

# Fraud in Science

The case of Dong-Pyou Han

Han *et al. Retrovirology* 2012, **9**(Suppl 2):P362  
<http://www.retrovirology.com/content/9/S2/P362>



RETROVIROLOGY

**POSTER PRESENTATION**

**Open Access**

# Eliciting broadly neutralizing antibodies against HIV-1 that target gp41 MPER

D Han<sup>3</sup>, H Habte<sup>3</sup>, Y Qin<sup>3</sup>, K Takamoto<sup>1</sup>, C LaBranche<sup>2</sup>, D Montefiori<sup>2</sup>, MW Cho<sup>3\*</sup>

*From* AIDS Vaccine 2012

Boston, MA, USA. 9-12 September 2012



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### Background

The membrane-proximal external region (MPER) of HIV-1 gp41 is highly conserved and is targeted by broadly neutralizing antibodies (bnAbs). Thus, it is an attractive target for AIDS vaccine development. Here, we describe a mini-protein that can induce bnAbs in rabbits.

- Highly conserved region of gp41
- Targeted by broadly neutralizing antibodies (bnAbs)
- Attractive target for AIDS vaccine



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### Methods

We generated a mini-protein that is structurally rigid, yet efficiently recognized by 2F5, 4E10 and Z13e1. It contains the C-terminal 54 a.a. of gp41 ectodomain (gp41-54Q), which includes the HR2 and the MPER. A 6xHis tag at the C-terminus was used to attach gp41-54Q to Zn-chitosan, which served as an antigen carrier/adjuvant. Rabbits were immunized subcutaneously, 4 times, using two different schedules (wks 0, 4, 9 and 16 vs. 0, 8, 16 and 24). A total of 9 animals were immunized with gp41-54Q in 3 independent experiments. Antibody responses were evaluated by ELISA and in neutralization assays using both TZM-bl and A3R5.7 cells.

- Creation of a structurally rigid mini-protein (gp41-54Q)
- Subcutaneous immunization of rabbits using different schedules (fast and slow)
- Evaluation: ELISA and neutralization assays



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### Results

Eight of nine rabbits mounted bnAbs (89%). Neutralizing activity was observed against all but two of 44 viruses evaluated to date, including 27 Tier 2 viruses from clades A, B, C, D, AE, and CRF02\_AG. Although Nabs could be detected after three immunizations, a fourth immunization was necessary for maximum neutralizing activity. The slower immunization regimen induced higher Nab titers, suggesting that longer rest periods improve affinity maturation. Neutralization inhibition analyses using various peptides identified one neutralizing epitope (N671, W672, F673 and D674) that overlaps with those recognized by Z13e1, 4E10 and 10E8 mAbs. Based on antibody absorption assays, there might be other non-linear epitopes. We are in the process of generating rabbit mAbs for more detailed analyses.

- 89% of the rabbits mounted bnAbs
- Maximum neutralizing activity after 4<sup>th</sup> immunization
- Slow immunization → higher titers of neutralizing antibodies.



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### Conclusion

We have successfully demonstrated that we can reproducibly induce bnAbs in rabbits using a mini-protein containing gp41 MPER. These results suggest that gp41 can be a promising vaccine immunogen.



Results lead to \$19  
million governmental  
research grants



## January 2013:

- External collaborator detects human antibodies (AB) in rabbit sera samples
- Dr. Michael Cho (direct supervisor of Han) reports misconduct findings to the Research Integrity Officer (RIO) of Iowa State University (ISU)
- Identity of delinquent is unknown



## February 2013:

- Dr. Cho provides evidence of spiked rabbit serum samples to RIO
- Office of Research Integrity (ORI) is informed about possible misconduct involving National Institute of Health funded research
- Identity of delinquent is still unknown



## February to August 2013:



- Multiple test have been performed to identify the delinquent



## August 2013:

- RIO is informed about evidence identifying Dr. Dong-Pyou Han as main suspect
- 8<sup>th</sup> August: The inquiry begins

## Allegations:

- Spiking samples of serum from rabbits immunized with gp41-54Q with human HIV ABs (starting 2009!)
- Spiking samples of serum from rabbits immunized with gp41-54Q with rabbit gp120 ABs
- Changing data in files of neutralization experiments to make it appear that rabbits immunized gp41-54Q and LAB gp41-64 produced bnAbs

22<sup>nd</sup> August 2013:

- Han confesses verbally
- A signed statement was provided by Han in October 2013

Research Misconduct Complaint (RMC) #002

To Dr. Charlotte Bronson

I (Dong Pyou Han) confess my misconducts on my research as indicated on the attached files. I am very ashamed myself about my misconduct. I did two kinds of my misconducts. First, in order to investigate a neutralizing activity of rabbit sera to , I sent the wrong samples that were added human or rabbit sera with a neutralizing activity as indicated in the attached file 1. Second, I have manipulated the data about a neutralizing activity. When I did the neutralizing assay with the non-spiking samples that are shown the neutralizing activity in the attached file 1, they have a weakly or no neutralizing activity. But, I manipulated their activity increased highly in order to look better as shown in the attached file 2. Now, I do not have the original files (data), which are stored in the computer files connected to an assay instrument (Bio-Tek).

The problem starts from the first samples that I sent to on 8/11/09. I found the samples were something wrong later. I have thought those samples were contaminated with human sera with a neutralizing activity. Because I worked the rabbits sera and human sera (CWRU4) at the same time though I do not remember the date, may be some samples were contaminated (mixed). Though later I found some samples were wrong and the data were from the wrong samples, I could not tell to Michael Cho. At that time, I was afraid of because the data were presented to our collaborators and others, and I hoped/expected other derivatives will be elicited a neutralizing activity. So, in order to show the neutralizing activity continuously I added the human sera with a neutralizing activity to the second samples that I sent to as indicated in the attached file 1. However, I falsified only

samples that showed some activity because I wanted them to look better. The abstract and presentation, which included the falsified or spiked samples' data, is included in the attached file 3.

I have regretted deeply the fact that I did and did not tell it. I was foolish, coward, and not frank. My misconduct is not done in order to hurt to someone. All cause by my foolishness and are my faulty and responsibility. I will resign with my responsibility about my misconduct.

September 30, 2013  
Han, Dong Pyou

Oct. 3, 2013  


Witnessed by:  
Charlotte R. Bronson Charlotte R. Bronson 10-3-13  
Dawn Brads-Pruce  10-3-2013

## The confession:

- He recognized that something was wrong with the samples, but did not pass this information
- Fraud started already in 2009 to cover up a sample mix up (at Case Western Reserve University (CWRU))
- Working with rabbit and human sera at the same time (contamination, mix up)
- According to him, he only spiked samples that showed neutralizing activity before spiking them
- He is ashamed about misconduct
- Was not done in order to hurt someone

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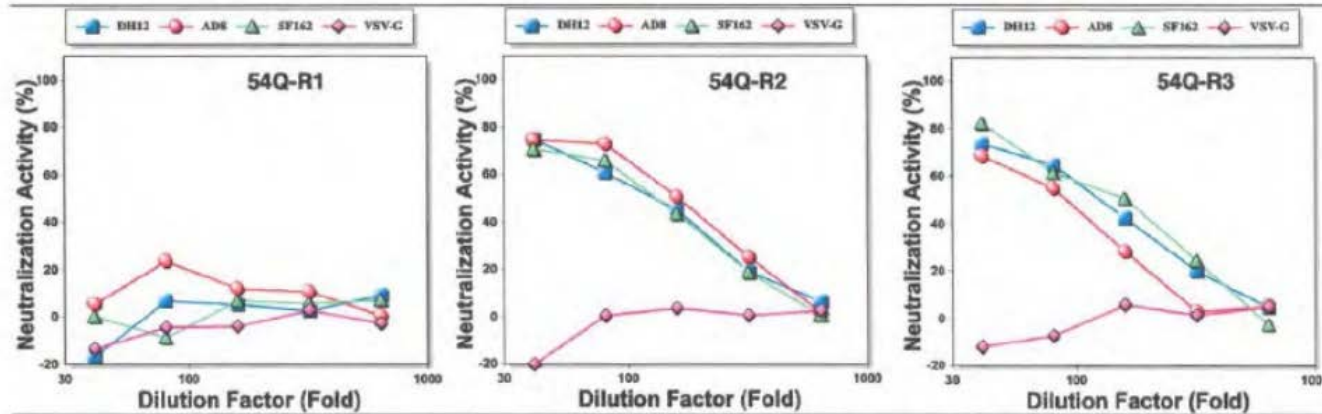
Witnessed by:  
Charlotte R. Bronson Charlotte R. Bronson 10-3-13  
Dawn Bradschauer DB 10-3-2013

*[Handwritten signature]*

Samples No	Immunogen	Notes	Person in Charge	hAb	Sent to	What was done to samples
1	gp41-54Q(T)	"Normal" (CWRU)	Doug	3/3 (Moderate)	Yes	Add human sera w NA to samples.*
2	gp41-54Q(T)	"Rapid" (CWRU)		3/3 (Low)		I am not clear about this sample. Or, nothing.
3	gp41-54Q(T)	in PBS (CWRU)		3/3 (Very Low)		I am not clear about this sample. Or, nothing.
4	gp41-54Q(T)	Repeat of "Normal"		2/3 (Moderate)	Yes	Add human sera w NA to samples.
5	gp41-54Q(T)	"Slow" immunization		3/3 (High)	Yes	Add human sera w NA to samples.
6	gp41-54Q(T)	50 µg (Low dose)		2 of 3	Yes (TBD)	Add rabbit gp120 Abs w NA to samples.**
7	gp41-54Q(T)	3rd repeat of "Normal"		2 of 3	Yes (TBD)	Add rabbit gp120 Abs w NA to samples.
8	gp41-54Q(T)	Repeat of "Slow"		2 of 3	Yes (TBD)	Add rabbit gp120 Abs w NA to samples.
9	gp41-54Q	Untrypsinized (with Tag)		No		No
10	HR1-54Q	(CWRU)		No	Yes	No
11	HR1-54Q	(BSU)		1 of 3	Yes	Add human sera w NA to samples.
12	54Q-OG(T)	"O group" sequence		1 of 3	Yes	Add human sera w NA to samples.
13	54Q(T) & 54Q-OG	Mixture		No		No
14	54Q(T) & E659D	Mixture		No		No
15	gp41-54Q(T)	Polyanhydride		No		No
16	gp41-54Q(AD8)	AD8 sequence		No		No
17	54Q-GHC	"High dose"-Zn-Chitosan		No		No
18	54Q-GHC	50 nm GNP		2/3 (High)	Yes	Add rabbit gp120 Abs w NA to samples.
19	54Q-Cys(T)	10 nm GNP		No		No
20	54Q-Cys(T)	50 nm GNP		1 of 3		Increase NA when manipulated the data.
21	Cys 54Q(T)	50 nm GNP		1 of 3		Increase NA when manipulated the data.
22	54Q-Cys(T)	PBS		No		No
23	54Q-GHC	Repeat 50 nm GNP		1 of 3	Yes (TBD)	Add rabbit gp120 Abs w NA to samples.
24	P4671/gp41-54Q-GHC	50 nm GNP		No		No
25	54Q-GHC	Zn-Chitosan		1 of 3	Yes (TBD)	Add rabbit gp120 Abs w NA to samples.
26	54Q-GHC	2nd repeat 50 nm GNP		2 of 3	Yes (TBD)	Add rabbit gp120 Abs w NA to samples.
27	gp120-OD	Zn-Chitosan		3/3 (not broad)	Yes	No
28	gp120-ODx3	Zn-Chitosan		3/3 (not broad)	Yes	No
29	gp120	Zn-Chitosan		3/3 (not broad)	Yes	No
30	gp120-OD-HR1-64	Zn-Chitosan		3/3 (not broad)	Yes	No

- Han provides lists, how samples have been manipulated

## NA of Rabbit Sera immunized w 54Q/Slow

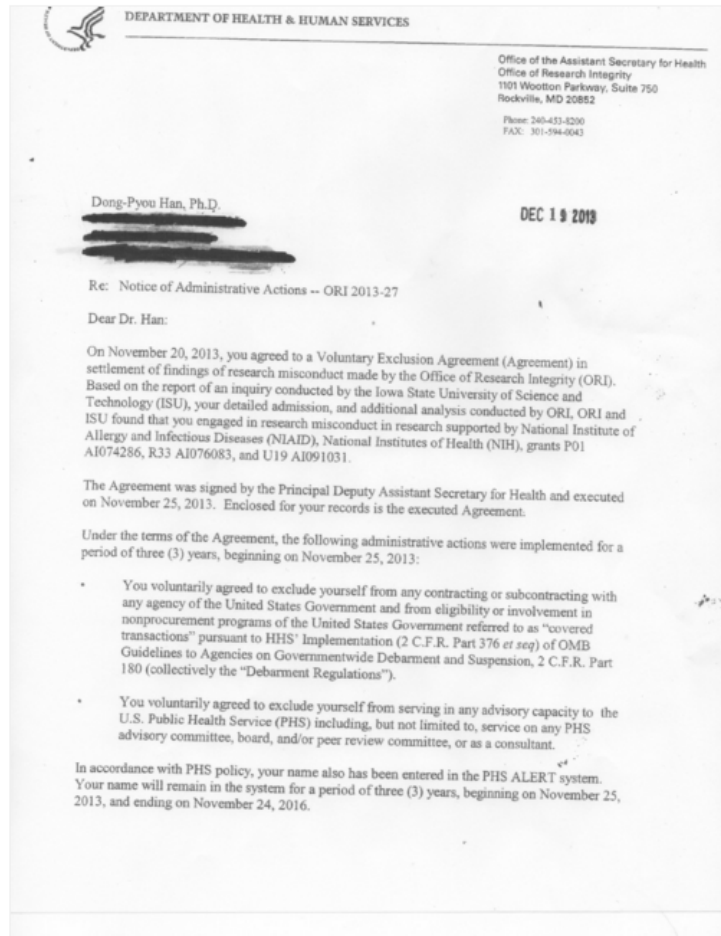


Samples No.	Immunogen	Notes	Person in Charge	baAb	Sent to	What was done to samples
7	gp11-54Q(T)	3rd repeat of "Normal"		2 of 3	Yes (TBD)	Add rabbit gp120 Abs w NA to samples.
8	gp41-54Q(T)	Repeat of "Slow"		2 of 3	Yes (TBD)	Add rabbit gp120 Abs w NA to samples.
9	gp11-54Q	Untrypsinized (with Tag)		No	No	

## Publishing of falsified data:

- 3 conference presentations
  - Keystone Symposia 2010, Banff, Canada
  - AIDS Vaccine 2011, Bangkok, Thailand
  - AIDS Vaccine 2012, Boston, USA
- 6 progress reports (2010-2012)
- 1 funded grant application
- 2 submitted grant applications
- 4 oral presentations at workshops and meetings





## December 2013:

- Exclusion of Han from participating in governmental funded research for in total three years



**RETRACTION**

**Open Access**

**Retraction:** eliciting broadly neutralizing  
antibodies against HIV-1 that target gp41 MPER

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**Retraction**

This poster presentation [1] has been retracted on request of the author Michael W Cho. The Office of Research Integrity at the US DHHS has determined that the first author Dong-Pyou Han committed research misconduct and the poster was prepared based on falsified data [2].

February 2014:

- Dr. Michael Cho requests the retraction of the poster presentation ( published in September 2009)

U.S. Department of Health & Human Services

**ORI** THE OFFICE OF RESEARCH INTEGRITY

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**Case Summary: Han, Dong-Pyou**

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Office of the Secretary  
Findings of Research Misconduct

AGENCY: Office of the Secretary, HHS.  
ACTION: Notice.  
SUMMARY: Notice is hereby given that the Office of Research Integrity (ORI) has taken final action in the following case:

Dong-Pyou Han, Ph.D., Iowa State University of Science and Technology: Based on the report of an inquiry conducted by the Iowa State University of Science and Technology (ISU), a detailed admission by the Respondent, and additional analysis conducted by ORI, ORI and ISU found that Dr. Dong-Pyou Han, former Research Assistant Professor, Department of Biomedical Services, ISU, engaged in research misconduct in research supported by National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), grants P01 AI074286, R33 AI076083, and U19 AI091031.

ORI and ISU found that the Respondent falsified results in research to develop a vaccine

## February 2014:

- Case summary is published online by ORI.
- Containing Han's actions of misconduct and terms of agreement with the government

The case of Dong-Pyou Han probably would have ended there, but...



Senator Charles Grassley, photo by Scott Applewhite

## February 2014:

- Senator Charles Grassley evinces doubt of the severeness of Han's penalty
- He indicates, that also lifetime funding bans can be issued



<http://www.cbsnews.com/news/scientist-dong-pyou-han-sentenced-prison-for-aids-research-fraud/>

## June 2014:

- After extensive media coverage of the case and furthermore, the public reaction of Senator Grassley:
  - Federal prosecutor pressed charges against Han
  - Han was arrested and the case brought before a grand jury



<http://www.washingtontimes.com/news/2014/jul/1/scientist-due-in-court-in-phony-aids-research-case/>

## February 2015:

- Han pled guilty to making false statements to receive NIH research grants

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NATURE | NEWS


## US vaccine researcher sentenced to prison for fraud

The case of Dong-Pyou Han illustrates the uneven nature of penalties for scientific misconduct.

Sara Reardon

01 July 2015 Updated: 01 July 2015


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Biomedical scientist Dong-Pyou Han (centre) confessed to fabricating and falsifying data on an HIV vaccine.

Charlie Neibergall/AP/REX

**The quiet revolutionary**



How the co-discovery of CRISPR explosively changed Emmanuelle Charpentier's life

The microbiologist spent years moving labs and relishing solitude. Then her work on gene-editing thrust her into the scientific spotlight.

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**Lost in space**



1<sup>st</sup> Juli 2015:

- Sentenced to **57 months** in prison
- Has to pay a **US\$7,2 million** fine
- **3 years** of supervised release



Thank you for your attention!

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