

## 研究论文

### H1N1流感病毒聚合酶片段的CpG抑制及其对密码子偏爱性的影响

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#### 摘要:

H1N1流感病毒的聚合酶具有RNA复制、转录等功能, 并且对流感病毒片段包装、子代繁殖及宿主适应性等有着重要作用。通过分析人、猪及禽类H1N1流感病毒聚合酶片段的二核苷酸频率及同义密码子的偏爱性, 发现不同宿主中, 流感病毒聚合酶片段的CpG频率最低, 且均被强烈抑制; 通过三类宿主间的比较发现, 人流感病毒抑制最为强烈, 且其CpG频率随年份呈下降趋势, 但2009年毒株的CpG频率突然上升。比较同义密码子使用频率发现, 含有CpG的同义密码子相对使用频率均小于1, 证明CpG抑制作用是影响同义密码子偏爱性的一个重要因素。以上结果暗示, CpG抑制对H1N1流感病毒的进化及跨宿主传播可能有重要影响。

**关键词:** H1N1 CpG抑制 同义密码子偏爱性 聚合酶

### The CpG Suppression of Polymerase Segments and Its Impact on Codon Usage Bias in H1N1 Influenza Virus

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#### Abstract:

The polymerase segments of H1N1 influenza virus are functional for catalyzing viral RNA transcription and replication, which also play a crucial role for the virus genome packaging, propagating and host adaption. In this research, the dinucleotide frequency and synonymous codon bias in the polymerase segments of the H1N1 influenza virus which were isolated from human, avian and swain were analyzed. The results showed that the frequency of the CpG dinucleotides were the lowest and were intensively suppressed across all 3 segments. The cross host comparison showed that the lowest CpG frequency was in human H1N1 influenza virus and the trend of CpG frequency was decreasing with the years. However, the frequency raised in year 2009 which accords with the evidence that the human H1N1 virus was transmitted from foreign hosts. Analyzing the relative synonymous codon usage (RSCU) in the polymerase segments, the frequency of the codons with CpG dinucleotides were all less than 1, which indicated CpG suppression was the main factor of the synonymous codon usage in H1N1 influenza virus genome. In summary, these results indicate that the CpG suppression have important impacts on the evolution and transmission of H1N1 influenza virus.

**Keywords:** CpG suppression Synonymous codon usage bias Polymerase

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#### 参考文献:

1. Palese P, Shah M. Orthomyxoviridae: The viruses and their replication. Fields Virology 4th Ed. Philadelphia, Lippincott Williams & Wilkins, 2007: 1647~1689
2. Huang TS, Palese P, Krystal M. Determination of influenza virus proteins required for genome replication. J Virol, 1990, 64(11): 5669~5673
3. Brownlee GG, Sharps JL. The RNA polymerase of influenza A virus is stabilized by interaction with its

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viral RNA promoter. *J Virol*, 2002, 76(14): 7103~7113

4. Perales B, Sanz-Ezquerro JJ, Gastaminza P, Ortega J, Santarén JF, Ortín J, Nieto A. The replication activity of influenza virus polymerase is linked to the capacity of the PA subunit to induce proteolysis. *J Virol*, 2000, 74(3): 1302~1312

5. Marsh GA, Rabadan R, Levine AJ, Palese P. Highly conserved regions of influenza A virus polymerase gene segments are critical for efficient viral RNA packaging. *J Virol*, 2008, 82(5): 2295~2304

6. Brower-Sinning R, Carter DM, Crevar CJ, Ghedin E, Ross TM, Benos PV. The role of RNA folding free energy in the evolution of the polymerase genes of the influenza A virus. *Genome Biol*, 2009, 10(2): R18

7. Hatta M, Hatta Y, Kim JH, Watanabe S, Shinya K, Nguyen T, Lien PS, Le QM, Kawaoka Y. Growth of H5N1 influenza A viruses in the upper respiratory tracts of mice. *PLoS Pathog*, 2007, 3(10): 1374~1379

8. Naffakh N, Massin P, Escricu N, Crescenzo-Chaigne B, van der Werf S. Genetic analysis of the compatibility between polymerase proteins from human and avian strains of influenza A viruses. *J Gen Virol*, 2000, 81(5): 1283~1291

9. Subbarao EK, London W, Murphy BR. A single amino acid in the PB2 gene of influenza A virus is a determinant of host range. *J Virol*, 1993, 67(4): 1761~1764

10. Karlin S, Mrazek J, Campbell AM. Compositional biases of bacterial genomes and evolutionary implications. *J Bacteriol*, 1997, 179(12): 3899~3913

11. Karlin S, Doerfler W, Cardon LR. Why is CpG suppressed in the genomes of virtually all small eukaryotic viruses but not in those of large eukaryotic viruses? *J Virology*, 1994, 68(5): 2889~2897

12. Goto M, Washio T, Tomita M. Causal analysis of CpG suppression in the mycoplasma genome. *Microb Comp Genomics*, 2000, 5(1): 51~58

13. Gentles AJ, Karlin S. Genomic CpG suppression in nuclear, organelle, and viral DNA. *Recent Dev Nucl Ac Res*, 2004, 1: 35~51

14. Shackelton LA, Parrish CR, Holmes EC. Evolutionary basis of codon usage and nucleotide composition bias in vertebrate DNA viruses. *J Mol Evol*, 2006, 62(5): 551~563

15. Tao P, Dai L, Luo M, Tang F, Tien P, Pan Z. Analysis of synonymous codon usage in classical swine fever virus. *Virus Genes*, 2009, 38(1): 104~112

16. Krieg AM. CpG motifs in bacterial DNA and their immune effects. *Annu Rev Immunol*, 2002, 20: 709~760

17. Ahn I, Jeong BJ, Bae SE, Jung J, Son HS. Genomic analysis of influenza A viruses, including avian flu (H5N1) strains. *Eur J Epidemiol*, 2006, 21(7): 511~519

18. Zhou T, Gu W, Ma J, Sun X, Lu Z. Analysis of synonymous codon usage in H5N1 virus and other influenza A virus. *Biosystems*, 2005, 81(1): 77~86

19. Bao Y, Bolotov P, Dernovoy D, Kiryutin B, Zaslavsky L, Tatusova T, Ostell J, Lipman D. The influenza virus resource at the National Center for Biotechnology Information, *J Virol*, 2008, 82(2): 596~601

20. Edgar RC. MUSCLE: Multiple sequence alignment with high accuracy and high throughput. *Nucl Acid Res*, 2004, 32(5): 1792~1797

21. Xia X, Xie Z. DAMBE: Data analysis in molecular biology and evolution. *J Hered*, 2001, 92(4): 371~373

22. McInerney JO. GCUA: General codon usage analysis. *Bioinformatics*, 1998, 14(4): 372~373

23. Johnson NP, Mueller J. Updating the accounts: Global mortality of the 1918-1920 "Spanish" influenza pandemic. *Bull Hist Med*, 2002, 76: 105~112

24. Woo PC, Wong BH, Huang Y, Lau SK, Yuen KY. Cytosine deamination and selection of CpG suppressed clones are the two major independent biological forces that shape codon usage bias in coronaviruses. *Virology*, 2007, 369(2): 431~442

25. Cullen BR. Role and mechanism of action of the APOBEC3 family of antiretroviral resistance factors. *J Virol*, 2006, 80(3): 1067~1076

26. Yu Q, König R, Pillai S, Chiles K, Kearney M, Palmer S, Richman D, Coffin JM, Landau NR. Single-strand specificity of APOBEC3G accounts for minus-strand deamination of the HIV genome. *Nat Struct Mol Biol*, 2004, 11(5): 435~442

27. Taubenberger JK, Reid AH, Lourens RM, Wang R, Jin G, Fanning TG. Characterization of the 1918 influenza virus polymerase genes. *Nature*, 2005, 437(6): 889~893

28. Smith GJ, Vijaykrishna D, Bahl J, Lycett SJ, Worobey M, Pybus OG, Ma SK, Cheung CL, Raghwani J, Bhatt S, Peiris JS, Guan Y, Rambaut A. Origins and evolutionary genomics of the 2009 swine-origin H1N1 influenza A epidemic. *Nature*, 2009, 459 (25): 1122~1125

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