Report

GISAID-ISIRV-WHO Training Workshop

Genetic Analyses of Influenza Viruses

Hong Kong Polytechnic University, 21-22 November 2015

The GISAID-ISIRV-WHO Training Workshop on *Genetic Analyses of Influenza Viruses* was organised by the GISAID Initiative in conjunction with ISIRV, the WHO Global Influenza Surveillance and Response System and the Hong Kong Polytechnic University, with generous financial support from the WHO, its Western Pacific Regional Office and ISIRV. The two-day workshop, held at the Polytechnic University on 21-22 November 2015, was opened by Dr Wenqing Zhang, Co-ordinator of the WHO Global Influenza Programme. It attracted 33 trainees from 24 countries, about half from East and Southeast Asia with others from Africa, South and Central America and Europe.

The purpose of the training workshop was to enable laboratories, particularly in Southeast Asia, to contribute to and benefit from the extensive genetic and related data available on influenza viruses, in relation to understanding the epidemiology of influenza, the evolution of the viruses and the emergence and spread of novel genetic and antigenic variants. Participants received instruction in the use of GISAID's EpiFlu™ database (hosted by the Federal Republic of Germany) and novel features of its new EpiFlu™ 2.0 platform, including advanced analysis tools for the identification (by display on annotated phylogenetic trees), and interpretation (using FluSurver) of mutations underlying the evolution and antigenic variation of human and animal influenza viruses.

Instruction was provided by:

Alex Chin, University of Hong Kong, Hong SAR, China.
Rebecca Garten, GISAID Database Technical Group member at the Influenza Division, Centers for Disease Control and Prevention, Atlanta, USA.
Alan Hay, GISAID Scientific Liaison Officer, The Francis Crick Institute, London, UK.
Naomi Komadina, GISAID Database Technical Group member at the WHO Collaborating Centre for Reference and Research on Influenza, Peter Doherty Institute, Melbourne, Australia.
Janice Lo, Head, WHO NIC, Centre for Health Protection, Hong Kong SAR, China.
Sebastian Maurer-Stroh, GISAID Database Technical Group member at the Bioinformatics Institute, Agency for Science, Technology and Research, Singapore.
John McCauley, Director, Crick Worldwide Influenza Centre, The Francis Crick Institute, London, UK.
Richard Neher, GISAID Database Technical Group member at the Max Planck Institute for Developmental Biology, Tuebingen, Germany.
Hui-Ling Yen, University of Hong Kong, Hong SAR, China.

The programme (attached) included:

Brief introductory lectures covering:

- Evolutionary aspects of human and animal influenza viruses (John McCauley)
- Surveillance of influenza – experience in Hong Kong (Janice Lo)
- Antiviral resistance (Hui-Ling Yen)
- GISAID – sharing and analysis of sequence data (Naomi Komadina)
- Submission and annotation of data (Rebecca Garten)
- Sequence analysis – alignment and phylogeny (Richard Neher)
- Interpretation of mutations using FluSurver (Sebastian Maurer-Stroh)

Hands-on bioinformatics training in:

- Submission (and annotation) of data
- Search and analysis of data
- Sequence alignment and phylogenetic analysis
- Identification and interpretation of mutations using FluSurver

Evaluation by about half of the participants (results attached) indicated their appreciation of both the content and quality of the brief lectures (68% very good/29% good) and hands-on instruction (67% very good/29% good) and the interactive nature of the workshop.

Finally, GISAID and ISIRV are extremely grateful to The Hong Kong Polytechnic University for providing the excellent facility and to Professor John Tam and colleagues, Teresa Chung, Amber Jiachi Chiou and Sukching Wan, of the Department of Applied Biology and Chemical Technology, for their efficient logistical support and their excellent hospitality.

GISAID-ISIRV Workshop on *Genetic Analyses of Influenza Viruses*
21-22 November 2015
Room Y824, 8th Floor Lee Shau Kee Building (Block Y), Department of Applied Biology and Chemical Technology, Hong Kong Polytechnic University

Programme

Saturday 21st November

08.30 - 09.00 **Registration**

09.00 - 09.15 **Welcome and Introduction-** *Alan Hay, John Tam*

09.15 - 10.45 **Brief introductory presentations**

- Evolutionary aspects of influenza - *John McCauley*
- Surveillance of influenza - Experience in Hong Kong - *Janice Lo*
- Antiviral resistance – *Hui-Ling Yen*
- GISAID - sharing and analysis of sequence data - *Naomi Komadina*
- Submission and annotation/curation of data -*Rebecca Garten*
- Sequence analysis - alignment/phylogeny - *Richard Neher*
- Interpretation of mutations (FluSurver) - *Sebastian Maurer-Stroh*

10.45 - 11.15 Refreshments

11.15 - 12.30 **Bioinformatics training – session 1**

- Submission of data, annotation - *Rebecca Garten*
- Search and analysis of data - *Naomi Komadina*

12.30 – 13.30 Lunch ***(Chinese Garden, 4th floor, S Building)***

13.30 – 15.00 **Bioinformatics training – session 1 (continued)**
- Sequence alignment and phylogenetic analysis - *Richard Neher*
- H5N1 clades - *Rebecca Garten*
- Phenotypically and epidemiologically interesting mutations (FluSurver) – *Sebastian Maurer-Stroh*

15.00 – 15.30 Refreshments

15.30 – 17.00 **Bioinformatics training – session 2**
- Analysis of own datasets (individual instruction)

Sunday 22nd November

09.00 – 13.00 **Bioinformatics training – session 3**

09.00 – 10.30 **Q & A/Trouble-shooting**

- GISAID Platform Use and Data upload - *Naomi Komadina, Rebecca Garten*

10.30 – 11.00 Refreshments

11.00 – 13.00 **Q & A/Trouble-shooting (continued)**

- Phylogenetic analysis - *Richard Neher*
- FluSurver use - *Sebastian Maurer-Stroh*

13.00 **Close of Workshop**

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Hong Kong Polytechnic University

PARTICIPANTS & TRAINERS

FIRST NAME	LAST NAME	INSTITUTION	COUNTRY
Mohamed Ali	Ben Hadj Kacem	Microbiology Laboratory, Charles Nicolle Hospital, Tunis	Tunisia
Karoline	Bragstad	Norwegian Institute of Public Health, Oslo	Norway
Jorge	Camara	Virology Institute, Cordoba	Argentina
Stanley	Chan	Centre for Health Protection, Hong Kong	Hong Kong SAR, China
Peter	Cheng	Centre for Health Protection, Hong Kong	Hong Kong SAR, China
Alex	Chin	University of Hong Kong	Hong Kong SAR, China
Amber Jiachi	Chiou	Hong Kong Polytechnic University	Hong Kong SAR, China
Malinee	Chittaganpitch	National Institute of Health, Nonthaburi	Thailand
Teresa	Chung	Hong Kong Polytechnic University	Hong Kong SAR, China
Bardach	Darmaa	National Centre for Communicable Diseases, Ulaanbataar	Mongolia
Vladimir	Drazenovic	Croatian Institute of Public Health, Zagreb	Croatia
Rebecca	Garten	CDC, Atlanta	USA
Ana Rita	Gonçalves Cabecinhas	University of Geneva Hospitals, Geneva	Switzerland
Julia	Guillebaud	Institute Pasteur of Madagascar, Antananarivo	Madagascar
Alan	Hay	The Francis Crick Institute, London	UK
Kisoon	Kim	Centre for Infectious Disease, NIH, KCDC, Chungcheongbuk-do	Republic of Korea
Heui Man	Kim	Centre for Infectious Disease, NIH, KCDC, Chungcheongbuk-do	Republic of Korea
Dae-Won	Kim	Centre for Infectious Disease, NIH, KCDC, Chungcheongbuk-do	Republic of Korea
Naomi	Komadina	Peter Doherty Institute, Melbourne	Australia

Vina Lea	Arguelles	Research Institute for Tropical Medicine, Muntinlupa City	Philippines
Janice	Lo	Centre for Health Protection, Hong Kong	Hong Kong SAR, China
Irma	Lopez Martinez	Institute of Diagnosis and Reference Epidemiology, Mexico D.F.	Mexico
Ann	Machablishvili	National Centre for Disease Control and Public Health, Tbilisi	Georgia
Sebastian	Maurer-Stroh	Bioinformatics Institute, A*STAR	Singapore
John	McCauley	The Francis Crick Institute, London	UK
Fernando	Motta	Institute Oswaldo Cruz, Rio de Janeiro	Brazil
Pretty	Multihartina	National Institute of Health Research and Development, Jakarta	Indonesia
Richard	Neher	Max Planck Institute for Developmental Biology, Tuebingen	Germany
Hoang Anh	Nguyen	Pasteur Institute of Ho Chi Minh City	Vietnam
Richard	Njouom	Pasteur Centre of Cameroon, Yaounde	Cameroon
Hana Apsari	Pawestri	National Institute of Health Research and Development, Jakarta	Indonesia
Kartika Dewi	Puspa	National Institute of Health Research and Development, Jakarta	Indonesia
Nor Aziyah Binti Mat	Rahim	Institute for Medical Research, Kuala Lumpur	Malaysia
Amany	Sheta	Central Public Health Laboratory, Cairo	Egypt
John	Tam	Hong Kong Polytechnic University	Hong Kong SAR, China
Titus	Tan	Research Institute for Tropical Medicine, Muntinlupa City	Philippines
Almiro Rogerio	Tivane	Laboratory of Virus Isolation, National Institute of Health	Mozambique
Florette	Treurnicht	National Institute for Communicable Diseases, Johannesburg	South Africa
Trang Thi Hong	Ung	National Institute of Hygiene and Epidemiology, Hanoi	Vietnam
Bishnu Prasad	Upadhyay	National Public Health Laboratory, Kathmandu	Nepal
Phengta	Vongphrachanh	National Centre for Laboratory and Epidemiology, Vientiane	Lao People's Democratic Republic
Sokhoun	Yann	Institute Pasteur in Cambodia, Phnom Penh	Cambodia
Hui-Ling	Yen	University of Hong Kong	Hong Kong SAR, China

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Summary of Evaluations

Session	**Very good**	**Good**	**Average**	**Poor**
Day 1 - Saturday 21st Nov				
09.15 - 10.45 **Brief introductory presentations** Evolutionary aspects of influenza - *John McCauley*	**10**	**5**	**1**	
09.15 - 10.45 **Brief introductory presentations** Surveillance of influenza - Experience in Hong Kong - *Janice Lo*	**12**	**4**		
09.15 - 10.45 **Brief introductory presentations** Antiviral resistance – *Hui-Ling Yen*	**11**	**5**		
09.15 - 10.45 **Brief introductory presentations** GISAID - sharing and analysis of sequence data - *Naomi Komadina*	**10**	**5**	**1**	
09.15 - 10.45 **Brief introductory presentations** Submission and annotation/curation of data -*Rebecca Garten*	**12**	**2**	**2**	
09.15 - 10.45 **Brief introductory presentations** Sequence analysis - alignment/phylogeny - *Richard Neher*	**9**	**7**		
09.15 - 10.45 **Brief introductory presentations** Interpretation of mutations (FluSurver) - *Sebastian Maurer-Stroh*	**12**	**4**		
11.15 - 12.30 **Bioinformatics training – session 1** Submission of data, annotation - *Rebecca Garten*	**10**	**4**	**1**	
11.15 - 12.30 **Bioinformatics training – session 1** Search and analysis of data - *Naomi Komadina*	**11**	**4**	**1**	
13.30 – 15.00 **Bioinformatics training – session 1 (continued)** Sequence alignment and phylogenetic analysis - *Richard Neher*	**9**	**7**		

13.30 – 15.00 **Bioinformatics training – session 1 (continued)** H5N1 clades - *Rebecca Garten*	**11**	**4**	**1**	
13.30 – 15.00 **Bioinformatics training – session 1 (continued)** Phenotypically and epidemiologically interesting mutations (FluSurver) - *Sebastian Maurer-Stroh*	**13**	**3**		
15.30 – 17.00 **Bioinformatics training – session 2** Analysis of own datasets (individual instruction)	**9**	**4**	**2**	
Day 2 - Sunday 22nd Nov				
Bioinformatics training – session 3 09.00 – 10.30 **Q & A/Trouble-shooting** GISAID Platform Use and Data upload - *Naomi Komadina, Rebecca Garten*	**10**	**6**		
11.00 – 13.00 **Q & A/Trouble-shooting (continued)** Phylogenetic analysis - *Richard Neher*	**10**	**4**		
11.00 – 13.00 **Q & A/Trouble-shooting (continued)** FluSurver use - *Sebastian Maurer-Stroh*	**10**	**5**		

Any other specific comments?

- There is a need for a publication by the WHO of a document serving as a reference in the phylogenetic study of influenza virus and for this to be updated regularly.
- The program was outstanding in terms of theoretical as well as practical aspects. Bioinformatics tools were the core area of the workshop and are most useful tools for all NICs for quick and uniform analysis and interpretation. If isirv –AVG could co-ordinate and organise a 3-5 day comprehensive training workshop on bioinformatics at a regional level, this will be useful for all NICs who are dedicated in surveillance, monitoring and response of influenza and respiratory viruses.
- While my experience with molecular biology is extensive, my exposure to influenza is limited. The intro presentations were very helpful for me to understand the specifics and parameters involved in flu research.
- The training was very thorough for the scope. I was still able to study afterwards because the instructors were able to properly emphasise the resources and web links that we can refer to.
- I appreciate the speakers' prepared informative presentations and actively supporting the training in bioinformatics. It is going to be very helpful for me in analysing influenza sequence data.
- This Workshop was so useful. From it I gained more knowledge on the access to GISAID, learned how to apply the software to find out flu data, analyse data, interpret analysed data, learned how to upload and submit data sets and learned how to make phylogenetic trees.
- I found this workshop really interesting and helpful. I knew the GISAID platform but didn't really know how to use it. Waiting now for the version 2.0.
- Yes, I found the practical particularly useful.

Would you recommend the Workshop to your colleagues?

Yes x 16

- Definitely, I always recommend and encourage my colleagues and juniors to attend such useful training programs in the future.
- I found it useful and pertinent for people working in the field!
- Yes of course! I would recommend this course not only to colleagues but also to friends who are in the same field.
- I would totally recommend the Workshop to my colleagues.
- Yes certainly x 2
- Yes I would like to recommend the Workshop to my colleagues and share what I learned.
- Absolutely

No x 0

What aspects of the Workshop did you like most? And least?

Most:

- The venue and arrangements for the workshop.
- Scientific and human quality of trainers.
- Bioinformatics however I found all are equally important and a system approach is always essential.
- Hands on training.
- Gaining a lot of technical and academic knowledge of influenza genetics.
- Having an application of how the data from different procedures combine to provide actual and useable information.
- The FluSurver tool, phylogenetic analysis and characterisation of mutations.
- Platform use and data upload.
- All trainers kindly explained how to use and apply the GISAID system including FluSurver and Nextflu.
- Uploading, submission, analysis and interpretation of the virus gene mutation.
- How to use GISAID.
- Training aspect on our own dataset
- FluSurver
- Bioinformatics Training sessions
- The fact that it was a small group. We could discuss with almost everybody what is almost impossible in bigger workshops. The possibility of using and analysing our own data. The availability and kindness of the different trainers (speakers).

Least:

- The short period of the workshop.
- The session on the analysis of own datasets had a lot of dead time, although this is understandable.
- H5N1 clades.
- Finding out the listing of influenza.
- Not so familiar with antiviral resistance.
- Not enough time to have an overview of what is possible to do with our data
- The Hong Kong style meal!!
- I think it would have been better to have a lunch buffet on Saturday. As we were running late in the schedule we had to rush for lunch. The buffet meal format allows people to be 'mobile' and discuss with more people, but this is just a detail!
- It was a little bit inconvenient to go to the bathroom.

Do you have any suggestions for improving such a Workshop?

- Define prerequisite knowledge before participation.
- Do more practice on selected strains carrying particular mutations starting from consensus sequences to GISAID submission, alignment and phylogenetic study
- Provision of sufficient time will be more productive in upcoming workshops.
- I think the training should start from alignment of a raw data or better if it is a continuation of a laboratory sequencing training.
- For analysis of own data sets, perhaps it would be quicker to provide sample data sets. Then if a locally-hosted GISAID platform in a closed network is possible, we can experience the interface of uploading and saving temporary data.

- If additional external resources could be provided regarding topics outside (but related to) the scope of the Workshop.
- Not really – it was fine the way it was.
- I think you should extend the time for analysis of phylogenetics and give the trainers more information about drug resistance.
- It would be better to check the computer networking system before the Workshop and provide sufficient computers.
- Slowing down the presentations.
- I would have liked to have had more time on sequence analysis.
- For beginners like me, it would have been better if participants were given a manual about how to submit, share and analyse sequence data, also interpretation and troubleshooting, so that it can be repeated again after returning home.
- Maybe it should have been run over 3 days instead of 2. This would have allowed for more digestion of the information that was in the presentations which could then have been spread over 2 days, with more guided training sessions.

Is there anything you would like to see at a future Workshop that was not included?

- Some explanation on the selection of sequence for analysis (when to construct a phylogenetic tree) & some interpretation of phylogenetic trees.
- Further use of bioinformatics applied to the influenza virus.
- Standardizing the selection of mutations and reference strains in the classification of influenza viruses.
- If possible, regional level workshop in such areas.
- It is better if this workshop is a continuation of a laboratory sequencing training.
- I have a few questions about sequence data generation such as biases in sequencing data have been discovered due to wet lab procedures (RNA extraction, PCR or sequence assembly). If resources on guidelines or important considerations to prevent biases are available, it would be great to also share this with us.
- Using phylogenetic trees to predict the future of the evolution of the influenza virus, some online tools for analysis like FluSurver.
- Sequence analysis of mutation.
- It was enough learning for 2 days. I really enjoyed the Workshop.
- More of the interpretation of the amino acid alignment sequence of the virus.
- More details about sequence alignments and phylogenetics and interpretation of mutations (FluSurver)
- Theoretical aspect of phylogeny.
- Was beautifully run.