AWARD NUMBER: W81XWH-20-1-0518

TITLE: Overcoming Hypomethylating Agents' Toxicity and Non-specificity Using an Aptamer-Based Strategy to Correct Aberrant DNA Methylation in Myelodysplastic Syndromes

PRINCIPAL INVESTIGATOR: Annalisa Di Ruscio

CONTRACTING ORGANIZATION: Beth Israel Deaconess Medical Center, Boston, MA

REPORT DATE: July 2021

TYPE OF REPORT: Annual Report

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

1. REPORT DATE
July 2021

2. REPORT TYPE
Annual Report

3. DATES COVERED
01Jul2020-30Jun2021

4. TITLE AND SUBTITLE
Overcoming Hypomethylating Agents’ Toxicity and Non-specificity Using an Aptamer-Based Strategy to Correct Aberrant DNA Methylation in Myelodysplastic Syndromes

5a. CONTRACT NUMBER
W81XWH-20-1-0518

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Annalisa Di Ruscio

E-Mail: adirusci@bidmc.harvard.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Beth Israel Deaconess Medical Center
330 Brookline Avenue
Boston, MA
02215-5491

8. PERFORMING ORGANIZATION REPORT

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR’S ACRONYM(S)

11. SPONSOR/MONITOR’S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
Myelodysplastic Syndromes (MDS) are a heterogeneous group of clonal hematopoietic malignancies leading to Acute Myeloid Leukemia (AML) in approximately 30 percent of the cases and the most common acquired bone marrow failure syndrome primarily among the elderly (older than age 65). Abnormal DNA methylation is the dominant mechanism for tumor suppressor gene silencing in the evolution of MDS to AML. However, the causes behind aberrant DNA methylation remain elusive. The currently approved hypomethylating protocols are based on two drugs: Azacitidine (AZA-CR) and Decitabine (AZA-dCR). Unfortunately, cytotoxic and global non-specific demethylation effects limit their clinical application. In this study, we propose to test an innovative RNA aptamer-based approach to target aberrant DNA methylation and achieve gene-specific demethylation. This approach is based on our previous discovery of an RNA-mediated regulation of DNA methylation. We have shown that RNAs interacting with the DNA methyltransferase 1 (DNMT1) – DiRs, inhibit its activity in a gene-specific manner. In light of this finding, we have developed RNA aptamers binding and inhibiting DNMT1. Herein, we aim to correct DNA methylation pattern globally and selectively using an RNA based approach. Therefore, two specific aims will be pursued: **Aim 1.** To reduce global DNA methylation by DNMT1-specific aptamers and **Aim 2.** To achieve selective demethylation by chimeric DNMT1-specific aptamers.

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
					USAMRMC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**		14	**19b. TELEPHONE NUMBER** *(include area code)*
Unclassified	Unclassified	Unclassified	Unclassified		

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

TABLE OF CONTENTS

	Page
1. Introduction	4
2. Keywords	4
3. Accomplishments	4
4. Impact	10
5. Changes/Problems	11
6. Products	11
7. Participants & Other Collaborating Organizations	13
8. Special Reporting Requirements	14
9. Appendices	14

1 INTRODUCTION:

Two distinct alterations of normal DNA methylation patterns occur in cancer: global hypo-methylation inducing genomic instability, and gene-specific hypermethylation. Myelodysplastic Syndromes (MDS) are a heterogeneous group of clonal hematopoietic malignancies leading to Acute Myeloid Leukemia (AML) in approximately 30 percent of the cases and the most common acquired bone marrow failure syndrome primarily among the elderly (older than age 65). Abnormal DNA methylation is the dominant mechanism for tumor suppressor gene silencing and clonal variation in the evolution of MDS to AML. However, the causes behind aberrant DNA methylation still remain elusive. The currently approved hypomethylating protocols are based on two drugs: Azacitidine (AZA-CR) and Decitabine (AZA-dCR). Unfortunately, cytotoxic and global non-specific demethylation effects limit their clinical application. In this study, we propose to test an innovative aptamer-based approach to target aberrant DNA methylation and achieve gene-specific demethylation in MDS. This approach is based on our previous discovery of an RNA-mediated regulation of the DNA methylation. We and others have shown that RNAs able to interact with the DNA methyltransferase 1 (DNMT1) – DiRs, inhibit its enzymatic activity in a gene-specific manner. In light of this, we have developed RNA aptamers able to bind and inhibit DNMT1. Here, we aim to correct DNA methylation pattern globally and selectively using an RNA based approach. Therefore, two specific aims will be pursued: **Aim 1**. To reduce global DNA methylation by DNMT1-specific aptamers and **Aim 2**. To achieve selective demethylation by chimeric DNMT1-specific aptamers.

2 KEYWORDS:

Myelodysplastic Syndromes, RNA aptamers, DNA methylation, demethylation, RNA therapeutics.

3 ACCOMPLISHMENTS:

What were the major goals of the project?

This proposal builds on the discovery that RNA can control cell type-specific DNA methylation. The ultimate goal of this research is to develop an RNA-aptamer-based platform to control global and gene-specific DNA methylation abnormalities. Introduction of this demethylating strategy will be instrumental in understanding the role of DNA methylation during normal development and disease and it will provide an innovative and targeted therapeutic agent to treat cancer and other conditions triggered by aberrant DNA methylation. Therefore, we propose the following two aims **Aim 1**. *To reduce global DNA methylation by DNMT1-specific aptamers*; **Aim 2**. *To achieve selective demethylation by DNMT1-chimeric aptamers*.

What was accomplished under these goals?

Aim 1. To reduce global DNA methylation by DNMT1-specific aptamers

The DNMT1-specific aptamers previously selected will be transfected in myeloid laboratory cell lines including K562, the MDS cell lines: MDS-92 and MDS-L (1). Expression changes will be evaluated by RNA Sequencing (RNA-Seq) and DNA methylation profile by Whole Genome Bisulfite Sequencing (WGBS). Changes in histone modifications occurring within the affected *loci* will be monitored by Chromatin Immunoprecipitation (ChIP)-Seq using histone marks associated with active promoters and transcriptional activity. Effects on proliferation and differentiation will be assessed in liquid and semi-solid clonogenic assays. These results will be compared to those obtained using the standard hypomethylating agent AZA-CR. Once established, the same approach will be carried out in primary MDS cells.

During the current funding period we have evaluated the DNMT1 specificity of the selected aptamers Ce-49 sh and Ce-10 sh as compared to the DNMT1-bait, by performing comparative binding experiments with the other main members of the DNMT family: DNMT3A and DNMT3B and with the

unrelated chromatin modifier lysine acetyltransferase 5 (KAT5). No significant interaction was recorded between the tested aptamers (that show the same specificity as DNMT1 bait) and the three control proteins (**Figure 1**). These data show that Ce-49 sh and Ce-10 sh have a strong affinity and are specific ligands for DNMT1 with apparent *in vitro* KDs within the nanomolar range.

To dissect the structural and dynamic properties of DNMT1 interaction with the selected aptamers, we conducted *in silico* molecular simulations in explicit waters for 300 nanoseconds (ns) with the parental R5– (DNMT1 bait), Ce-49 sh– or Ce-10 sh–DNMT1 complexes, respectively. The values of the root mean square deviation (RMSD) of the trajectory structures versus the starting models indicate stability of the system during the entire simulation with slightly dissimilar behaviour of the Ce-10 sh–DNMT1. In Ce10 sh–DNMT1, the RMSD values exhibited by either the complex or each individual component were higher to some degree than those observed in R5–DNMT1 and Ce-49 sh–DNMT1 complexes. Additionally, the number of persistent hydrogen bonds within the last 150 ns simulation resulted more stable at the aptamer-protein interfaces for the R5 and Ce-49 sh complexes than the Ce-10 sh-DNMT1 interface. These findings suggest that Ce-10 sh–DNMT1 complex undergoes to greater rearrangement in the time scale used, revealing important structural determinants related to the aptamer sequence and responsible for the stability of the aptamer complexes with the target. These results validate the complex stability and confirm a similar binding modality between the selected aptamers and the parental sequence with DNMT1. Further, the DNMT1-bait and Ce-49 sh and Ce-10-2 sh were unable to interfere *in vitro* with the enzymatic activity of DNMT3A/B, thus confirming the high affinity and selectivity of the aptamers for DNMT1(**Figure 2**).

We also evaluated the transcriptional activation brought about by DNMT1 aptamers in other cell lines in which the *CEBPA* promoter is methylated and the mRNA is expressed at low-to-undetectable levels such as A549, Calu-1, and U937. Upon transfection with the DNMT1-specific aptamers, we observed effective increase of *CEBPA* levels, whereas no changes occurred when the control oligonucleotide was used. As a result of DNMT1 inhibition cell viability was reduced 60 to 40% in Calu-1, A549 and U937.

To estimate the extent of the effect on DNA methylation resulting from the DNMT1-specific aptamers, the genome-scale methylome profile was assessed by the EPIC array platform on K562 cells transfected with Ce-49 sh and Ce-10 sh. The differential methylation analyses revealed significant reduction of DNA methylation across thousands of CpG covered by the array in the aptamer-treated cells as compared to the control. Nearly 16.000 and 14.000 differentially methylated regions (DMRs) were detected for the Ce-49 sh and Ce-10-2 sh samples, respectively with more than 60% overlap between the two (**Figure 3**). Gene ontology (GO) analyses for "biological process" of genes corresponding to the overlapping hypo-methylated CpGs included among the top ranked, GO terms belonging to epigenetic modification, regulation of transcription and gene expression, consistently with the aptamer function. Altogether, our results support the potential use of these newly generated aptamers as a novel approach to block DNMT1 activity, restore the expression of genes silenced by DNA methylation and reduce cell viability of cancer cells.

Aim 2. To achieve selective demethylation by DNMT1-chimeric aptamers

RNA oligonucleotides can be utilized as gene specific demethylating agents. In this aim, we will design DNMT1chimeric aptamers able to: 1) anchor to a specific genomic location and 2) inhibit DNMT1 enzymatic activity. This approach will exploit the ability of RNA to assume triplex RNA-DNA helix structures (2-8).

During this initial funding period, we started designing DNMT1-chimeric aptamers targeting the *CEBPA* locus. The following strategy was adopted in order to deliver the aptamers into the human lung epithelial carcinoma cell line A549. The DNMT1-specific aptamer Ce-49 sh sequence was fused with the gene specific sequence (*targeting region*) in combination with an RNA sequence allowing annealing with an aptamer binding a chosen cell-type specific surface marker (*sticky*), hereafter indicated as Ce-49-SP-sticky. The reasoning behind such design was to evaluate both specificity for the chosen locus and selectivity for the targeted cell type (**Figure 4**). In this experiment, we annealed the

targeting aptamer (GL21.T) recognizing the AXL transmembrane receptor, a surface marker of A549 cells, to the Ce-49-SP-sticky. Our preliminary data demonstrated over two-fold increase of *CEBPA* expression in cells treated (at 400nM) with the targeting CHIMERA (the duplex obtained annealing GL21.T with Ce-49-SP-sticky), as compared to the negative control (a sequence not binding DNMT1) while a moderate increase was observed upon transfection with the Ce-49 sh alone. This observation suggests that in the context of the CHIMERA both, the uptake of the GL21.T targeting aptamer by the AXL-expressing cells and the ability of Ce-49-SP-sticky moiety to inhibit DNMT1 within the *CEBPA* locus and promote mRNA expression, are preserved (**Figure 5**). Notably, cells treated with the CHIMERA exhibited a decrease in cell viability to a lesser extent than cells transfected with the Ce-49 sh alone, hinting to a lower toxicity of the former versus the latter approach.

Currently, a similar approach is ongoing on K562, using two cell specific targeting aptamers GL21.T and Gint4.T, that recognize the respective AXL and the PDFGR beta markers expressed on K562 cell surface and will enable us to define the efficiency of different CHIMERAs.

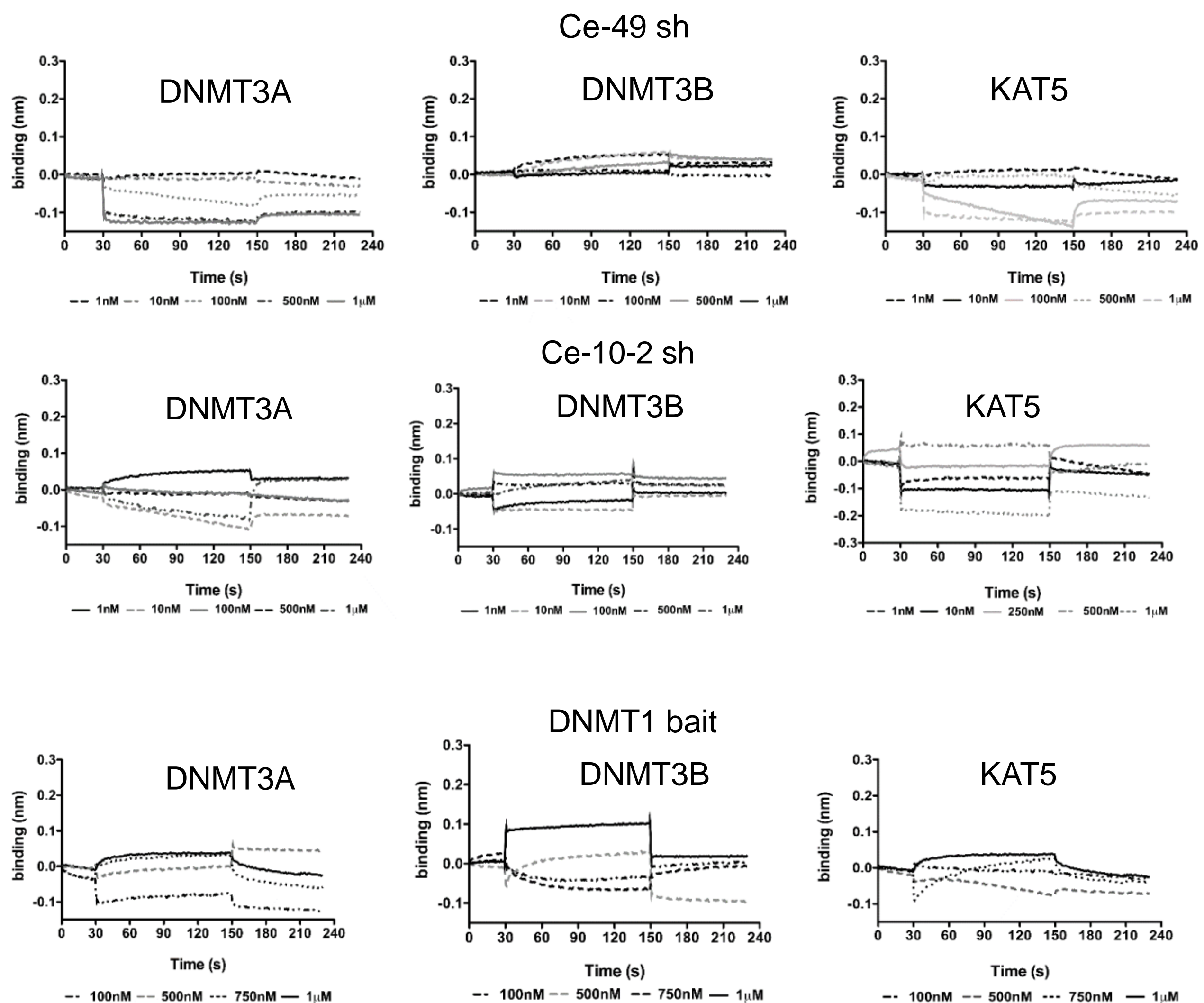

Figure 1. Aptamer specificity. Binding measured by bio-layer interferometry of Ce-49 sh (**upper panel**), Ce-10-2 sh (**middle panel**) and DNMT1 bait (**lower panel**) to DNMT3A, DNMT3B and KAT5 protein immobilized on separate biosensors. Aptamers were tested at the reported concentrations.

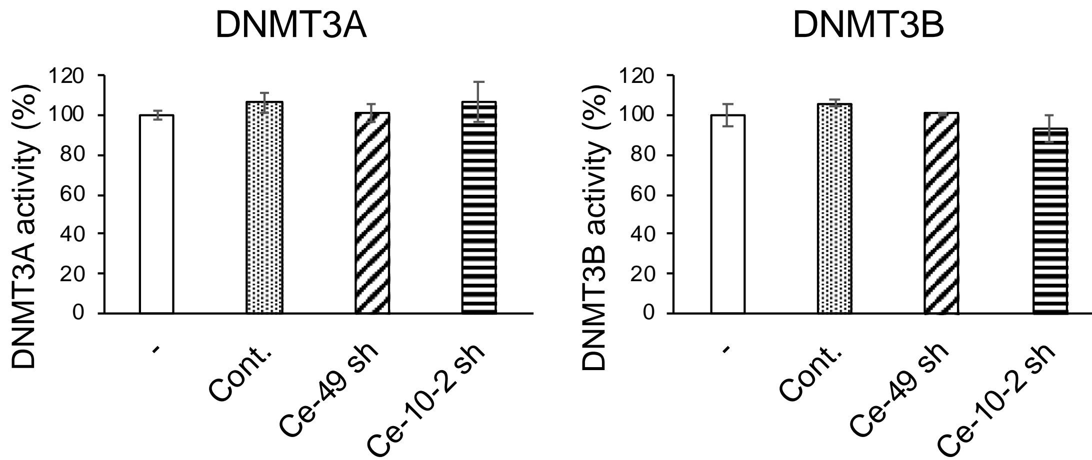

Figure 2. Functional activity. Activity of purified DNMT3A (**left panel**) or B (**right panel**) proteins was analysed in vitro in the absence (-) or in the presence of indicated aptamers and expressed as percentage relative to the activity of DNMT protein alone. Bars depict mean ± SD (n=2).

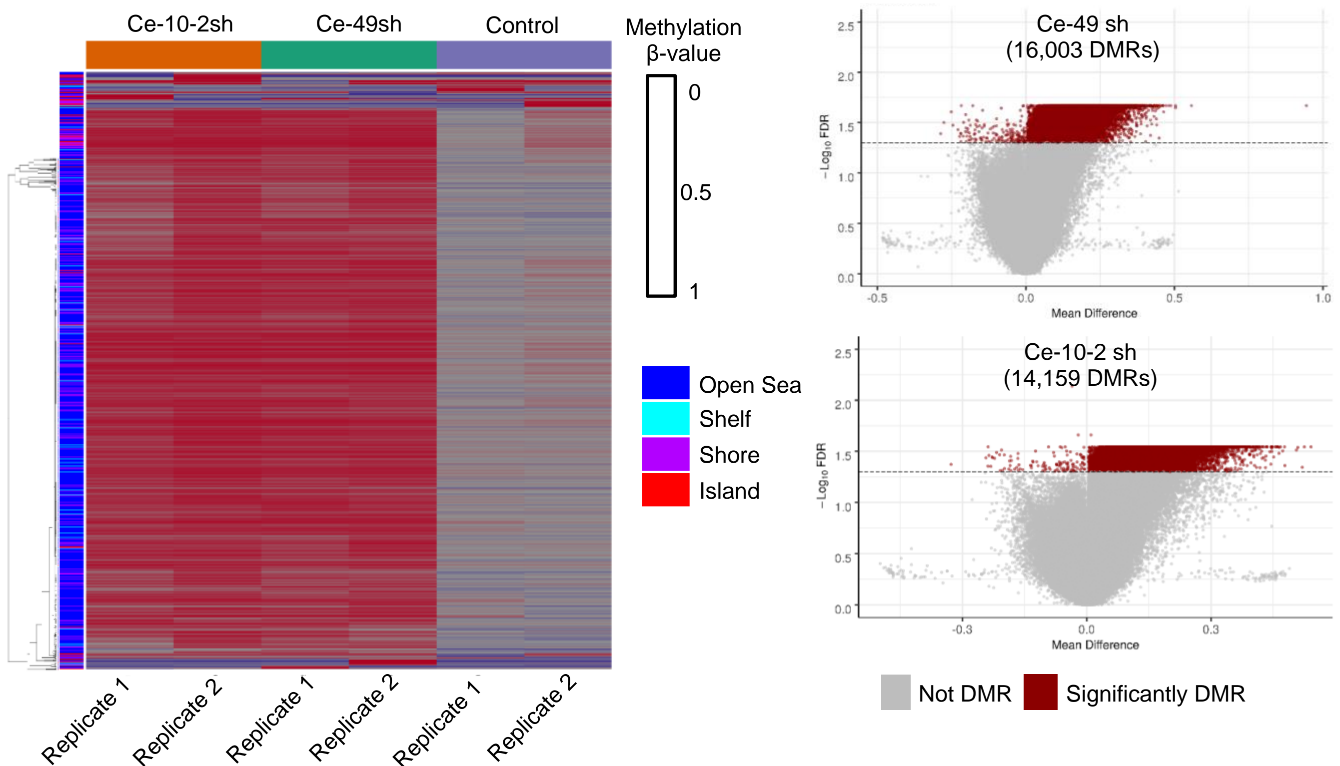

Figure 3. DNA methylation analyses. Heatmap of differentially methylated CpG regions (DMR) in K562 transfected with Ce-49 sh, Ce-10-2 sh or or control (Cont.) aptamers, on the left. Volcano plots on the right, reporting the significant differentially methylated regions (DMRs) for Ce-49 sh (upper panel) and Ce-10-2 sh (lower panel).

GL21.T sticky

Ce-49-SP sticky

Figure 4. Schematic of the aptamer design. xxxx indicates $4xC_3$ carbon linker. The red box indicates the RNA containing 2'F Pyrimidyne (GL21.T). The light purple box indicates the RNA containing 2'F Pyrimidyne and 2'O-methil purines (sticky). The green box indicates the DNA (Gene specific sequence). The blue box indicates the RNA containing 2'F Pyrimidyne (Ce-49 sh).

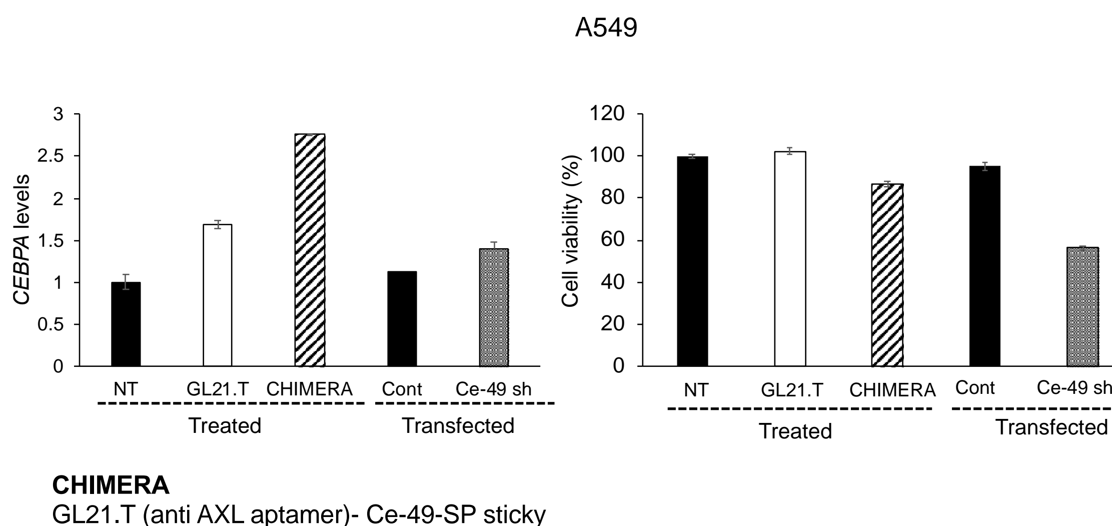

Figure 5. Gene specific activation by DNMT1-chimeric aptamers. *CEBPA* expression upon treatment with the CHIMERA aptamer, as compared to the control (left panel). Cell viability of A549 cells treated or transfected with the indicated aptamers or Cont. after 72 hours. Bars depict mean ± SD (n=2).

References

1. Tsujioka T, Matsuoka A, Tohyama Y, Tohyama K. Approach to new therapeutics: investigation by the use of MDS-derived cell lines. Curr Pharm Des. 2012;18(22):3204-14. Epub 2012/05/11. doi: CPD-EPUB-20120507-014 [pii]. PubMed PMID: 22571700.
2. Lee JS, Burkholder GD, Latimer LJ, Haug BL, Braun RP. A monoclonal antibody to triplex DNA binds to eucaryotic chromosomes. Nucleic Acids Res. 1987;15(3):1047-61. PubMed PMID: 2434928; PMCID: 340507.
3. Hanvey JC, Shimizu M, Wells RD. Intramolecular DNA triplexes in supercoiled plasmids. Proceedings of the National Academy of Sciences of the United States of America. 1988;85(17):6292-6. PubMed PMID: 3413097; PMCID: 281955.

4. Rajagopal P, Feigon J. Triple-strand formation in the homopurine:homopyrimidine DNA oligonucleotides d(G-A)4 and d(T-C)4. Nature. 1989;339(6226):637-40. doi: 10.1038/339637a0. PubMed PMID: 2733796.
5. Yu K, Roy D, Huang FT, Lieber MR. Detection and structural analysis of R-loops. Methods in enzymology. 2006;409:316-29. doi: 10.1016/S0076-6879(05)09018-X. PubMed PMID: 16793409.
6. Ginno PA, Lott PL, Christensen HC, Korf I, Chedin F. R-loop formation is a distinctive characteristic of unmethylated human CpG island promoters. Molecular cell. 2012;45(6):814-25. doi: 10.1016/j.molcel.2012.01.017. PubMed PMID: 22387027; PMCID: 3319272.
7. Perrouault L, Asseline U, Rivalle C, Thuong NT, Bisagni E, Giovannangeli C, Le Doan T, Helene C. Sequence-specific artificial photo-induced endonucleases based on triple helix-forming oligonucleotides. Nature. 1990;344(6264):358-60. doi: 10.1038/344358a0. PubMed PMID: 2156170.
8. Sklenar V, Feigon J. Formation of a stable triplex from a single DNA strand. Nature. 1990;345(6278):836-8. doi: 10.1038/345836a0. PubMed PMID: 2359461.

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

BIDMC expects that all postdocs and grad students supported by NIH funding utilize an Individual Development Plan (IDP) to set academic and career goals and facilitate conversations with their PIs. PIs are encouraged to use whatever format best facilitates the professional development of the postdoc or grad student. BIDMC offers resources to support mentees and PIs in implementing IDPs. Now available for the PIs to use for all postdocs is the annual performance evaluation document which standardizes the review process.

How were the results disseminated to communities of interest?

Nothing to Report

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

a) We will complete RNA sequencing in K562 transfected with the DNMT1-specific aptamers and look at histone modifications. In parallel, we will analyze the effect of the DNMT1-specific aptamers in the MDS cell lines: MDS-92 and MDS-L;
b) We will compare the effect of the DNMT1-specific aptamers with those obtained by approved hypomethylating agent Azacitidine;
c) We will assess the ability of the DNMT1-chimeric aptamer to induce demethylation and expression of *CEBPA* in A549 and K562;
d) We will assess the ability of the DNMT1-chimeric aptamers to induce demethylation and expression of another gene *P15*;
e) We will compare on-target versus off-target effects of the DNMT1-chimeric aptamers.

4 IMPACT:

What was the impact on the development of the principal discipline(s) of the project?
Nothing to Report

What was the impact on other disciplines?
Nothing to Report

What was the impact on technology transfer?
Nothing to Report

What was the impact on society beyond science and technology?
Nothing to Report

5 CHANGES/PROBLEMS:

The project was started on November 2020 due to a delay in the human protocol approval. In addition, recruitment of the post-doctoral fellow was deferred due the COVID 19 pandemic.

Changes in approach and reasons for change
Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them
Nothing to Report

Changes that had a significant impact on expenditures
The project was started on November 2020 due to a delay in the human protocol approval. Recruitment of the post-doctoral fellow was deferred due the COVID 19 pandemic.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Nothing to Report

Significant changes in use or care of human subjects
Nothing to Report

Significant changes in use or care of vertebrate animals
Nothing to Report

Significant changes in use of biohazards and/or select agents
Nothing to Report

6 PRODUCTS:

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

Journal publications.

1) Esposito, C. L., I. Autiero, M. A. Basal, A. Sandomenico, S. Ummarino, M. Borchiellini, M. Ruvo, S. Catuogno, A. K. Ebralidze, V. de Franciscis and **A. Di Ruscio** (2020). "Targeted systematic evolution of an RNA platform neutralizing DNMT1 function and controlling DNA methylation" (*under consideration*)

2) Ummarino S, Hausman C, **Di Ruscio A**. The PARP Way to Epigenetic Changes. Genes (Basel). 2021 Mar 20;12(3):446. doi: 10.3390/genes12030446. PMID: 33804735; PMCID: PMC8003872.
Yes.

3) van der Kouwe E, Heller G, Czibere A, Pulikkan JA, Agreiter C, Castilla LH, Delwel R, **Di Ruscio A**, Ebralidze AK, Forte M, Grebien F, Heyes E, Kazianka L, Klinger J, Kornauth C, Le T, Lind K, Barbosa IAM, Pemovska T, Pichler AS, Schmolke AS, Schweicker CM, Sill H, Sperr WR, Spittler A, Surapally S, Trinh BQ, Valent P, Vanura K, Welner RS, Zuber J, Tenen DG, Staber PB. Core binding factor leukemia hijacks T-cell prone PU.1 antisense promoter. Blood. 2021 May 19:blood.2020008971. doi: 10.1182/blood.2020008971. PMID: 34010414
Yes.

4) Trinh BQ, Ummarino S, Zhang Y, Ebralidze AK, Bassal MA, Nguyen TM, Heller G, Coffey R, Tenen DE, van der Kouwe E, Fabiani E, Gurnari C, Wu CS, Espinosa Angarica V, Yang H, Chen S, Zhang H, Thurm AR, Marchi F, Levantini E, Staber PB, Zhang P, Voso MT, Pandolfi PP, Kobayashi SS, Chai L, **Di Ruscio A**, Tenen DG. Myeloid lncRNA LOUP Mediates Opposing Regulatory Effects of RUNX1 and RUNX1-ETO in t(8;21) AML. Blood. 2021 May 10:blood.2020007920. doi: 10.1182/blood.2020007920. PMID: 33971010
Yes.

Books or other non-periodical, one-time publications.
Nothing to Report

Other publications, conference papers and presentations.

1) Systematic Evolution of an RNA Platform Neutralizing DNMT1 Function" Esposito C. L, Autiero I, Bassal A.M, Sandomenico A, Ummarino S, Borchiellini M, Menotti R, Catuogno S, Ebralidze A, De Franciscis V, Di Ruscio A. **(2020)** *Virtual 6th RNA BIOLOGY SYMPOSIUM.* Virtual conference Singapore. *October 1st-2nd* (Oral Presentation);

2) Systematic evolution of an RNA platform neutralizing DNMT1 function Esposito C. L, Autiero I, Bassal A.M, Sandomenico A, Ummarino S, Borchiellini M, Menotti R, Catuogno S, Ebralidze A, De Franciscis V, Di Ruscio A. **(2020)** *OTS oligo meeting. 16th Annual Meeting of the Oligonucleotide Therapeutics Society.* Virtual conference, September 27th-30th (Poster);

3) An Engineered RNA Platform to Neutralize DNMT1 Function and Control DNA Methylation for Myelodysplastic Syndrome" Esposito C. L, Autiero I, Bassal A.M, Sandomenico A, Ummarino S, Borchiellini M, Menotti R, Catuogno S, Ebralidze A, De Franciscis V, Di Ruscio A. **(2020)** *62nd ASH Annual Meeting and Exposition.* Virtual conference. December 5th-8th (Poster).

- **Website(s) or other Internet site(s)**
  Nothing to Report

- **Technologies or techniques**
  Nothing to Report

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

  Italian Provisional Patent Application No. 102019000019822 (filed on October 2019)
  DNMT1-SPECIFIC APTAMERS AND USES THEREOF which can be found in
  Abstract: Disclosed is a polynucleotide/an oligonucleotide capable of inhibiting DNA methyltransferase 1 (DNMT1) and uses thereof. Also disclosed are methods of treating diseases using the polynucleotide/oligonucleotide and methods of producing the polynucleotide/oligonucleotide thereof.

- **Other Products**
  Nothing to Report

7 PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Annalisa Di Ruscio
Project Role: Principal Investigator
Researcher Identifier (e.g. ORCID ID): 0000-0002-9705-4245
Nearest person month worked: 5
Contribution to Project: Dr. Di Ruscio is overseeing the direction of the project and focusing
Funding Support: This grant, NIH grant R00 and discretionary funds

Name: Alexander K. Ebralidze
Project Role: Key personnel
Researcher Identifier (e.g. ORCID ID): 0000-0001-7081-9343
Nearest person month worked: 0.24

Contribution to Project: Dr. Ebralidze is focusing on the design of DNMT1-specific aptamers and Aim2.
Funding Support: This grant, NIH grant R50

Name: Lucrezia Rinaldi
Project Role: Postdoctoral Fellow
Researcher Identifier (e.g. ORCID ID): 0000-0002-3054-8072
Nearest person month worked: 4.9

Contribution to Project: Dr. Rinaldi is focusing on Aim 1 and 2
Funding Support: This grant

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
On June, 30 2021 the R00 granted to Dr. Di Ruscio was completed

What other organizations were involved as partners?
Nothing to Report

8 SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

Not applicable

9 APPENDICES: