Liu, B., Li, J., . . . Sun, M. (2011). miR-21 downregulates the tumor suppressor P12 CDK2AP1 and stimulates cell proliferation and invasion. *J Cell Biochem, 112*(3), 872-880. doi:10.1002/jcb.22995

Zhou, B., Li, C., Qi, W., Zhang, Y., Zhang, F., Wu, J. X., . . . Zhai, Q. W. (2012). Downregulation of miR-181a upregulates sirtuin-1 (SIRT1) and improves hepatic insulin sensitivity. *Diabetologia, 55*(7), 2032-2043. doi:10.1007/s00125-012-2539-8

Zhou, Y., Wan, G., Spizzo, R., Ivan, C., Mathur, R., Hu, X., . . . Lu, X. (2014). miR-203 induces oxaliplatin resistance in colorectal cancer cells by negatively regulating ATM kinase. *Mol Oncol, 8*(1), 83-92. doi:10.1016/j.molonc.2013.09.004

Zhu, D. X., Miao, K. R., Fang, C., Fan, L., Zhu, W., Zhu, H. Y., . . . Li, J. Y. (2011). Aberrant microRNA expression in Chinese patients with chronic lymphocytic leukemia. *Leuk Res, 35*(6), 730-734. doi:10.1016/j.leukres.2010.11.005

Zhu, J., He, F., Hu, S., & Yu, J. (2008). On the nature of human housekeeping genes. *Trends Genet, 24*(10), 481-484. doi:10.1016/j.tig.2008.08.004

Zhu, J., He, F., Song, S., Wang, J., & Yu, J. (2008). How many human genes can be defined as housekeeping with current expression data? *BMC Genomics, 9*, 172. doi:10.1186/1471-2164-9-172

Zhu, S., Wu, H., Wu, F., Nie, D., Sheng, S., & Mo, Y. Y. (2008). MicroRNA-21 targets tumor suppressor genes in invasion and metastasis. *Cell Res, 18*(3), 350-359. doi:10.1038/cr.2008.24

Zhu, W., Shan, X., Wang, T., Shu, Y., & Liu, P. (2010). miR-181b modulates multidrug resistance by targeting BCL2 in human cancer cell lines. *Int J Cancer, 127*(11), 2520-2529. doi:10.1002/ijc.25260

Zhu, Y., Wu, J., Li, S., Ma, R., Cao, H., Ji, M., . . . Tang, J. (2013). The function role of miR-181a in chemosensitivity to adriamycin by targeting Bcl-2 in low-invasive breast cancer cells. *Cell Physiol Biochem, 32*(5), 1225-1237. doi:10.1159/000354521

Zhuang, L. K., Xu, G. P., Pan, X. R., Lou, Y. J., Zou, Q. P., Xia, D., . . . Tong, J. H. (2014). MicroRNA-181a-mediated downregulation of AC9 protein decreases intracellular cAMP level and inhibits ATRA-induced APL cell differentiation. *Cell Death Dis, 5*, e1161. doi:10.1038/cddis.2014.130

Zou, C., Chen, J., Chen, K., Wang, S., Cao, Y., Zhang, J., . . . Tang, H. (2015). Functional analysis of miR-181a and Fas involved in hepatitis B virus-related hepatocellular carcinoma pathogenesis. *Exp Cell Res, 331*(2), 352-361. doi:10.1016/j.yexcr.2014.11.007

Zou, C., Li, Y., Cao, Y., Zhang, J., Jiang, J., Sheng, Y., . . . Tang, H. (2014). Up-regulated MicroRNA-181a induces carcinogenesis in hepatitis B virus-related hepatocellular carcinoma by targeting E2F5. *BMC Cancer, 14*, 97. doi:10.1186/1471-2407-14-97

BIODATA OF STUDENT

Yaghma Masood was born in Rampur, India. She was the second child from four siblings. She had primary and secondary education from Abdullah Girls' Senior Secondary School, Aligarh, India. Yaghma Masood is a Dentist and a lecturer at the Department of Dentistry and Oral Health, La Trobe University, Australia. She was graduated with first class in Bachelor of Dental Surgery from Aligarh Muslim University, Aligarh, India in 2005. She received her master's degree with merit in Experimental Oral Pathology in 2007 from Barts and the London, Queen Mary University of London, UK. In 2008, she joined Universiti Teknologi MARA as a Lecturer. Due to her strong interest in research, she continued her further studies for PhD. In 2013, She entrolled in Doctor of Philosophy program at Faculty of Medicine and Health Sciences, Universiti Putra Malaysia. Her research focus in PhD was on the role of microRNAs in head and Neck Cancer. During her candidature, she published one article as first author at international level with impact factor 2.249. She has submitted two more articles for publication. Her other research interests include oral cancer, dental caries and oral health related quality of life. Yaghma is a co-investigator for three research grants for the research projects on oral cancer, dental caries and oral health related quality of life. She has published more than 15 peer reviewed journal articles and book chapters, many of which are in leading journals. He is also a reviewer for many reputed journals including Angle Orthodontics.

LIST OF PUBLICATION

Published Articles

Masood Y., Kqueen CY., Rajadurai P. Role of miRNA in Head and Neck Squamous Cell Carcinoma. 2014. Expert Review of Anticancer Therapy, 2014; 1-15. (ISI Impact Factor 2.279).

Articles with Prepared Manuscript and under Submission

Masood Y., Mohtarrudin N., Subha TS., Rajadurai P., Kqueen CY. Hsa-microRNA-181a-2-3p as biomarker for head and neck cancer in patients: a bioinformatic and clinical study and the therapeutic implication.

Masood Y., Mohtarrudin N., Subha TS., Rajadurai P., Kqueen CY. Hsa-microRNA-663 as biomarker for head and neck cancer in patients: a bioinformatic and clinical study and the therapeutic implication.

UNIVERSITI PUTRA MALAYSIA

STATUS CONFIRMATION FOR THESIS / PROJECT REPORT AND COPYRIGHT

ACADEMIC SESSION : _____

TITLE OF THESIS / PROJECT REPORT :

_____

_____

_____

NAME OF STUDENT : _____

I acknowledge that the copyright and other intellectual property in the thesis/project report belonged to Universiti Putra Malaysia and I agree to allow this thesis/project report to be placed at the library under the following terms:

1. This thesis/project report is the property of Universiti Putra Malaysia.
2. The library of Universiti Putra Malaysia has the right to make copies for educational purposes only.
3. The library of Universiti Putra Malaysia is allowed to make copies of this thesis for academic exchange.

I declare that this thesis is classified as :

*Please tick (√)

☐	**CONFIDENTIAL**	(Contain confidential information under Official Secret Act 1972).
☐	**RESTRICTED**	(Contains restricted information as specified by the organization/institution where research was done).
☐	**OPEN ACCESS**	I agree that my thesis/project report to be published as hard copy or online open access.

This thesis is submitted for :

☐	**PATENT**	Embargo from_____ until _____ (date) (date)

Approved by:

_____	_____
(Signature of Student)	(Signature of Chairman of Supervisory Committee)
New IC No/ Passport No.:	Name:
Date :	Date :

[Note : If the thesis is CONFIDENTIAL or RESTRICTED, please attach with the letter from the organization/institution with period and reasons for confidentially or restricted.]