

**AWARD NUMBER: W81XWH-18-1-0444**

**TITLE: Identification of lncRNAs Required for Synthetic Lethal Interactions with Mutant KRAS in Pancreatic Cancer**

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**CONTRACTING ORGANIZATION: University of Mississippi Medical Center**

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# REPORT DOCUMENTATION PAGE

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**1. INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

In pancreatic cancer, mutant RAS is a major oncogenic driver, yet, there is lack of drugs against this oncogenic RAS. Thus, there is an urgent need for identification of novel therapeutic targets associated with mutant RAS in pancreatic cancer. Long non-coding RNAs (lncRNAs) are RNA molecules lacking the coding capacity with molecular weight of > 200 nucleotides in length. Increasing evidence indicates that lncRNAs function as master gene regulators, thus impacting diverse cellular functions and disease processes. We hypothesize that lncRNAs can play an important role in regulating RAS pathway by synthetic lethal interaction with mutant KRAS.

**2. KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Pancreas, cancer, RNA

**3. ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

**What were the major goals of the project?**

*List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.*

1) Screen for synthetic lethal interactions between KRAS and lncRNAs using the genome-wide CRISPR/Cas9-based libraries lncRNA libraries and 2) Functional characterization of candidate synthetic lethal lncRNAs in pancreatic

**What was accomplished under these goals?**

*For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.*

Built on our preliminary studies that we generated two CRISPR/Cas9-based libraries (knockout and activation) were created and we performed genome wide screens using these two libraries to identify lncRNAs which can have synthetic interactions with the mutant KRAS in pancreatic cancer. Those gRNA (guide RNA) clones lost in the lncRNA KO library, or those gRNA clones enriched in the lncRNA activation library, are potential candidates which were examined for further verification. Future studies will validate and characterize these candidate lncRNAs and determine how they are involved in the synthetic lethal interactions with mutant KRAS.

**What opportunities for training and professional development has the project provided?**

*If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. “Training” activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. “Professional development” activities result in increased knowledge or skill in one’s area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.*

none

**How were the results disseminated to communities of interest?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.*

Publications and abstracts were presented

**What do you plan to do during the next reporting period to accomplish the goals?**

*If this is the final report, state "Nothing to Report."*

*Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.*

The project end date was 9/14/2022.

4. **IMPACT:** *Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

**What was the impact on the development of the principal discipline(s) of the project?**

*If there is nothing significant to report during this reporting period, state "Nothing to Report."*

*Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).*

Nothing to report

**What was the impact on other disciplines?**

*If there is nothing significant to report during this reporting period, state "Nothing to Report."*

*Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.*

Nothing to report

**What was the impact on technology transfer?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:*

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report

**What was the impact on society beyond science and technology?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:*

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report

**5. CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, “Nothing to Report,” if applicable:*

**Changes in approach and reasons for change**

*Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.*

No changes to report

**Actual or anticipated problems or delays and actions or plans to resolve them**

*Describe problems or delays encountered during the reporting period and actions or plans to resolve them.*

No problems to report

**Changes that had a significant impact on expenditures**

*Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.*

No changes to report

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

*Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.*

**Significant changes in use or care of human subjects**

No changes to report

## Significant changes in use or care of vertebrate animals

No vertebrate animals were used

## Significant changes in use of biohazards and/or select agents

No changes to report

6. **PRODUCTS:** *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state “Nothing to Report.”*

- **Publications, conference papers, and presentations**

*Report only the major publication(s) resulting from the work under this award.*

[Emerging roles of lncRNAs in the post-transcriptional regulation in cancer.](#)

He RZ, Luo DX, **Mo YY**. Genes Dis. 2019 Feb 11;6(1):6-15. doi: 10.1016/j.gendis.2019.01.003. eCollection 2019 Mar.

[LncRNA IPW inhibits growth of ductal carcinoma in situ by downregulating ID2 through miR-29c.](#)

Deshpande RP, Sharma S, Liu Y, Pandey PR, Pei X, Wu K, Wu SY, Tyagi A, Zhao D, **Mo YY**, Watabe K. Breast

Cancer Res. 2022 Jan 25;24(1):6. doi: 10.1186/s13058-022-01504-4. PMID: 35078502 **Free PMC article.**

[lncRNA RMST Enhances DNMT3 Expression through Interaction with HuR.](#)

Peng WX, Koirala P, Zhang W, Ni C, Wang Z, Yang L, **Mo YY**. Mol Ther. 2020 Jan 8;28(1):9-18. doi:

10.1016/j.ymthe.2019.09.024. Epub 2019 Oct 4. PMID: 31636039 **Free PMC article.**



[Stabilization of UCA1 by N6-methyladenosine RNA methylation modification promotes colorectal cancer progression.](#)

He RZ, Jiang J, Hu X, Lei M, Li J, Luo W, Duan L, Hu Z, **Mo YY**, Luo DX, Peng WX. Cancer Cell Int. 2021 Nov 22;21(1):616. doi: 10.1186/s12935-021-02288-x. PMID: 34809621

**Journal publications.** *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

**Books or other non-periodical, one-time publications.** *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

none

**Other publications, conference papers and presentations.** *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (\*) if presentation produced a manuscript.*

[Emerging roles of lncRNAs in the post-transcriptional regulation in cancer.](#)

He RZ, Luo DX, Mo YY. *Genes Dis.* 2019 Feb 11;6(1):6-15. doi: 10.1016/j.gendis.2019.01.003. eCollection 2019 Mar.

[LncRNA IPW inhibits growth of ductal carcinoma in situ by downregulating ID2 through miR-29c.](#)

Deshpande RP, Sharma S, Liu Y, Pandey PR, Pei X, Wu K, Wu SY, Tyagi A, Zhao D, Mo YY, Watabe K. *Breast Cancer*

Res. 2022 Jan 25;24(1):6. doi: 10.1186/s13058-022-01504-4. PMID: 35078502 **Free PMC article.** 

[lncRNA RMST Enhances DNMT3 Expression through Interaction with HuR.](#)

Peng WX, Koirala P, Zhang W, Ni C, Wang Z, Yang L, Mo YY. *Mol Ther.* 2020 Jan 8;28(1):9-18. doi: 10.1016/j.ymthe.2019.09.024.

- **Website(s) or other Internet site(s)**

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

PubMed

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

none

- **Inventions, patent applications, and/or licenses**

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

none

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- data or databases;

- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

**7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

**What individuals have worked on the project?**

*Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate “no change”.*

Example:

*Name: Mary Smith  
 Project Role: Graduate Student  
 Researcher Identifier (e.g. ORCID ID): 1234567  
 Nearest person month worked: 5*

*Contribution to Project: Ms. Smith has performed work in the area of combined error-control and constrained coding.*

*Funding Support: The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Name: Yin-Yuan Mo  
 No Change



**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.*

**What other organizations were involved as partners?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.*

*Provide the following information for each partnership:*

*Organization Name:*

*Location of Organization: (if foreign location list country)*

*Partner’s contribution to the project (identify one or more)*

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner’s facilities for project activities);*
- *Collaboration (e.g., partner’s staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner’s staff use each other’s facilities, work at each other’s site); and*
- *Other.*

Nothing to Report

## 8. SPECIAL REPORTING REQUIREMENTS

**COLLABORATIVE AWARDS:** *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ebrap.org/eBRAP/public/index.htm> for each unique award.*

**QUAD CHARTS:** *If applicable, the Quad Chart (available on <https://www.usamraa.army.mil/Pages/Resources.aspx>) should be updated and submitted with attachments.*

9. **APPENDICES:** *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*