PIBB 生物化学与生物物理进展
Progress in Biochemistry and Biophysics
2008, 35(12): 1387~1393
www.pibb.ac.cn

Prevalence of Avian Influenza Virus Receptor in Human Respiratory Tract*

ZHANG Zeng-Feng[1,2], FAN Xiao-Hui[3], LI Kang-Sheng[1], HUANG Kai[1,2], LUO Dian-Zhong[4], FENG Zhen-Bo[4], WEI Min-Yi[4], GUAN Yi[1,2], CHEN Hong-Lin[1,2], ZHANG Jin-Xia[1,2]**

([1]*International Institute of Infection and Immunity, Shantou University Medical College, Guangdong* 515031, China;
[2]*State Key Laboratory for Emerging Infectious Diseases, Department of Microbiology; The University of Hong Kong,* Hong Kong, China;
[3]*Department of Microbiology and Immunology, Guangxi Medical University, Nanning* 530021, China
[4]*Department of Pathology, Guangxi Medical University, Nanning* 530021, China)

Abstract SAα2,6 and SAα2,3 linked sialic acid molecules on epithelial cell membrane served as receptors for influenza virus, which are specifically recognized by human and avian influenza viruses, respectively. The distribution of these two species of sialic acids in human respiratory tract from different anatomical sites and different age groups was investigated. The results showed that SAα2,3Gal species was prevalent in respiratory bronchiole and lung alveolar epithelium, but was infrequent in trachea, bronchus and bronchiole. On the contrary, the SAα2,6Gal species was more common in the trachea and bronchus and to a lesser degree in the alveolar epithelium. When compared the expression levels of SAα2,6Gal and α2,3Gal in the respiratory tract among different age groups, no significant difference was found. In the *ex vivo* H5N1 virus infection study, alveolus epithelium were found to be more susceptible to avian influenza than trachea and bronchus epithelial cells. These results suggest that the human respiratory tract, to some extent, is permissive for avian influenza viruses. The currently-observed limited human to human transmission of H5N1 virus may be associated with the different abundance of SAα2,3Gal linkages in human upper respiratory tract among individuals.

Key words influenza A virus, sialic acid receptors, SAα2,6Gal linkage, SAα2,3Gal linkage, H5N1

Avian H5N1 influenza virus currently circulating in poultry in Eurasian and African countries have caused repeated infection in humans since 2004, constituting a significant and persistent pandemic threat[1~3]. So far, approximately 387 human cases have been confirmed, with a majority occurring in children or young adults[3, 4]. Genetic and epidemiological findings suggest that most of those human infections were directly introduced from avian species. However, the mechanism of interspecies transmission from avian species to humans has still not been fully described[3].

Host tropism of influenza virus is restricted by receptor specificity. The binding of influenza virus to host cells is mediated via the viral surface protein haemagglutinin, which recognizes cell surface glycoproteins containing terminal sialic acid residues. Previous studies have revealed that avian influenza A virus preferentially bind to sialic acid linked to galactose by an α2,3-linkage (SAα2,3Gal), while human influenza virus bind to α2,6-linked sialic acids (SAα2,6Gal)[5~7]. As SAα2,3Gal is predominant in the gastrointestinal epithelium of ducks[8], while SAα2,6Gal is predominant in the tracheal epithelium of humans[9], these different linkage types and their distribution have been considered as the major barrier for interspecies transmission between avian species and humans[10]. Furthermore, as pigs express both SAα2,3Gal and SAα2,6Gal in their tracheal epithelium, and support the growth of both human and avian influenza A viruses, it was hypothesized that pigs may act as "mixing vessels" for the reassortment of avian and human influenza viruses, or the adaptation of avian virus to SAα2,6Gal linkages, thereby facilitating the emergence of human pandemic influenza strains[11].

*This work was supported by The Research Grants Council of The Hong Kong SAR Government (7488/05M) and the Research Fund for the Control of Infectious Diseases of the Health, Welfare and Food Bureau of the Hong Kong SAR Government, the Li Ka Shing Foundation, the Providence Foundation in memory of The late Dr. Lui Hac Minh, and grants from The National Natural Science Foundation of China (30571674, 30771988).
**Corresponding author. Tel: 852-28199830, Fax: 852-28199827
E-mail: zhangajx@hkucc.hku.hk
Received: April 1, 2008 Accepted: July 16, 2008

Two recent studies demonstrated SAα2,3Gal linkages expression and influenza virus binding in the bronchioles and alveoli of the human respiratory tract, indicating that avian influenza virus can replicate relatively efficiently in the lower respiratory tract, providing a possible explanation for inefficient human-to-human transmission of avian influenza viruses[12, 13]. H5N1 virus was also found to be able to infect epithelial cells of the human upper respiratory tract in an *ex vivo* infection model[14]. However, the prevalence and extent of SAα2,3Gal and SAα2,6Gal expression in the human respiratory tract from different anatomical sites and different age groups have not been systematically investigated.

In this report we studied the distribution and prevalence of sialic acid receptors in the airway epithelia throughout the human respiratory tract of different age groups. Our results demonstrated that SAα2,6Gal linkage receptor predominates in trachea and bronchus, while SAα2,3Gal linkage is only patchily expressed in trachea and bronchus of a small number of individuals, but more prevalent in alveolar epithelia. In the *ex vivo* infection study, we also demonstrated that alveolar cells were more susceptible than trachea and bronchus epithelial cells to avian influenza H5N1 virus infection. These findings suggest that the human respiratory tract is permissive for avian influenza A viruses, some people are more susceptible to H5N1 infection may be due to the higher expression of SAα2,3Gal in their upper respiratory tract.

1 Materials and methods

1.1 Tissue samples

To study influenza receptor distribution in the human respiratory tract, a total of 142 paraffin-embedded respiratory tissue sections from 72 patients were randomly selected from archival collections of autopsy and biopsy samples between 1994 and 2006 in several local hospitals in Guangxi and Guangdong provinces, China. The age of the patients ranged from antenatal to 76 years old. Different parts of the respiratory tract were included based on the availability of tissues, and were histologically classified as trachea (10 sections), bronchus (40 sections), bronchioles (44 sections) and alveolus (48 sections) (in Table 1).

The postnatal development of the lung may reach completion within the first 2 years of life, and children's lungs do not reach adult volume until 18～24 years of age[15]. During this phase the majority of the growth occurs through an increase in the volume of existing alveoli[15]. Therefore, based on the development of the human respiratory system, patients were classified into four different age groups: antenates (foetal), infants (< 2 years), children (2～18 years) and adults (> 18 years) (Table 1)

Table 1 Distribution of differential age groups and tracheobronchial grades in 72 cases

Age groups	No. of cases	No. of sections	Tracheobronchial grades			
			Trachea	Bronchus	Bronchiole	Alveoli
Fetus	12	35	4	9	11	11
< 2 years	16	33	2	7	11	13
2～18 years	10	19	2	1	8	8
> 18 years	34	55	2	23	14	16
Total	72	142	10	40	44	48

1.2 Lectin histochemical staining of human airway tissues

Expression of SAα2,3Gal and SAα2,6Gal linkages in epithelial tissues of trachea, bronchi, bronchioles and alveoli was examined using the sialic acid linkage specific lectins: *Sambucus nigra* agglutinin (SNA, EY Laboratories, Inc., California, USA), and *Maackia amurensis* agglutinin (MAA-Ⅱ, Vector Laboratories, California, USA), which specifically recognize SAα2,6Gal and SAα2,3Gal linkages, respectively. Paraffin-embedded tissue sections mounted on glass slides were deparaffinized, rehydrated and then incubated consecutively for 15 min with avidin D and biotin solutions (Vector Laboratories) to block nonspecific binding of endogenous biotin and avidin. Tissues were incubated with biotin-labeled MAA-Ⅱ(1 mg/L) or SNA(1 mg/L) for 60 min at room temperature, and then with streptavidin/peroxidase complex reagent (Vector Laboratories) for 30 min followed by color development

using 3,3'-diaminobenzidine(DAB, Vector Laboratories) according to the manufacturer's instructions. Duck's intestine tissue, which has been known to have only SAα2,3Gal linkages, and pig trachea tissue, which has been shown to present both SAα2,3Gal and SAα2,6Gal linkages, were used as positive controls. Sections incubated with PBS were set up as negative controls. Images were captured with a microscope (Nikon eclipse 80*i*) equipped with a digital camera (Spot Pursuit, Diagnostic Instruments, Inc. Michigan, USA) and Spot™ computer software.

All lectin histochemical staining sections were reviewed independently by two pathologist. Relative expression level was classified based on the positive cell number, but not the staining intensity, and counted as high expression (+++ with > 50% of respiratory epithelial cells positive), medium (++ with 30%～50% cells positive), low (+ with 1%～30% cells positive) and undetectable (all epithelial cells negative). All statistical analyses were performed using Statistical Package for the Social Sciences 11.5 (SPSS, Inc., Chicago, IL). Kruskal-Wallis (multitude independent samples) and Mann-Whitney (2 independent samples) analysis were tested for statistical significance. The result were significant when $P < 0.05$.

1.3 *Ex vivo* infection of human lung tissues

H5N1 virus, A/HK/212/03 isolated from human[16], DK/GX/3546/05 randomly selected from a large panel of poultry isolates that have previously been characterized[1,17,18], were used in *ex vivo* viral infection study. A human H3N2 influenza virus, A/ST/602/04, was also included as control. These viruses were passaged once in 10-day embryonated chicken eggs, allantoic fluid from inoculated eggs was collected, $TCID_{50}$s were determined in MDCK cells. Viruses were stored at –80℃ until use.

Eight cases of surgically-removed human respiratory tract tissues from lung cancer or non-cancer patients were obtained from local hospitals in Guangdong province following local Institutional Ethical Review Board-approved protocols. The specimens were kept in cold MEM medium containing antibiotics under aseptic conditions and transported to the laboratory immediately. After brief washing in MEM to remove blood, tissues were cut into small pieces of about 0.2 cm×0.2 cm×0.2 cm and transferred to T25 culture flasks for virus inoculation.

Tissues were infected with 10^3 $TCID_{50}$ of H5N1 virus in a 500 μl inoculum. A separate flask of tissue was incubated with 500 μl PBS as a negative control. The inoculum was removed after one hours incubation at 37℃/5% CO_2, and tissues were further incubated at 37℃/5% CO_2 for 24 h in 3 ml of serum-free F12K Nutrient Mixture (GIBCO, New York, USA) supplemented with 25 mmol/L HEPES Buffer Solution and 1% Antibiotic-Antimycotic(GIBCO). The infected tissues were then fixed in 10% neutral formalin for 24 h and histological sections prepared for immunohistochemical staining.

1.4 Immunohistochemical staining of tissues

For detection of influenza A nucleoprotein (NP) in human tissues, sections were blocked with 1% bovine serum albumin/PBS, stained with an anti-influenza nucleoprotein monoclonal antibody (17H4 clone) raised with H5N1 strain CK/Yu22/02[1] at 1∶5 000 dilution at 4℃ for overnight and then incubated with biotin conjugated goat anti-mouse IgG, (Calbiochem) at 1∶2 000 dilution for 30 min at room temperature, incubated with streptavidin/peroxidase complex reagent (Vector Laboratories) for 30 min at room temperature. Color development and images capture were carried out as described above. H5N1 virus infected mouse lung tissue were used as positive controls for NP staining. Tissue sections incubated with PBS were set up as negative controls.

2 Results

2.1 Distribution of influenza virus sialic acid receptors in human respiratory tissue

SAα2,6 linkage and SAα2,3 linkage sialic acid were stained with SNA and MAA-Ⅱ, respectively. Only the sialic acids expressed on the apical epithelial surface were recognized and counted as positive in this study. The numbers and percentage of anatomical sites expressing SAα2,3Gal and SAα2,6Gal, are summarized in Table 2. As shown in Figure 1, SAα2,3Gal expression was more regularly observed in lower, rather than upper respiratory epithelial cells, with 81.25% of examined alveolar tissue produced positive staining. However, the expression of SAα2,3Gal was only observed in 20%, 27.50% and 38.64% of trachea, bronchus and bronchiole sections, respectively, and the expression pattern was sporadic (Table 2 and Figure 1, $P < 0.01$). This result is consistent with the previous reports that H5N1 virus tends to bind and infect SAα2,3Gal expressing alveolus cells in human lung and to a less extend in trachea and bronchus[13, 19]. In contrast, the expression

of human influenza virus receptor, SAα2,6Gal, was detected in all trachea and bronchus tissue sections, and to a lesser degree in alveolar epithelium (Table 2 and Figure 1, $P < 0.05$). However, there was no significant difference for SAα2,6Gal or α2,3Gal receptor expression levels in the respiratory tract among different age groups, including antenates, infants, children and adults.

Table 2 Distribution of SAα-2,3Gal and SAα-2,6Gal receptor in different anatomical sites of human

Anatomical sites	Number of sections	SAα-2,3Gal					SAα-2,6Gal				
		–	+	++	+++	Positive rate	–	+	++	+++	Positive rate
Trachea	10	8	2	0	0	20.00	0	1	5	4	100
Bronchus	40	29	9	2	0	27.50	0	7	7	26	100
Bronchiole	44	27	16	1	0	38.64	8	17	8	11	81.82
Alveoli	48	9	13	15	11	81.25*	19	15	11	3	60.42**
Total	142	73	40	18	11	48.65	27	40	31	44	80.98

*$P < 0.01$; **$P < 0.05$.

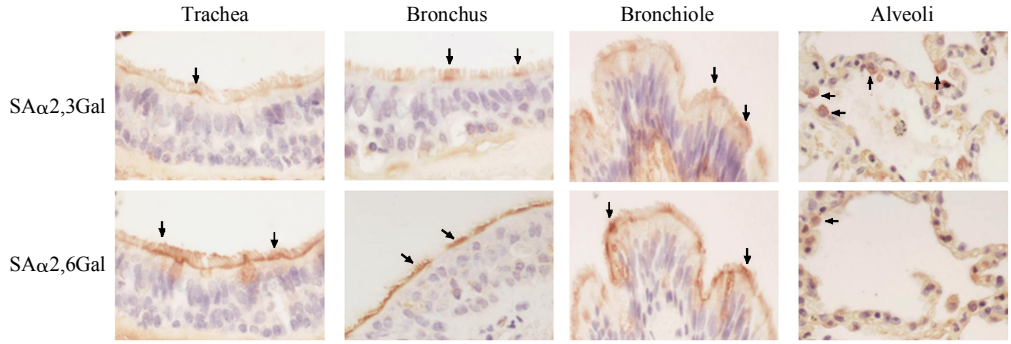

Fig. 1 Detection of SAα2,3Gal linkages and SAα2,6Gal linkages expression(brown) in human respiratory tract tissues by lectin histochemical staining with MAA-Ⅱ and SNA, respectively in trachea, bronchus, bronchiole and alveoli

Arrow heads indicate positive staining. The original magnification was 400×.

2.2 Avian H5N1 virus infection in human respiratory tract tissues

Previous reports suggested that alveolar cells in the lung is the major site for avian H5N1 virus replication in human infection[12~14], but the infection in human upper respiratory tract is still not very clear[14]. We therefore studied H5N1 virus *ex vivo* infection of surgically removed human respiratory tissues. Infection of epithelial cells in trachea, bronchus, bronchiole and alveolus was examined for the presence of the influenza viral antigen nucleoprotein (NP).

A/HK/212/03 was the isolate of a fatal human H5N1 infection[16], and previous receptor binding characterization indicated this virus bears higher affinity to human receptor compared with other H5N1 strains tested[20]. As demonstrated by immunohistochemical staining of NP protein in Figure 2a, NP positive epitthilail cells were observed in bronchial, bronchiolar, and alveolar epithelial cells. And this virus appears to infect the epithelial cells in these tissues with similar efficiency. As most of the human infections were caused by direct poultry to human transmission, it is note worthy to investigate if pure avian type H5N1 viruses are able to infect human respiratory tissues. We then used an avian H5N1 isolates, DK/GX/3546/05, which has typical avian type receptor in haemagglutinin gene, to infect human respiratory tissues. As demonstrated in Figure 2b, infection levels were highest in alveolus cells and lower in bronchus and bronchiole. This result is consistent with the level of SAα2,3Gal receptor expression. It is worthy to note that no NP positive cells were observed in tracheal epithelium following these two H5N1 viruses infection.

Infection of respiratory tissue with H3N2 human isolate, A/ST/602/04, was also carried out to compare with those avian H5N1 isolates. As shown in Figure 2c, many NP positive cells were observed in the epithelium from trachea to alveoli. This is consistent with the distribution of SAα2,6Gal influenza virus receptor.

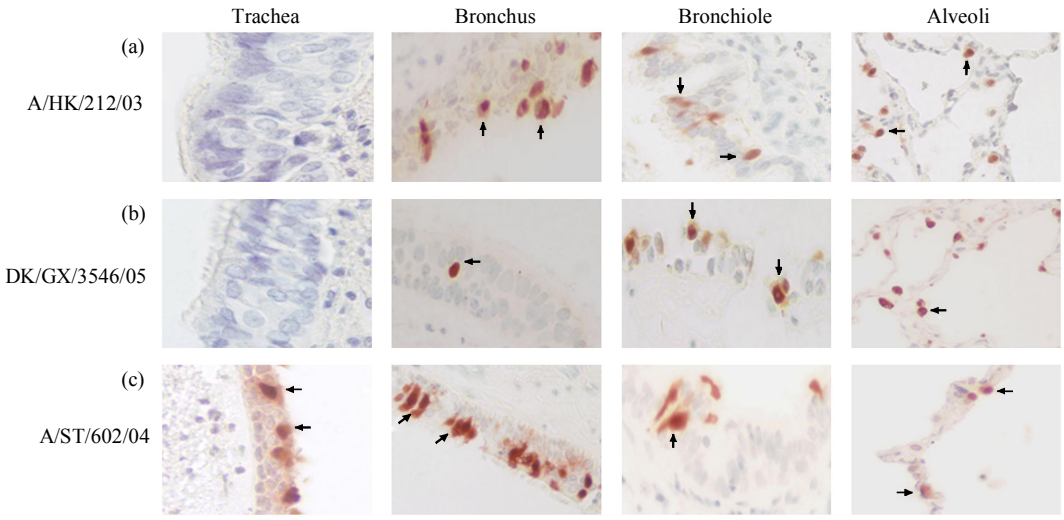

Fig. 2 Detection of influenza viral nucleoprotein(brown) in infection with H5N1 virus was demonstrated in the surgical removed trachea, bronchus, bronchiole and alveolus tissues in *ex vivo* infection with different viruses

(a) A/HK/212/03. (b) DK/GX/3546/05. (c) One H3N2 human influenza virus (A/ST/602/04) used as control. The original magnification was 400×.

3 Discussion

The mechanism by which H5N1 influenza virus transmits from birds to human is not yet understood. Human and avian influenza viruses have different receptor specificities and thus cross-species transmission is restricted. However, in recent years, beside H5N1 virus, two other subtypes of avian influenza virus, H7N7 and H9N2, have also caused human infections[21, 22]. Previous studies of H5N1 virus have shown that the human lower respiratory tract binds higher amount of H5N1, suggested the tissue tropism of avian influenza infections in human[12, 13, 23]. In an another similar study of H5N1 infection in human, viral genome and antigens were detected in type Ⅱ alveolar epithelial cells, also in ciliated and non-ciliated trachea epithelial cells[24]. It remains to be determined if the presence of SAα2,3Gal in the upper respiratory tract would predispose towards susceptibility to H5N1 virus infection. Furthermore, the different anatomical distribution of SAα2,3Gal and SAα2,6Gal in the human respiratory tract has not been systematically investigated. This study for the first time demonstrates the prevalence and extent of SAα2,3Gal sialic acid receptor expression in human respiratory tract tissues.

Our results showed that avian type influenza receptor, SAα2,3Gal, existed predominantly in human lower respiratory epithelium, i.e. bronchioles and alveoli. But in trachea and bronchus, the expression was only sporadically and patchily distributed. This may imply that avian H5N1 influenza virus is more likely to cause lower respiratory tract infection with consequent development of the severe pneumonia observed in the majority of H5N1 infection cases. On the other hand, SAα2,6Gal linkage receptors are ubiquitous in the upper respiratory tract and to a lesser degree in the lower respiratory system, which may explain why seasonal human influenza virus are mostly restricted to upper respiratory tract.

Previous study of human H5N1 infection indicated that respiratory bronchiole and alveolar cells were the major target cells of H5N1 virus replication[24]. To study the susceptibility of human respiratory tissue to H5N1 viral infection, we performed *ex vivo* infection experiments. In consistent with other reports, our results indicated that alveolar epithelial cells are more susceptible to H5N1 than other cells. Moreover, sporadic H5N1 infection of in bronchiolar, bronchial and tracheal epitheliums was also observed. And these supported the distribution of SAα2,3Gal receptor in respiratory tract.

Are some people more susceptible to avian influenza virus infection? This study demonstrated that SAα2,3Gal is prevalent in lung alveolus cells in virtually all cases examined, but only detected in a small number of epithelial cells in the upper respiratory tract of a small portion of people. The molecular mechanism for this differential expression

of SAα2,3Gal in human upper respiratory tract is still not known, though a study had indicated that there was differential expression of related enzymes in human tissues [25]. However, this differential expression of SAα2,3Gal in the upper respiratory tract may explain why some people are more susceptible than others to H5N1 influenza infection. Besides viral factors, the currently-observed limited human to human transmission of H5N1 virus may also be associated with the expression and distribution of this receptor.

References

1 Li K S, Guan Y, Wang J, *et al*. Genesis of a highly pathogenic and potentially pandemic H5N1 influenza virus in eastern Asia. Nature, 2004, **430**(6996): 209～213

2 World Health Organization Global Influenza Program Surveillance Network. Evolution of H5N1 Avian Influenza Viruses in Asia. Emerg Inf Dis, 2005, **11**: 1515～1521

3 Beigel J H, Farrar J, Han A M, *et al*. Avian influenza A (H5N1) infection in humans. N Engl J Med, 2005, **353**(13): 1374～1385

4 World Health organization. Cumulative number of confirmed human cases of avian influenza A/(H5N1). http://www.who.int/csr/disease/avian_influenza/country/cases_ table_2008 _09_10/en/ index.html.

5 Rogers G N, Paulson J C. Receptor determinants of human and animal influenza virus isolates: differences in receptor specificity of the H3 hemagglutinin based on species origin. Virology, 1983, **127** (2): 361～373

6 Rogers G N, D′Souza B L. Receptor binding properties of human and animal H1 influenza virus isolates. Virology, 1989, **173** (2): 317～322

7 Connor R J, Kawaoka Y, Webster R G, *et al*. Receptor specificity in human, avian, and equine H2 and H3 influenza virus isolates. Virology, 1994, **205**(1): 17～23

8 Ito T, Suzuki Y, Suzuki A, *et al*. Recognition of N-glycolylneuraminic acid linked to galactose by the α2,3 linkage is associated with intestinal replication of influenza A in ducks. J Virol, 2000, **74**(19): 9300～9305

9 Couceiro J N, Paulson J C, Baum L G. Influenza virus strains selectively recognize sialyloligosaccharides on human respiratory epithelium: the role of the host cell in selection of hemagglutinin receptor specificity. Virus Res, 1993, **29**(2): 155～165

10 Suzuki Y, Ito T, Suzuki T, *et al*. Sialic acid species as a determinant of the host range of influenza A viruses. J Virol, 2000, **74** (24): 11825～11831

11 Ito T, Nelson J, Couceiro S S, *et al*. Molecular basis for the generation in pigs of influenza A viruses pandemic potential. J Virol, 1998, **72**(9): 7367～7373

12 Shinya K, Ebina M, Yamada S, *et al*. Avian flu: influenza virus receptors in the human airway. Nature, 2006, **440**(7083): 435～436

13 van Riel D, Munster V J, de Wit E, *et al*. H5N1 virus attachment to lower respiratory tract. Science, 2006, **312**(5772): 399

14 Nicholls J M, Chan M C W, Chan W Y, *et al*. Tropism of avian influenza A (H5N1) in the upper and lower respiratory tract. Nature Medicine, 2007, **13**(2): 147～149

15 Haddad G G, Pérez Fontán J J. Development of the respiratory system. In: Nelson W E, Behrman R E, Kliegman R M, Arvin A M, eds. Nelson Textbook of Pediatrics. 15th. Philadelphia: WB Saunders Company, 1996. 1165～1167

16 Peiris J S M, Yu W C, Leung C W, *et al*. Re-emergence of fatal human influenza A subtype H5N1 disease. Lancet, 2004, **363**(9409): 617～619

17 Chen H, Smith G J D, Li K S, *et al*. Establishment of multiple sub-lineages of H5N1 influenza virus in Asia-implications for pandemic control. Proc Nat Acad Sci USA, 2006, **103** (8): 2845～2850

18 Smith G J D, Fan X H, Wang J, *et al*. Emergence and predominance of an H5N1 influenza variant in China. Proc Natl Acad Sci USA, 2006, **103**: 16936～16941

19 Skehel J, Wiley D. Receptor binding and membrane fusion in virus entry: the influenza hemagglutinin. Annu Rev Biochem, 2000, **69**: 531～569

20 Gambaryan A, Alexander T, Galina P, *et al*. Evolution of the receptor binding of influenza A (H5) viruses. Virology, 2006, **344** (2):432～438

21 Fouchier R A, Schneeberger P M, Rozendaal F W, *et al*. Avian influenza A virus (H7N7) associated with human conjunctivitis and a fatal case of acute respiratory distress syndrome. Proc Natl Acad Sci USA, 2004, **101**(5): 1356～1361.

22 Peiris M, Yuen K Y, Leung C W, *et al*. Human infection with influenza H9N2. Lancet 1999, **354**(9182): 916～917

23 Uiprasertkul M, Puthavathana P, Sangsiriwut K, *et al*. Influenza A H5N1 replication sites in humans. Emerg Infect Dis, 2005, **11** (7): 1036～1041

24 Gu J, Xie Z G, Gao Z C, *et al*. H5N1 infection of the respiratory tract and beyond: a molecular pathology study. Lancet, 2007, **370** (9593): 1137～1145

25 Kitagawa H, Paulson J C. Differential expression of five sialytransferase genes in human tissues. J Biochem Chem, 1994, **269** (27): 17872～17878

人呼吸道禽流感病毒受体的分布趋势 *

张增峰[1,2] 樊晓晖[3] 李康生[1] 黄 楷[1,2] 罗殿中[4] 冯振博[4]
韦敏怡[4] 管 轶[1,2] 陈鸿霖[1,2] 张锦霞[1,2]**

([1]汕头大学医学院国际感染与免疫研究所，汕头 515031；[2]香港大学医学院微生物系，新发传染病国家重点实验室，香港；
[3]广西医科大学微生物与免疫学教研室，南宁 530021；[4]广西医科大学病理学教研室，南宁 530021)

摘要 禽类流感病毒和人类流感病毒具有很强的受体识别特异性，分别与唾液酸 α-2,3Gal 和 α-2,6Gal 受体分子结合而感染各自的宿主细胞．这种受体结合特异性是流感病毒在禽类和人类之间跨种属传递的主要障碍．应用凝集素组织化学染色技术，探讨人呼吸道各解剖学部位流感病毒唾液酸受体的分布特征．结果显示，唾液酸 α-2,3Gal受体， 即禽类流感受体，主要分布在下呼吸道的呼吸部即呼吸细支气管和肺泡， 而在主气管、支气管和细支气管仅少量分布．相反，人类流感病毒受体，唾液酸 α-2,6Gal 受体在气管、支气管呈高密度分布，随着支气管分级逐渐降低分布减少，至肺泡分布最少．但比较人呼吸道发育成熟过程中，唾液酸 α-2,3Gal 和 α-2,6Gal 受体的表达，未发现明显差别．禽流感 H5N1 病毒体外感染人呼吸道组织试验结果表明，肺泡上皮较支气管和气管上皮易感染，与唾液酸 α-2,3Gal 受体分布特点相符合．结果提示，人呼吸道可被禽流感病毒感染，目前 H5N1 病毒极少发生人传人的特点，可能与个体间上呼吸道唾液酸 α-2,3Gal 受体表达差异有关．

关键词 A 型流感病毒，唾液酸，SAα2,6Gal 受体，SAα2,3Gal 受体，H5N1 病毒
学科分类号 R373.1+3，R26

---

* 香港特区政府研究资助局 (7488/05M), 香港特区卫生福利食品署传染病控制研究基金、李嘉诚基金会和国家自然科学基金面上资助项目 (30571674, 30771988).

** 通讯联系人.
Tel: 852-28199830, Fax: 852-28199827, E-mail: zhangajx@hkucc.hku.hk

收稿日期：2008-04-01，接受日期：2008-07-16