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Details of the Collaborative Activity

2020-21

Name of the Collaborating Institute: NITTE Deemed to be University, Mangalore, Karnataka, India

Activities:

Student Observership

1. A student (Ms. Farha Fazul) of MHA has undertaken Observer-ship at Justice KS Hegde Charitable Hospital from 7th -28th Sep 2020

- **Joint Research projects:**

1. Challenges at Technology adaption in academic learning among students during Covid-19 lock down at selected institutions of Mangalore.
2. Dr. Neetha Kamath, Niite Usha institute of Nursing Sciences and Mrs, Renita Priya D'Souza, YNC.

- **Joint Publication:**

Shruthi K, Nandakishore B, **Irfan K, Koumar RC**. Repertoires of MicroRNA-30 Family as Gate-keepers in Lung Cancer. *Frontiers in Bioscience-Scholar*. 2021

ATTESTED

Dr.Gangadhara Somayaji K.S.
Registrar
Yenepoya(Deemed to be University)
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Mangalore- 575 018, Karnataka

JKSHCH/MS/ 183 /2020-21

Date: 28.09.2020

CERTIFICATE

This is to certify that Ms. Farha Fazul, III semester MHA student of Yenepoya Medical College has completed 15 days observership from 07.09.2020 to 28.09.2020 at the following departments of our hospital:

a) Dialysis Unit – Compliance to NABH standards

b) HR department – Performance Appraisal

c) Quality Department – Incident Reporting

Major (Dr) Shivakumar Hiremath
Medical Superintendent.

Major (Dr.) Shivakumar Hiremath
Medical Superintendent
Justice K.S. Hegde Charitable Hospital
Medical Science Complex, University Road
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Review

Repertoires of MicroRNA-30 family as gate-keepers in lung cancer

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[2]*Department of Pulmonary Medicine, K S Hegde Medical Academy, Nitte (Deemed to be University), Deralakatte, Mangaluru, 575018 Karnataka, India*
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TABLE OF CONTENTS

1. *Abstract*
2. *Introduction*
3. *MicroRNAS*
4. *miR-30 family*
5. *miR-30 and lung cancer*
    - *5.1 Role of miR-30 in proliferation, cell cycle regulation and apoptosis*
    - *5.2 Role of miR-30 in epithelial-mesenchymal transition (EMT)*
    - *5.3 Role of miR-30 in drug resistance*
    - *5.4 Clinical significance*
    - *5.5 Biomarkers*
6. *Future prospect*
7. *Conclusions*
8. *Author contributions*
9. *Ethics approval and consent to participate*
10. *Acknowledgment*
11. *Funding*
12. *Conflict of interest*
13. *References*

1. Abstract

Lung cancer is a prominent global health issue responsible for the highest fraction of cancer-related mortality. The disease burden has incited the investigation of associated molecular pathways, to explore better therapeutic possibilities. MicroRNAs are extensively studied in recent years for their pivotal role in the regulation of several tumorigenic pathways. MicroRNA-30 (miR-30) family is primarily investigated in case of non-small cell lung cancer (NSCLC) and has been found to play the role of a tumour suppressor. There are six members of miR-30 family: miR-30a, miR-30b, miR-30c-1, miR-30c-2, miR-30d and miR-30e. They regulate several imperative signalling pathways like p53, PI3K/AKT, resulting in the modulation of key carcinogenic events involving cell proliferation, apoptosis, metastasis, epithelial-mesenchymal transition, and drug resistance. Their altered levels are documented in NSCLC tissue and blood samples. They are suggested as biomarkers of disease progression and therapeutic outcomes in lung cancer. They possess immense therapeutic potential in the treatment of lung cancer and combat the emerging problem of drug resistance by modulating prime regulatory axes. However, there are many limitations in the existing studies, and additional research is required for the comprehensive understanding of pathways so that the tumour suppressive potential of miR-30 can be translated into clinical benefits. In this review, we present a deeper understanding of the regulatory role and clinical significance of miR-30 and have emphasized the emerging roles in lung cancer.

Submitted: 9 December 2020 Revised: 4 February 2021 Accepted: 2 March 2021 Published: 3 December 2021

2. Introduction

Lung cancer is the most frequently diagnosed neoplasm, with 2.09 million new cases diagnosed in the year 2018 [1]. Even though the recent statistics by Siegel *et al.* [2] suggests that the death rates associated with lung cancer have decreased, mortality has increased over the years, from 1.59 million deaths in 2012 [3] to 1.76 million in 2018 [1]. Tobacco cigarette smoking (active and passive) is the principal risk factor, with exposure to air pollution, occupational exposure to asbestos, radon, metals, radiation therapy, human immunodeficiency virus (HIV) infection, alcohol consumption, and genetic susceptibility including epigenetics being other causal factors [4, 5]. Non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) are the two main types of lung cancer with NSCLC being the most common. Histologically, squamous cell carcinoma, adenocarcinoma, and large cell carcinoma are the major subtypes of NSCLC. Additionally, the presence of specific DNA mutations (*EGFR*, *ALK* and *ROS1*) allow further molecular classification.

Early-stage detection of NSCLC offers surgical resection as a treatment with most favourable prognosis, and survival rates can reach up to 90% [6]. However, the disease is asymptomatic and is often diagnosed at later stages (stage III/IV) making it difficult to offer any kind of curative treatments with survival rates sinking up to 15% [7]. Treatment modules include surgery, radiation therapy, interventional pulmonology and chemotherapy or a combination of the same. Besides these, immunotherapy seems promising, such as PD-1/PD-L1 inhibitors which include Nivolumab. Pembrolizumab (Keytruda) targeting PD-1 and Atezolizumab (Tecentriq) targeting PD-L1 [6]. The IV stage of lung carcinoma metastasizes to distant organs that include brain, bones, and adrenal glands. High-grade squamous cell and adenocarcinomas have exhibited overexpression of certain genes that include high smooth muscle actin (ACTA), c-MET and focal adhesion kinase (FAK) that regulate type 1 matrix metalloprotease (MMP14) [8].

MicroRNAs (miRNAs) are small RNA molecules which can regulate several target genes, thus regulating complex regulatory pathways. Role of miRNAs is evident in health and disease as observed by growing number of reports [9, 10]. Many miRNAs like miR-21, miR-30, miR-34, miR-210 etc. are studied for their role in carcinogenesis, diagnosis, prognosis, and therapeutic potential in lung cancer [11]. Most importantly, several studies have shown a significant downregulation and tumour suppressive potential of miR-30 family members in lung cancer [12–14]. This review discusses an extensive overview of the current research on the role of miRNAs in lung cancer with a major focus on miR-30 family.

3. MicroRNAS

MicroRNAs (miRNAs) are endogenous, highly conserved, small non-coding RNA molecules involved in the regulation of gene expression [15, 16]. Mature miRNAs are single-stranded RNAs containing 18–25 nucleotides, which are the end products of processed primary and precursor miRNAs [17]. Approximately 1000 nucleotide long primary miRNA (Pri-miRNA) is processed using the microprocessor complex to produce 70 nucleotide long stem-looped precursor miRNA (pre-miRNA) in the nucleus. This pre-miRNA is transported to the cytoplasm using Exportin-5 and processed to mature single stranded miRNA using DICER [18]. With the advent of high throughput techniques, an increasing number of miRNAs are being sequenced. The latest miRBase registers 48,860 mature miRNA sequences from 271 organisms, and human genome encodes for 2,654 of them [19].

Duplex miRNA is loaded on to Argonaute along with other associated proteins comprising the RNA induced silencing complex (RISC). Argonaute proteins form the fundamental component of RISC performing endonucleolytic cleavage of target mRNA based on the guide (miRNA) and target strand (3' UTR of mRNA) complementarity, resulting in gene silencing. Repression of gene expression can also result from translational inhibition if miRNA-mRNA possesses partial complementarity [15, 20]. The canonical pathway for miRNA biogenesis [18] and its mechanism of target inhibition is described in Fig. 1.

Different miRNAs are assembled into families indicating a derivation from a common ancestor. The miRNA family also hint towards similar sequence, secondary structure, and/or shared biological function [16]. Sister miRNAs of the family mostly share conserved seed sequence resulting in the silence of common target genes and hence shared regulatory role. Nevertheless, recent evidence suggests that complementarity may extend beyond seed region (3' end of miRNA) resulting in diverse target profiles for the miRNAs of the same family [21].

Post-transcriptional crosstalk between miRNA and mRNA results in the complex regulation network leading to minimization of transcriptional noise, maintenance of threshold protein or mRNA levels, and/or acting as switch-like repression [22, 23]. These attributes of miRNA have made it relevant in most physiological and pathological conditions, including cancer [24]. The genomic locations of more than half of the miRNA population are at fragile sites signifying its relevance in cancer [25]. The deregulated expression levels of various miRNAs in several cancers have been documented, and they may act as either oncogenes or tumour suppressors depending upon their targets [26]. Also, some miRNAs do possess tissue specificity substantiating their regulatory role in differentiation status and tissue identity, as well as its therapeutic potential [27]

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Supplementary material: Supplementary material associated with this article can be found, in the online version, at https://www.fbscience.com/Scholar/articles/10.52586/S558.

Keywords: Lung cancer; miR-30 family; Biomarker; Therapeutic potential; Signalling pathway; Tumour-suppressor

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LETTER OF ACCEPTANCE

March 19, 2021

Dear author/s: **Shruthi Kanthaje[1], Nandakishore Baikunje[2], Irfan Kandal[3], Chandrahas Koumar Ratnacaram[1,*]**

Affiliation:

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[3]Department of Pulmonary Medicine, Yenepoya (Deemed to be University), University Road, Deralakatte, Mangaluru, Karnataka, India-575018

It's a great pleasure to inform you that, after the peer review process, your article, "**Repertoires of MicroRNA-30 Family as Gate-keepers in Lung Cancer**" has been accepted and considered for publication in **Frontiers in Bioscience-Scholar**.

Thank you for submitting your work to this journal. We hope you submit another articles in future.

Best regards,

Sincerely yours,

Editorial office

Frontiers in Bioscience-Scholar

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NITTE
(Deemed to be University)

ETHICS COMMITTEE
NITTE USHA INSTITUTE OF NURSING SCIENCES

(Established under Section 3 of UGC Act 1956)
Placed under Category 'A' by MHRD, GoI. Accredited with 'A' Grade by NAAC.

NUINS/CON/NU/IEC/2020-21 | 833

09.06.2020

To

Dr. Neetha Kamath,
Associate Professor,
Nitte Usha Institute of Nursing Sciences,
Kotekar Beeri Road, Paneer,
Deralakatte.

Dear Dr. Neetha,

Sub : Protocol titled "Challenges of technology adoption in academic learning among nursing students during COVID 19 lockdown at selected institution of Mangalore."

We have received from you 3 copies each of the following documents:

- Protocol titled "Challenges of technology adoption in academic learning among nursing students during COVID 19 lockdown at selected institution of Mangalore."
- Participant information sheet and Informed Consent.

At the ethics committee meeting held on 09th June 2020 the committee has reviewed and approved the documents supporting the above mentioned study to be carried out under the guidance of the Chief Investigator.

The members who attended this meeting held on 09th June 2020 at which your proposal was discussed, are listed below :

1.	Dr. Vinitha Pai, Professor & Deputy Director of Ph D, Yenepoya Deemed University	:	Chairperson
2.	Dr. Shishir Kumar, Psychiatrist, Dept. of Psychiatry, KSHEMA	:	Member
3.	Dr. Fatima D Silva, Principal, NUINS	:	Member
4.	Dr. Sabitha Nayak, Vice-Principal, NUINS	:	Member
5.	Dr. Jacintha Veigas, Professor, NUINS	:	Member
6.	Dr. Praveen Rai, Assoc. Professor, NUCSER	:	Member
7.	Dr. Nalini M., HOD, Dept. of Psychiatry, NUINS	:	Member
8.	Prof. Sujatha R, HOD, Dept. of Pediatrics, NUINS	:	Member
9.	Sr. Dhanya, Principal, Athena College of Nursing, Mangalore:		Ethicist
10.	Mrs. Meenakshi, MRD, Justice K.S. Hegde Charitable Hospital:		Legal Expert

All members voted for the proposed trial and none of the members voted against the proposed trial.

Yours truly,

Vinitha Rai

Chairperson
Institutional Ethics Committee.

ATTESTED
Dr. Gangadhara Somayaji K S
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University Road, Deralakatte
Mangalore-575 018, Karnataka

TO WHOMSOEVER IT MAY CONCERN

This is to certify that Dr.Neetha Kamath working as an Associate Professor in Nitte Usha Institute of Nursing Sciences. NITTE (Deemed to be University) has collaborated with Mrs. Renita Priya Dsouza working as Assistant Professor in Yenepoya Nursing College, Yenepoya Deemed to be University for the research project titled "Challenges at technology adoption in academic learning among students during the COVID-19 lockdown at selected institutions of Mangalore." from June 2020 onwards till the publication.

19/11/2020

Seal and signature of concerned authority

Principal
Nitte Usha Institute of Nursing Sciences
Deralakatte, Mangalore - 575 018

NITTE USHA INSTITUTE OF NURSING SCIENCES

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No:- YEC-1/2020/036

YENEPOYA ETHICS COMMITTEE - 1

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YEC-1 Approval Letter

Reference: **Protocol no. YEC-1/2020/036 titled, "Challenges at technology adoption in academic learning among students during the COVID-19 lockdown at selected institutions of Mangalore"**

Names of all research team members

No	Name	Role in the research team	Designation/ Affiliation
1	Dr. Devina E Rodrigues	Principal Investigator	Professor, Nursing Research, Father Muller's College of nursing, Mangalore
2	Ms. Renita Priya D Souza	Co-Investigator	Assistant Professor, Child Health Nursing, YNC
3	Dr. Neetha Kamath	Co-Investigator	Professor, Community Health Nursing, Nitte Usha Institute of Nursing Science, Mangalore

It is hereby confirmed that neither the PI nor any of the research team members have participated in the decision making process of YEC-1.

The following YEC-1 member(s) declared a conflict of interest for the protocol and recused themselves.

No	Name	Position in YEC-1	Designation
	None		

The YEC-1 reviewed the protocol and related documents as listed below:

No	Document Name	Version	Date
1	Protocol	2	11-07-2020
2	Participant Information Sheet	2	11-07-2020
3	Informed Consent	2	11-07-2020

YEC-1 hereby approves the protocol no. YEC-1/2020/036 and the related documents as listed above and this approval is valid from 14-07-2020 to 13-01-2021

Any data collected before or beyond the validity period shall be considered as protocol deviation and liable to action.

It is the responsibility of the Principal Investigator to:

1. Provide correct, updated contact details and respond to YEC-1 communications without delay.
2. Adhere to the current regulatory guidelines
3. Adhere to the undertaking signed by the PI.
4. Adhere only to the approved version of protocol (and related documents)
5. Restrict recruitment to the approved sample size of **708**
6. Obtain written approval of YEC-1 before any proposed change in the protocol (amendment) is implemented in the prescribed format **(Ann01/SOP9B/v3)**
7. Report to YEC-1 any deviation from the guidelines/approved version of the protocol without delay (including change in research team members) in the

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prescribed format **(Ann01/SOP11/v3** - Initial report and **Ann02/SOP11/v3** - Detailed report)

8. As per the current regulatory guidelines, report to YEC-1 all serious adverse events in the prescribed format **(Ann01/SOP12 v3** - Onsite SAE and **Ann02/SOP12/v3** - Offsite SAE) and their follow-up actions.
9. Submit continuing review form one month before the end of validity of this approval **(Ann04/SOP10/v3)**
10. Report to YEC-1 an adverse event/change in risk to participants (excluding

All communications with YEC-1 should be sent by email to ethcom@yenepoya.edu.in
YEC-1 functions in accordance with Declaration of Helsinki (2013), National Ethical Guidelines for Biomedical and Health Research Involving Human Participants (2017) and New Drugs and Clinical Trials Rules (2019).
YEC-1 is re-registered with the Office of the Drugs Controller General of India with Re-Registration no. ECR/521/Inst/KA/2014/RR-17 valid from 04/09/2017 to 03/09/2020 and re-recognized by Forum for Ethical Review Committees for Asia and the Western Pacific Region (FERCAP) for a period of 5 years from 26 November 2019.

Dr. Uma Kulkarni
Member-Secretary, YEC-1

Date: 14-07-2020

Secretary
Yenepoya Ethics Committee-1

Important Dates:	
YEC-1 approval:	14-07-2020 to 13-01-2021
Date for continuing review/completion report	13-12-2020

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Joint Memorandum of Understanding (Herein after referred to as "Agreement") is made and executed on **1st January 2021** at Mangalore

Between

YENEPOYA MEDICAL COLLEGE HOSPITAL, (YMCH), Deralakatte, Mangalore – 575 018. **(First Party)** &

MEDICAL SUPERINTENDENT
YENEPOYA MEDICAL COLLEGE HOSPITAL
MANGALORE-575 018

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Major (Dr.) Shivakumar Hiremath
Medical Superintendent
Justice K.S. Hegde Charitable Hospital
Medical Science Complex, University Road
Deralakatte, MANGALORE - 575 018

JUSTICE K.S. HEGDE CHARITABLE HOSPITAL, Deralakatte, Mangalore – 575 018, **(Second Party)**

Collectively referred to as parties

- Oncology treatment requires a holistic approach of surgical, medical and radiation oncology services.
- First party will utilize services of radiation oncology from second party for holistic treatment.
- Second party will offer radiation oncology services to patients of first party.
- Second party will hold consultation service once a week at YMCH on a fixed day and time and participate in treatment plan for oncology patients admitted by first party.
- Second party shall send required documents/information as required under TPA requirements in respect of patients which are referred by first party for Radiation Oncology services.
- First party will upload the preauths for all modes of treatment (Medical, Surgical and Radiation Oncology) including sub-preauths if required.
- Second party will allocate specific time for Patients of first party, for the Radiation Therapy.
- Second party will charge basic package rates as fixed by SAST (Suvarna Arogya Suraksha Trust) subsequent revisions there off to all the patients referred from first party for providing radiation oncology services including the patients who do not come under the Ambit of SAST.
- First party is allowed to deduct 10% on the basic package rate as the package rates fixed by SAST also covers other expenses like investigation charges, travelling allowance, ambulance charges in case of death and discharge medicines.

MEDICAL SUPERINTENDENT
YENEPOYA MEDICAL COLLEGE HOSPITAL
MANGALORE-575 018

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- First party shall be responsible to make the payment of Bills within 30 days from the date of submission of claim by second party i.e. after the completion of fractions of radiation therapy as detailed in RT plan or termination of treatment.
- Both parties have mutually agreed to enter into this agreement for a period of one year from the date of entering into this agreement. The agreement can be extended further upon mutual consent of both parties.
- In case of any dispute or difference in relation to this agreement between parties the same shall be resolved by mutual negotiations with senior management.
- In case the dispute is unresolved, either party has the right to terminate the agreement by giving one month prior notice by means of registered letter or a letter delivered at the office and duly acknowledged by the other party.

First Party
MEDICAL SUPERINTENDENT
YENEPOYA MEDICAL COLLEGE HOSPITAL
MANGALORE-575 018

Second Party
Major (Dr.) Shivakumar Hiremath
Medical Superintendent
Justice K.S. Hegde Charitable Hospital
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Witness:

1.
Asst.Medical Superintendent
Yenepoya Medical College Hospital
Mangalore-575018

2.

Witness:

1.

2.

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