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GENETIC SHIFT AND GENETIC DRIFT IN INFLUENZA

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ABSTRACT

Genetic shift can be defined as a natural process whereby accumulation of mutations is seen in genes that are responsible for encoding antigens. These alterations produce variations (alterations) in the same way they appear in the immune system. Antigenic drift is a small change when compared to antigenic shift which is a major change or variation. Influenza viruses evolve through antigenic shift and drift on its surface proteins Hemagglutinin (HA) and Neuraminidase (NA). Genetic shift leads to the formation of a whole new subtype as in this case two or more strains of viruses or the viruses themselves combine. This growing nature of the virus has led to the need for finding newer vaccines. Evolution is seen in all living forms. Changes in genotypes and phenotypes make up a population from one generation to the other. This is a phenomenon similar to the genetic shift and drift of influenza virus. Immunity also plays a major role with the help of antibodies towards fighting the mutated virus entering our body. The continuous variations caused in the influenza virus due to genetic shift and genetic drift has led to the formation of newer strains and thus the necessity for newer vaccines to arise.

Keywords: Genetic shift; genetic drift; influenza virus; mutation

INTRODUCTION

Genetic Shift

Genetic shift is a natural process whereby accumulation of mutations in genes take place **[1]**. The genes are responsible for encoding the antigens **[2]**. These variations/alterations appear the same way they appear in the immune system **[3]**. Genetic shift is a major change when compared to genetic drift. Influenza viruses evolve through an antigenic shift on its surface protein HA and NA **[4]**. Genetic shift leads to the formation of a whole new subtype as in this case two or more strains of viruses combine or when the viruses themselves combine. This growing nature of the virus due to its reassortment has led to the need for the discovery of newer vaccines. The antigenic shift can cause a major variation and most people do not come across the same or similar strains constantly in their lifespan. The emerging high impact diseases are Severe acute respiratory syndrome (SARS), Ebola fever, and influenza in humans. These viral diseases occur when an established animal virus switches hosts into humans and get subsequently transmitted within the human populations **[5]**. This suggests that the boosting of natural immunity is indeed a quintessential factor inorder to improve the growing influenza vaccine **[6]**.

Genetic Drift

Genetic drift is a smaller change when compared to genetic shift. This is a smaller mutation in the surfaces of the proteins Hemagglutinin and Neuraminidase genes that will make the protein almost unrecognizable to the already existing host immunity **[7]**. This variation is continuous among influenza strains **[8]**. Small changes in genetic shift accumulate to form bigger variations which thereby leads to genetic shift. The changes happening on the surface of hemagglutinin protein from one form to another form is less recognizable and can infect both vaccinated and non vaccinated people **[9]**.

This evolution of influenza through antigenic shift and antigenic shift i.e understanding of the evolution of influenza is necessary for the formulation of a newer vaccine. Epidemics happen due to these shifts and drifts. Apart from this, cross species virus transmission takes place and emergence of new epidemic diseases are seen. Transfer of virus to new hosts will include contact between the virus and the host, infection of one individual leading to its outbreak **[10]**.

Structure of Influenza Virus

The structure of influenza virus and its viral protein function are responsible for the antigenic shift and antigenic drift **[11]**. The main subtypes of influenza virus - Influenza A, B and C are generally segmented, negatively stranded RNA genomes **[12]**. Characterization of the influenza virus is with the help of its surface proteins, Hemagglutinin (HA) and Neuraminidase (NA) **[13]**. The main attribution for the shift and drift seen in the virus should be given to RNA dependent RNA polymerase. Influenza viruses are highly adaptive with strongly immunogenic surface proteins **[14]**.

Most flu cases are caused by the Influenza A virus especially the ones seen in epidemics and pandemics **[15]**. The influenza A virus is most commonly seen to be affecting a variety of animal species although the influenza B virus is seen in humans, and can lead to local outbreaks **[16, 17]**. The influenza C virus is of little concern due to its morphological and genetic differences and its non symptomatic nature. The three subtypes have variable structures and the virion particles can be ovoid or spherical in shape **[18]**.

As mentioned earlier, the surface of influenza virus contains proteins, HA and NA which will exist as spikes. These spikes generally determine the subtype of Influenza virus. They are also important in the immune response against the virus; antibodies **[19]**. Influenza virus spreads by virus containing aerosols or by fomites or sometimes by coming in contact with infected people **[20]**. Since the composition of flu changes with time , the vaccine for flu is also reviewed each year. The age and health statuses of the person taking the vaccine for flu will play an important role. In the effect of the vaccine **[21]**. Normal flu vaccines can have side effects like mild fever and aching of muscles in children, runny nose, headache, sore throat and cough **[22-24]**.

Evolution of Influenza Virus

Organisms generally encounter different environmental interactions. There will be certain responses to these interactions which define the genetic makeup of the organism. Genotype will usually remain constant from an environment to another. But occasional mutations happen leading to a change or evolution. When the same kind of genotype is subjected to different environments, phenotypes are produced. This is similar to how the genetic makeup of influenza virus changes by accumulation of shifts and thus leading to genetic drift **[25]**.

Influenza virus can evolve by drug mechanisms such as evolution of virus by mutation and selection (in a stepwise fashion); seen in genetic drift **[26]**. Thereby, genetic shift and genetic drift are the main mechanism by which the influenza virus evolves leading to newer strains and newer subtypes that become unrecognizable to the human immune system **[27, 28]**.

Evolution of influenza virus is said to have a lot of speculations. The origin is slightly unclear and studies have shown that pigs may serve as the intermediate host in genetic exchange between influenza viruses in avians and humans **[29]**.

The general feature on how a new strain is caused is by reassortment that allow viruses to evolve through natural conditions **[30]**. This reassortment is very similar to chromosome crossover events, as different viral strains may come in contact and transfer the genetic information. The cause of shift is reassortment while the cause of genetic drift is RNA synthesis **[31, 32]**.

Mutation and selection cause variation during evolution. Influenza viruses show a very high mutation rate and this is due to the integration of faulty nucleotides occurring during the replication of the virus **[33]**.

Every decade a new strain of virus arises due to this same reason. For the regard of mutation, such extremely high rates of mutation are not matched by any other organism **[34]**.

Necessity of Vaccine

Though antigenic drift is a small change, as the virus replicates , the changes keep taking place continuously and as discussed earlier, these small changes will accumulate which will thereby result in the formation of a newer strain. This new strain may not be identifiable by the immune system **[35]**. The antibodies that may have been created by the immune system earlier for the response will be unable to identify and protect from the newly formed virus **[36]**.

Immunity plays an important role in any individual towards fighting any pathogens with the help of the circulating antibodies secreted by the clonal-B cells. To a great extent, protection is produced by these circulating antibodies present in the blood. Therefore, the better immunised we are, the better chances we have towards saving ourselves from being exposed to mutated virus **[37]**.

Major few pandemics that have occurred, including the recent Novel Corona Virus disease 2019, is due to antigenic shift **[38]**. The continuous shift and drift nearly made it impossible for the development of flu vaccines and its proper treatment **[39]**. Therefore, it has become a necessity to find a universal flu vaccine **[40]**. Seasonal influenza is common but every flu season is different and millions of people get the flu every year . An annual flu vaccine is one of the best ways to help against the flu. Flu vaccines cause antibodies which develop in the body after weeks of vaccination. These antibodies provide protection against infection with viruses that are used to make the vaccine **[41, 42]**.

The biological characteristics of influenza viruses indicate that future influenza pandemics are inevitable **[43]**. Therefore, specific measures are to be taken for the control of such influenza pandemics **[44, 45]**.

CONCLUSION

The continuous variation caused in influenza virus is due to genetic shift and genetic drift . This has led to the formation of newer strains and thus the need for newer vaccines arise. Development of flu vaccines and medications that will treat the influenza virus is becoming difficult and researchers and scientists are hoping to develop an effective vaccine that will target a part of the virus which is not affected by these changes. This can hopefully lead to a universal flu vaccine. It is the remarkable ability of influenza virus to escape host defence mechanisms by altering the antigenic character. The alterations of the antigenic character by the molecular mechanisms control the epidemics/pandemics of influenza. The annual influenza epidemics are caused by this rapid evolution the virus undergoes. For selecting suitable vaccine strains the antigenicity of the circulating influenza virus should be monitored.

REFERENCES

[1] Jones S, Nelson-Sathi S, Wang Y, Prasad R, Rayen S, Nandel V, *et al*. Evolutionary, genetic, structural characterization and its functional implications for the influenza A (H1N1) infection outbreak in India from 2009 to 2017. Sci Rep [Internet]. 2019 Oct 11;9(1):14690. Available from: http://dx.doi.org/10.1038/s41598-019-51097-w

[2] Scholtissek C. Pandemic influenza: antigenic shift [Internet]. Perspectives in Medical Virology. 2002. p. 87–100. Available from: http://dx.doi.org/10.1016/s0168-7069(02)07005-2

[3] Biswas D, Dutta M, Sarmah K, Yadav K, Buragohain M, Sarma K, *et al*. Genetic characterisation of influenza A(H1N1)pdm09 viruses circulating in Assam, Northeast India during 2009-2015. Indian J Med Microbiol [Internet]. 2019 Jan;37(1):42–9. Available from: http://dx.doi.org/10.4103/ijmm.IJMM_18_416

[4] Rogers SM, Tamkee P, Summers B, Balabahadra S, Marks M, Kingsley DM, *et al*. GENETIC SIGNATURE OF ADAPTIVE PEAK SHIFT IN THREESPINE STICKLEBACK [Internet]. Vol. 66, Evolution. 2012. p. 2439–50. Available from: http://dx.doi.org/10.1111/j.1558-5646.2012.01622.x

[5] Rhetoric: Flu Vaccine [Internet]. Encyclopedia of Health Communication. Available from: http://dx.doi.org/10.4135/9781483346427.n459

[6] Rossenkhan R, Rolland M, Labuschagne JPL, Ferreira R-C, Magaret CA, Carpp LN, *et al*. Combining Viral Genetics and Statistical Modeling to Improve HIV-1 Time-of-infection Estimation towards Enhanced Vaccine Efficacy Assessment. Viruses [Internet]. 2019 Jul 3;11(7). Available from: http://dx.doi.org/10.3390/v11070607

[7] Naeem A, Elbakkouri K, Alfaiz A, Hamed ME, Alsaran H, AlOtaiby S, *et al*. Antigenic drift of hemagglutinin and neuraminidase in seasonal H1N1 influenza viruses from Saudi Arabia in 2014 to 2015. J Med Virol [Internet]. 2020 Mar 11; Available from: http://dx.doi.org/10.1002/jmv.25759

[8.] Ryt-Hansen P, Pedersen AG, Larsen I, Kristensen CS, Krog JS, Wacheck S, *et al*. Substantial Antigenic Drift in the Hemagglutinin Protein of Swine Influenza A Viruses. Viruses [Internet]. 2020 Feb 23;12(2). Available from: http://dx.doi.org/10.3390/v12020248

[9] Boni MF. Vaccination and antigenic drift in influenza [Internet]. Vol. 26, Vaccine. 2008. p. C8–14. Available from: http://dx.doi.org/10.1016/j.vaccine.2008.04.011

[10] Francis F, Chen J, Yong L, Bosquee E. Aphid Feeding on Plant Lectins Falling Virus Transmission Rates: A Multicase Study. J Econ Entomol [Internet]. 2020 Jun 9; Available from: http://dx.doi.org/10.1093/jee/toaa104

[11] Paramasivam A, Vijayashree Priyadharsini J, Raghunandhakumar S. N6-adenosine methylation (m6A): a promising new molecular target in hypertension and cardiovascular diseases. Hypertens Res [Internet]. 2020 Feb;43(2):153–4. Available from: http://dx.doi.org/10.1038/s41440-019-0338-z

[12] Fischer WB. Viral Membrane Proteins: Structure, Function, and Drug Design [Internet]. Springer Science &

Business Media; 2007. 292 p. Available from: https://play.google.com/store/books/details?id=x5j0ASqUj9gC

[13] Smiline ASG, Vijayashree JP, Paramasivam A. Molecular characterization of plasmid-encoded blaTEM, blaSHV and blaCTX-M among extended spectrum β-lactamases [ESBLs] producing Acinetobacter baumannii [Internet]. Vol. 75, British Journal of Biomedical Science. 2018. p. 200–2. Available from: http://dx.doi.org/10.1080/09674845.2018.1492207

[14] Girija As S, Priyadharsini J V. CLSI based antibiogram profile and the detection of MDR and XDR strains of isolated from urine samples. Med J Islam Repub Iran [Internet]. 2019 Feb 8;33:3. Available from: http://dx.doi.org/10.34171/mjiri.33.3

[15] Billington J, Deschamps I, Erck SC, Gerberding JL, Hanon E, Ivol S, *et al*. Developing Vaccines for SARS-CoV-2 and Future Epidemics and Pandemics: Applying Lessons from Past Outbreaks. Health Secur [Internet]. 2020 Apr 29; Available from: http://dx.doi.org/10.1089/hs.2020.0043

[16] Van Hoecke L, Verbeke R, De Vlieger D, Dewitte H, Roose K, Van Nevel S, *et al*. mRNA Encoding a Bispecific Single Domain Antibody Construct Protects against Influenza A Virus Infection in Mice. Mol Ther Nucleic Acids [Internet]. 2020 May 1;20:777–87. Available from: http://dx.doi.org/10.1016/j.omtn.2020.04.015

[17] Hu L-F, Chang X, Ye Y, Wang Z-X, Shao Y-B, Shi W, *et al*. Stenotrophomonas maltophilia resistance to trimethoprim/sulfamethoxazole mediated by acquisition of sul and dfrA genes in a plasmid-mediated class 1 integron [Internet]. Vol. 37, International Journal of Antimicrobial Agents. 2011. p. 230–4. Available from: http://dx.doi.org/10.1016/j.ijantimicag.2010.10.025

[18] Kordyukova LV, Mintaev RR, Rtishchev AA, Kunda MS, Ryzhova NN, Abramchuk SS, *et al*. Filamentous versus Spherical Morphology: A Case Study of the Recombinant A/WSN/33 (H1N1) Virus. Microsc Microanal [Internet]. 2020 Apr;26(2):297–309. Available from: http://dx.doi.org/10.1017/S1431927620000069

[19] Delaveris CS, Webster ER, Banik SM, Boxer SG, Bertozzi CR. Membrane-tethered mucin-like polypeptides sterically inhibit binding and slow fusion kinetics of influenza A virus. Proc Natl Acad Sci U S A [Internet]. 2020 May 26; Available from: http://dx.doi.org/10.1073/pnas.1921962117

[20] Selvakumar R, Np M. COMPARISON IN BENEFITS OF HERBAL MOUTHWASHES WITH CHLORHEXIDINE MOUTHWASH: A REVIEW [Internet]. Vol. 10, Asian Journal of Pharmaceutical and Clinical Research. 2017. p. 3. Available from: http://dx.doi.org/10.22159/ajpcr.2017.v10i2.13304

[21] Priyadharsini JV, Vijayashree Priyadharsini J, Smiline Girija AS, Paramasivam A. In silico analysis of virulence genes in an emerging dental pathogen A. baumannii and related species [Internet]. Vol. 94, Archives of Oral Biology. 2018. p. 93–8. Available from: http://dx.doi.org/10.1016/j.archoralbio.2018.07.001

[22] M MA, Geetha RV, Thangavelu L. Evaluation oEvaluation of anti-inflammatory action of Laurus nobilis-an in vitro studyf anti-inflammatory action of Laurus nobilis-an in vitro study [Internet]. Vol. 10, International Journal of Research in Pharmaceutical Sciences. 2019. p. 1209–13. Available from: http://dx.doi.org/10.26452/ijrps.v10i2.408

[23] Marickar RF, Geetha RV, Neelakantan P. Efficacy of contemporary and novel Intracanal medicaments against enterococcus faecalis. J Clin Pediatr Dent [Internet]. 2014 Autumn;39(1):47–50. Available from: http://dx.doi.org/10.17796/jcpd.39.1.wmw9768314h56666

[24] Shahana RY, Muralidharan NP. Efficacy of mouth rinse in maintaining oral health of patients attending orthodontic clinics [Internet]. Vol. 9, Research Journal of Pharmacy and Technology. 2016. p. 1991. Available from: http://dx.doi.org/10.5958/0974-360x.2016.00406.6

[25] Sun Y-M, Lu C, Wu Z-Y. Spinocerebellar ataxia: relationship between phenotype and genotype - a review [Internet]. Vol. 90, Clinical Genetics. 2016. p. 305–14. Available from:

http://dx.doi.org/10.1111/cge.12808

[26] Ou L, Qin K, Yang Z-X, Bie M-J. [The Effects and Mechanisms of Dihydroartemisinin on Influenza A Virus H1N1 Induces TNF-α and IL-6 Expression in Bronchial Epithelial Cells]. Sichuan Da Xue Xue Bao Yi Xue Ban [Internet]. 2020 Mar;51(2):171–7. Available from: http://dx.doi.org/10.12182/20200360604

[27] Gupte S. Influenza Complete Spectrum - I - ECAB [Internet]. Elsevier Health Sciences; 2012. 129 p. Available from: https://play.google.com/store/books/details?id=4xYMIbA8SYkC

[28] Shahzan MS, Sohaib Shahzan M, Smiline Girija AS, Vijayashree Priyadharsini J. A computational study targeting the mutated L321F of ERG11 gene in C. albicans, associated with fluconazole resistance with bioactive compounds from Acacia nilotica [Internet]. Vol. 29, Journal de Mycologie Médicale. 2019. p. 303–9. Available from: http://dx.doi.org/10.1016/j.mycmed.2019.100899

[29] Brown JD, Stallknecht DE. Wild Bird Surveillance for the Avian Influenza Virus [Internet]. Avian Influenza Virus. 2008. p. 85–97. Available from: http://dx.doi.org/10.1007/978-1-59745-279-3_11

[30] Roossinck MJ. Plant Virus Evolution [Internet]. Springer Science & Business Media; 2008. 224 p. Available from: https://play.google.com/store/books/details?id=caKwoL29oikC

[31] Vaishali M, Geetha RV. Antibacterial activity of Orange peel oil on Streptococcus mutans and Enterococcus-An In-vitro study [Internet]. Vol. 11, Research Journal of Pharmacy and Technology. 2018. p. 513. Available from: http://dx.doi.org/10.5958/0974-360x.2018.00094.x

[32] Priyadharsini JV, Vijayashree Priyadharsini J, Smiline Girija AS, Paramasivam A. An insight into the emergence of Acinetobacter baumannii as an oro-dental pathogen and its drug resistance gene profile – An in silico approach [Internet]. Vol. 4, Heliyon. 2018. p. e01051. Available from: http://dx.doi.org/10.1016/j.heliyon.2018.e01051

[33] Li R, Zhang T, Xu J, Chang J, Xu B. Isolation of two novel reassortant H3N6 avian influenza viruses from long-distance migratory birds in Jiangxi Province, China. Microbiologyopen

[Internet]. 2020 May 28;e1060. Available from: http://dx.doi.org/10.1002/mbo3.1060

[34] Kato Y, Takahashi K, Ito F, Suzuki S, Fukui K, Mimaki M, *et al*. Novel oseltamivir-resistant mutations distant from the active site of influenza B neuraminidase. J Biomol Struct Dyn [Internet]. 2020 May 25;1–10. Available from: http://dx.doi.org/10.1080/07391102.2020.1765872

[35.] Bot A, Bona CA. Genetic Immunization [Internet]. Springer Science & Business Media; 2013. 180 p. Available from: https://play.google.com/store/books/details?id=642-BwAAQBAJ

[36] Choi J-H, Ko M-K, Shin SH, You S-H, Jo H-E, Jo H, *et al*. Improved foot-and-mouth disease vaccine, O TWN-R, protects pigs against SEA topotype virus occurred in South Korea. Vet Microbiol [Internet]. 2019 Sep;236:108374. Available from: http://dx.doi.org/10.1016/j.vetmic.2019.07.026

[37] Donma MM, Donma O. The effects of allium sativum on immunity within the scope of COVID-19 infection. Med Hypotheses [Internet]. 2020 Jun 2;144:109934. Available from: http://dx.doi.org/10.1016/j.mehy.2020.109934

[38] Ramesh N, Siddaiah A, Joseph B. Tackling Corona Virus Disease 2019 (COVID 19) in Workplaces. Indian J Occup Environ Med [Internet]. 2020 Jan;24(1):16–8. Available from: http://dx.doi.org/10.4103/ijoem.IJOEM_49_20

[39] Pratha AA, Ashwatha Pratha A, Geetha RV. Awareness on Hepatitis-B vaccination among dental students-A Questionnaire Survey [Internet]. Vol. 10, Research Journal of Pharmacy and Technology. 2017. p. 1360. Available from: http://dx.doi.org/10.5958/0974-360x.2017.00240.2

[40] Abbasi J. FLU-v, a Universal Flu Vaccine Candidate, Advances in Trial. JAMA [Internet]. 2020 Apr 14;323(14):1336. Available from: http://dx.doi.org/10.1001/jama.2020.4138

[41] Mayor S. Intranasal flu vaccine provides similar protection to injected flu vaccine, finds study [Internet]. BMJ. 2016. p. i4481. Available from: http://dx.doi.org/10.1136/bmj.i4481

[42] Girija SA, Jayaseelan VP, Arumugam P. Prevalence of VIM- and GIM-

producing Acinetobacter baumannii from patients with severe urinary tract infection. Acta Microbiol Immunol Hung [Internet]. 2018 Dec 1;65(4):539–50. Available from: http://dx.doi.org/10.1556/030.65.2018.038

[43] Ashwin KS, Muralidharan NP. Vancomycin-resistant enterococcus (VRE) vs Methicillin-resistant Staphylococcus Aureus (MRSA). Indian J Med Microbiol [Internet]. 2015 Feb;33 Suppl:166–7. Available from: http://dx.doi.org/10.4103/0255-0857.150976

[44] Girija ASS, Smiline Girija AS, Vijayashree Priyadharsini J, Paramasivam A. Plasmid-encoded resistance to trimethoprim/sulfamethoxazole mediated by dfrA1, dfrA5, sul1 and sul2 among Acinetobacter baumannii isolated from urine samples of patients with severe urinary tract infection [Internet]. Vol. 17, Journal of Global Antimicrobial Resistance. 2019. p. 145–6. Available from: http://dx.doi.org/10.1016/j.jgar.2019.04.001

[45] Gischke M, Ulrich R, I Fatola O, Scheibner D, Salaheldin AH, Crossley B, *et al*. Insertion of Basic Amino Acids in the Hemagglutinin Cleavage Site of H4N2 Avian Influenza Virus (AIV)-Reduced Virus Fitness in Chickens is Restored by Reassortment with Highly Pathogenic H5N1 AIV. Int J Mol Sci [Internet]. 2020 Mar 28;21(7). Available from: http://dx.doi.org/10.3390/ijms21072353