

CONFIDENTIAL

**Report of the Inquiry into the Allegation of
Research Misconduct by Dr. Georgiy Aslanidi**

Submitted to Dr. David Norton, Vice President for Research

July 8, 2016

DIO 6242

Executive Summary

The Inquiry addressed an allegation brought against Dr. Georgiy Aslanidi (Respondent) by Dr. Arun Srivastava, (Complainant), Professor and Division Chief, and Dr. Roland Herzog, (Complainant), Professor, both from the Division of Cellular & Molecular Therapy, Department of Pediatrics, College of Medicine, University of Florida (UF). According to Drs. Srivastava and Herzog, there were falsified and/or fabricated figures in 3 journal articles from 2011 through 2016 (namely Figure 3 in Article 1, Figure 4 in Article 2 and Figure 6 in Article 3) (Page 3745 in Attachment 1a, Page 297 in Attachment 1b, Page 22 in Attachment 1c).

According to the National Institutes of Health (NIH) regulation, 42 Code of Federal Regulations (CFR), Parts 50 and 93 and the UF policy for Dealing with Conduct in Research, “fabrication is making up data or results and recording or reporting them” and “falsification is manipulating research materials, equipment or processes, or changing or omitting data or results such that the research is not accurately represented in the research record”. Further, a finding of research misconduct, according to federal policy and the UF policy requires that: 1) there is a significant departure from accepted practices of the relevant research community; and 2) the misconduct be committed intentionally, knowingly or recklessly; and 3) the allegation be proven by a preponderance of evidence.

Preliminary information-gathering and preliminary fact-finding from the inquiry indicated that:

- Allegations 1, 2 and 3 for Figure 3A in Article 1, Figure 4 in Article 2 and Figure 6 in Article 3 may have substance. Thus, it was determined that these allegations warranted further investigation.
- Allegation 1 for Figure 3B in Article 1 did not have substance. Thus, it was determined that this allegation did not warrant further investigation.

Description of the Allegation: See Attachment 2. A schematic representation of the allegation of fabrication for Figure 3A in Article 1 is provided in Attachment 3.

Name and Position of the Respondent:

Dr. Georgiy Aslanidi, Research Assistant Professor, Department of Pediatrics, College of Medicine, UF.

PHS/NIH Support Information:

Awards referenced in the “Acknowledgements” section of published Articles used in the Inquiry Report.

Allegation 1: This research was supported in part by:

1. The Wistar Institute Consortium Agreement award to UF with prime award P01 HL-078810 from NIH/NHLBI; R. Herzog (PI); Immune Responses to AAV-Mediated Fix Gene Transfer: PROJ 3 Strategies to Prevent Cytotoxic T Lymphocyte Responses to the Transgene Product in Viral Gene Transfer

2. R01 AI051390, NIH/NIAID; R. Herzog (PI) ; Immunology of Factor IX Gene Transfer to Liver
3. R01 HL076901, NIH/NHLBI; A. Srivastava (PI); Human Parvovirus B19 Vectors: Mechanism of Transduction
4. P01 DK058327, NIH/NIDDK; A. Srivastava (PI); Recombinant AAV for Correction of Genetic Abnormalities
5. R01 HL097088, NIH/NHLBI; R. Herzog (Contact PI), A. Srivastava, Guangping Gao, Sergei Zolotukhin; Next Generation of Recombinant AAV Serotype Vectors for Gene Therapy

Allegations 2 and 3: This research was supported in part by:

1. Children's Miracle Network; G. Aslanidi (PI) – Gift awards
2. Children's Miracle Network; Chen Ling (PI) – Gift awards

Applicable Regulations:

1. National Institutes of Health (NIH) regulation, 42 Code of Federal Regulations (CFR), Parts 50 and 93 found at <http://www.admin.ufl.edu/DDD/attach06-07/R10101-0704.pdf> and https://ori.hhs.gov/sites/default/files/42_cfr_parts_50_and_93_2005.pdf.
2. UF Regulation 6C1-1.0101; Policy for Dealing with Conduct in Research found at <http://www.admin.ufl.edu/DDD/attach06-07/R10101-0704.pdf>.

Inquiry Process:

The inquiry process was conducted by Dr. Brandi Ormerod, Associate Professor and Director of Graduate Student Diversity and Professional Development, Department of Biomedical Engineering, College of Engineering, and Dr. Irene Cooke and Mr. Michael Scian, Director and Assistant Director, respectively, of the Division of Research Compliance, Office of Research, UF.

The following steps were taken:

1. Notice of Inquiry was provided to the Respondent on April 8, 2016, and his comments to the Notice of Inquiry were solicited (Attachments 4a and 4b).
2. Review of sequestered information including laboratory notebooks, flow cytometry data, electronic files and folders, and e-mails.
3. E-mail correspondence with Dr. Rao.
4. Discussions with Drs. Srivastava and Herzog.
5. Interview with Dr. Aslanidi on May 13, 2016. The interview was recorded and the recording was provided to Dr. Aslanidi for his review and comment (Attachments 5a and 5b).

Results of the Inquiry Process:

1. Review of sequestered information for Figure 3 in Article 1:

An extensive search of the laboratory note books, flow cytometry data and electronic files that were available yielded no original data, records or images. However, there were laboratory presentations, e-mails, abstracts, posters and powerpoint presentations that contained Figure 3A; some with 3 panels, some with the fabricated 5 panels. A summary of the findings from the review of this information is provided below:

- Figure 3 experiments looked at the adeno-associated virus (AAV)–enhanced green fluorescent protein (EGFP) vector-mediated transduction of primary human monocyte-derived dendritic cells in the presence of nuclear factor kappa-light-chain enhancer of activated B cell (NF-kB) modulators with flow cytometry (Figure 3A) and western blot analyses (Figure 3B) (Page 3745, Attachment 1a).
- The results obtained from the experiments conducted for Figures 3A and 3B were shown in presentations by Dr. Rao at laboratory meetings on June 22, 2009, September 11, 2009 and November 2, 2009 (Slide 38 in Attachment 6a, Slide 39 in Attachment 6b, and Slides 43 and 47 in Attachment 6c). All these

presentations contained Figure 3A with 3 panels. Dr. Jayandharan Rao, was a post-doc for Dr. Srivastava from 2007 to 2009.

- Dr. Rao returned to his home country, India, in December 2009.
- In January 2010, Dr. Srivastava submitted an abstract to the American Society of Gene and Cell Therapy (ASGCT) for their annual conference in May 2010. The abstract contained Figure 3A with 3 panels, similar to the one presented by Dr. Rao at previous laboratory meetings on June 22, 2009, September 11, 2009 and November 2, 2009 (Slide 38 in Attachment 6a, Slide 39 in Attachment 6b and Slide 43 in Attachment 6c). It also contained Figure 3B with portions of the western blot presented by Dr. Rao at the laboratory meeting on November 2, 2009 (Slide 47 in Attachment 6c). The abstract was published in the ASGCT Abstract Booklet (#370 on page S143) (Attachment 7).
- On March 27, 2010, Dr. Srivastava sent a reminder e-mail to Dr. Rao to provide a draft of the article (Attachment 8). This e-mail also contained the statement "*George is repeating the human DC (dendritic cell) experiment*".
- On April 8, 2010, Dr. Srivastava sent an e-mail to Dr. Aslanidi asking him to review an abstract for the upcoming UF Pediatric Science day in May, 2010 (Attachment 9). This abstract was similar to the ASGCT abstract submitted earlier in January 2010 and did not mention cytokines. Dr. Aslanidi replied within an hour on April 8, 2010, with the addition of the statement "*VP-16 as well as cytokines maturation cocktail (TNF-alpha, IL-1beta and PGE2) led to a 19-fold increase in EGFP expression suggesting the involvement of the NF-kB pathway in AAV-mediated transduction*" (Attachment 9a).
- There was a poster (file name = G) with Dr. Aslanidi as the first author, and a powerpoint presentation (file name = Aslanidi G) with Dr. Aslanidi as the author, from Dr. Srivastava's electronic folders dated May 10, 2010 (Attachments 10 and 11). Importantly, both showed Figure 3A with 5 panels and Figure 3B (Slides 13 and 14 in Attachment 11) with portions of the western blot presented by Dr. Rao at the laboratory meeting on November 2, 2009 (Slides 43 and 47 in Attachment 6c).
- On May 12, 2010, Dr. Rao sent the first draft of Article 1 from India to Dr. Srivastava (Attachment 12). Significantly, this draft contained the Figure 3A with 3 panels (Page 35, Attachment 12) as presented by Dr. Rao at previous laboratory meetings on June 22, 2009, September 11, 2009 and November 2, 2009 (Slide 38 in Attachment 6a, Slide 39 in Attachment 6b and Slide 43 in Attachment 6c). It also contained Figure 3B (Page 35, Attachment 12) with portions of the western blot presented by Dr. Rao at the laboratory meeting on November 2, 2009 (Slide 47 in Attachment 6c).
- On July 5, 2010, Dr. Srivastava sent a revised article draft to all co-authors with the Figure 3A with 5 panels (Page 37, Attachment 13) and Figure 3B (Page 37, Attachment 13) with portions of the western blot presented by Dr. Rao at the laboratory meeting on November 2, 2009 (Slide 47 in Attachment 6c).
- This Figure 3A with 5 panels was subsequently repeated in all articles and presentations that contained this Figure 3A.

2. E-mail correspondence with Dr. Rao for Figure 3 in Article 1:

A summary from the e-mail correspondence is provided below:

- Dr. Rao agreed that Figure 3A in Article 1 was fabricated.
- Dr. Rao did not have the expertise to work with dendritic cells (Response 3a, Page 3, Attachment 14).
- In April 2009, Dr. Aslanidi organized a meeting with Drs. Rao and Srivastava to discuss AAV experiments with dendritic cells (Attachment 15).
- Dr. Aslanidi led the group's work with AAV and dendritic cells from April to December 2009 (Response 3c, Page 3, Attachment 14).
- In May 2009, Dr. Aslanidi sent an email to Dr. Rao with a summary of AAV and dendritic cell maturation data (Attachment 16), which appeared as Table 1 in Article 1 (Page 3746 in Attachment 1a). This showed that Dr. Aslanidi worked on AAV-dendritic cell experiments in Fall 2009.
- In addition, in August 2009, Dr. Aslanidi sent another email to Dr. Rao with results of an additional AAV and dendritic cell experiment (Attachment 17). While these results were not included in Article 1, they

were present in the poster (file name = G) (Attachment 10). This showed that Dr. Aslanidi worked on AAV-dendritic cell experiments in Fall 2009.

- In addition, in September 2009, Dr. Aslanidi sent another email to Dr. Rao with results of an additional AAV and dendritic cell experiment (Attachment 18). While these results were not included in the article, poster or powerpoint presentation, it showed that Dr. Aslanidi worked on AAV-dendritic cell experiments in Fall 2009.
- Dr. Rao did not have access to the flow cytometry raw data and software after he returned to India in December 2009 (Response 1 for Figure 3A, Page 4, Attachment 14). Both were needed in order to change the flow cytometry data.
- Dr. Rao did not do any flow cytometric analysis (Attachment 19).

3. Discussions with Drs. Srivastava and Herzog for Figure 3A and 3B in Article 1:

Key points of the discussions with Drs. Srivastava and Herzog are provided below:

- Drs. Srivastava and Herzog stated that Figure 3A in Article 1 was fabricated.
- Dr. Srivastava's expertise is on work with AAV vectors.
- As a post-doc in Dr. Srivastava's laboratory, Dr. Rao worked on AAV vectors in HeLa cells. He did not have dendritic cell or flow cytometry expertise.
- Dr. Aslanidi approached Drs. Rao and Srivastava in March 2009 to discuss experiments with AAV and dendritic cells.
- Dr. Aslanidi acquired AAV expertise as a post doc in Dr. Sergei Zolotukhin's laboratory at UF from 2005-2008. Dr. Aslanidi then acquired dendritic cell expertise as a post doc in Urology at UF from 2008-2010.
- Dr. Aslanidi provided Dr. Srivastava with the figures and tables during the preparation of the article on flash drives rather than via e-mail.
- As a senior investigator, researcher and professor, Dr. Srivastava did not work in the laboratory for the experiments in Article 1.
- Dr. Srivastava understood the principles of flow cytometry but did not know how to run the process.
- Dr. Aslanidi was given first co-authorship on Article 1 because of his extensive contribution with AAV and dendritic cell work.

4. Interview with Dr. Aslanidi (Attachment 5):

Key points of the interview with Dr. Aslanidi are provided below.

For Figure 3 in Article 1:

- Dr. Aslanidi agreed that Figure 3A in Article 1 was fabricated.
- Dr. Srivastava had not worked in the laboratory for many years.
- Dr. Aslanidi's only initial contribution in 2009 was to provide "monocytes derived dendritic preps" (Attachment 4b).
- Dr. Aslanidi produced Figure 2 and Table 1 for Article 1 in Fall 2010, after initial reviews of Article 1 for publication recommended that additional experiments be conducted (Attachments 4b and 5a, and Pages 3745 and 3746 in Attachment 1a).
- Dr. Aslanidi was provided Figure 3A with 5 panels and Figure 3B for his poster (Attachment 10) and powerpoint presentation (Slides 13 and 14 in Attachment 11) in May 2010 but did not remember who provided them.
- There were many other AAV and dendritic cell experiments that were conducted but not included in Article 1 (Attachment 4b).
- Dr. Aslanidi did not conduct the flow cytometry experiments for Figure 3A.
- Dr. Aslanidi did not have flow cytometry expertise prior to 2011, but stated that there were people to ask for help and he could have done this prior to 2011.

- Dr. Aslanidi added the “Cytokine” statement in the UF Pediatric Science Day abstract to indicate that cytokines are required to stimulate immature dendritic cells to mature cells (Attachment 9).
- Dr. Aslanidi had a language barrier early in his career.
- Dr. Rao was not involved in the preparation of dendritic cells.

For Figure 4 in Article 2 and Figure 6 in Article 3:

- Dr. Aslanidi stated that the so called “range of exposure” was actually minimum and maximum intensity of bioluminescence in photons emitted per second per cm² (Page 297 in Attachment 1b and Page 22 in Attachment 1c).
- Dr. Aslanidi agreed that cutting off the numbers in the figures in Articles 2 and 3 was probably a mistake, but the intensity of the bioluminescence signal was shown by color in both figures (Page 297 in Attachment 1b and Page 22 in Attachment 1c).
- Dr. Aslanidi stated that readers could infer bioluminescence by color using the description in the figure caption for Figure 4 in Article 2 and in the scale depicted in Figure 6 of Article 3 along with the associated figure caption (Page 297 in Attachment 1b and Page 22 in Attachment 1c).

Conclusion of the Inquiry Process:

For Figure 3A in Article 1:

Drs. Rao, Srivastava, Herzog and Aslanidi all agreed that Figure 3A in Article 1 was fabricated. Thus, the allegation has substance and warrants further investigation. However, while it appeared that the fabrication was first seen in the poster (file name = Aslanidi G) and powerpoint presentation (file name = Aslanidi G) dated May 10, 2010, it is not clear at this time, who was responsible for this fabrication. This warrants additional investigation.

For Figure 3B in Article 1:

It was determined that the while the western blot presented in Dr. Rao’s November 22, 2009, laboratory presentation was not shown in its entirety in Figure 3B in Article 1, the western blot bands that were presented were the same as that in the laboratory presentation. Thus, the allegation does not have substance and does not warrant further investigation.

For Figure 4 in Article 2 and Figure 6 in Article 3:

Minimum and maximum bioluminescence intensities can be affected by background, binning, focal stop and exposure time settings. Varying these parameters could influence the appearance of size of a tumor, yet information about these parameters was not provided in the figure captions or the methods section of Articles 2 or 3. Further, information about the signals and details about how these settings were controlled across images taken weeks apart was also not presented in the methods section of either article. Additionally, for Figure 6 in Article 3, discrepancies in the manuscript confuse which cancer cell type the mice were injected with, the long-time intervals between when groups imaging sessions require a careful description of imaging parameters given that bioluminescent intensities are compared and the lack of labeling on the graphs in Figure 6B bring into question whether separate mice or regions within the same mice were imaged. Although variable imaging settings may be standardized in the photons emitted per second per cm² settings used in the articles, all of these reasons warrant additional investigation.

Charges to Consider for the Investigation:

1. Determine who fabricated Figure 3A in Article 1.
2. Determine whether Figure 4 in Article 2 and Figure 6 in Article 3 were fabricated or falsified.
3. Determine whether the allegations meet the definition of research misconduct; in this case, fabrication or falsification.

4. Determine whether there was a significant departure from the accepted practices of the relevant research community.
5. Determine whether the fabrication or falsification (if present) was unintentional or intentional, knowing or reckless based on the facts of the case.
6. Determine whether the allegation can be proven by a preponderance of evidence.

Figure 3 Retraction:

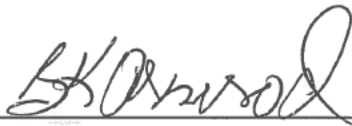
Dr. Srivastava is already collaborating with the PNAS journal to either retract Figure 3 or the entire article, depending on what is feasible. In addition, it is recommended that Figure 3A be corrected wherever it has been published (e.g. videos/ PubMed, etc.).

Submitted by the Inquiry Committee Members (in alphabetical order) on July 8, 2016.



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