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Global Distribution of Rubella Virus Genotypes

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Abstract
Rubella virus is an RNA virus that has RNA genome and belonging to genus Rubivirus and family Matonaviridae, and Rubella is a viral infection which can cause fetal death or congenital defects. The World Health Organization (WHO) recognizes 12 genotypes for Rubella virus genome include 1B, 1C, 1D, 1E, 1F, 1G, 1H, 1I, 1J, 2A, 2B, and 2C, and 1provisional genotype, 1a. Genotype1E,which has been confirmed as the most frequent genotype in China, has circulated continuouslysince its first isolation in 2001.

Despite recent developments in wholegenome sequencing technologies, the number of available complete genome sequences of rubella virus is still less than 50 in GenBank. Among these sequences are only 13 complete genome sequences of genotype 2B isolates The genome of RV is a single molecule of positive-strand RNA of approximately 10 kb with a GC content of 69.5 %, by far the most of any RNA virus sequenced to date.[16] The 5' end of the RNA has a 7-methyl-guanosine cap. **Cell, Gene and Therapy, Vol.2, Number 4, Winter 1st, 2021; 142- 145**

Introduction

Rubella virus is an RNA virus that has RNA genome and belonging to genus Rubivirus and family Matonaviridae (formerly belonged to Togaviridae), and Rubella is a viral infection which can cause fetal death or congenital defects, which is known as a congenital rubella syndrome (CRS), if infection ocure during early pregnancy, and in some cases usually presents with mild disease with up to 50% of cases being asymptomatic.[1]

Rubella virus (RV) contains a single-stranded positive-sense (positive-polarity) RNA genome with 9,762 nucleotides in length, exclusive of the 3_ poly A tract, and encoding two non-structural (P90 and P150) and also 3 structural proteins (one of which is nucleocapsid and two envelope [E1 and E2]).[2,3] RV is genetically classified into 13 genotypes, and is a member of the *Togaviridae* family, normally result in a benign illness, however in some adults' cases arthritis and arthralgia have been observed. [4] Also, there are Less frequent complications which are reported in some cases about both encephalitis and thrombocytopenia.[5]

The World Health Organization (WHO) recognizes 12 genotypes for Rubella virus genome include 1B, 1C, 1D, 1E, 1F, 1G, 1H, 1I, 1J, 2A, 2B, and 2C, and 1provisional genotype, 1a. Among them, genotypes 1E and 2B have wide geographic distributionsOver the past 14 years, a total of three wild-type RV genotypes, 1E, 1F, and 2B, have been identified in ChinaTo date, the WHO introduced 12 RV genotypes, 1B, 1C, 1D, 1E, 1F, 1G, 1H, 1I, 1J, 2A, 2B, and 2C, and 1 provisional genotype, 1a. Among them, genotypes 1E and 2B have wide geographic distributions.

Chinese Rubella virological surveillance was atarted in 1999. Over the past 14 years, a entire of 3 wild-type RV genotypes, 1E, 1F, and 2B, have been recognized in China. The RV genotype 1F was reported in 2002; it was considered inactive and probably extinct. Genotype1E,which has been confirmed as the most frequent genotype in China, has circulated continuouslysince its first isolation in 2001. However, the epidemic pattern of genotype 2B inChina is different from that of genotype 1E. Before 2010, the detection of genotype 2B viruses was infrequent; they were only found in 2000 and 2008. Since 2011, perhaps owing to multiple introductions, a new lineage of the 2B virus has become endemic to the mainland of China. [6]

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A genotype 1E strain was initially detected in France in 1995. In 1997, it spread to North America .Genotype 1E strains replaced the circulating strains (1F and 2B) and became the major epidemic strain in China after 2001. In the late 2000s, genotype 2B strains, first isolated in Israel 1968, have become the dominant RV genotype globally (Rubella virus nomenclature update). In Japan, the rubella endemic was attributed to five indigenous genotypes 1a, 1C, 1D, 1E, and 1J. RV genotype 1E strains have started to spread since 2010, followed by genotype 2B strains replacing 1E strains since 2011. Genotype 2B strains caused the most recent rubella outbreak, which peaked in 2013. The mechanism of the genotypic shift remains largely unclear was the first rubella outbreak with the genotype 2B virus.Genotype Iviruses circulate widely in North America, Europe and Asia (Hong Kong, China and Japan), while genotype II virusescirculate in China, India and Israel.[7]

Previous reports showed that nine genotypes (1B, 1C, 1D, 1E, 1F, 1G, 2A, 2B, and 2C) and four provisional genotypes 1a, 1h, 1i, and 1j are present in Europe, North America, South America, and Asia whereas genotype 2B frequently circulates in Asian countries. [8] In China, virological surveillance for rubella started in 1999, and continuous surveillance data indicate that two RV genotypes, namely 1E and 2B, have co-circulated in recent years.[9] Rubella virus was declared eliminated from the United States in 2005.[10] Genotype 1G has been reporting in the Americas over a 7-year span, indicating that these viruses are likely to be endemic. In Brazil.[11] Genotype I viruses circulate widely in North America, Europe and Asia (Hong Kong, China and Japan), while genotype II viruses circulate in China, India and Israel.[12]

In China, the previously endemic RV genotypes were likely 2A and 1F (before 2002) but both were replaced by genotype 1E12. Although genotype 1E is currently detected most frequently, an increasing number of genotype 2B viruses are now detected. Some of the genotype 2B viruses are believed to be imported, while others are likely due to endemic transmission.[13] Two rubella virus genotypes have been discovered: genotype I, which circulates in Asia, Europe, North and South America; and genotype II which overlaps with genotype I in Asia.[14]

The genotype 1E and 2B viruses had wide geographic distribution and were frequently found in the world in recent years .In addition, genotype 1E wasthe predominant genotype circulated in China since itwas first found in 2001.[15]

Despite recent developments in whole genome sequencing methods, the number of available whole genome sequences of rubella virus is still less than 50 in GenBank. Among these sequences are only 13 complete genome sequences of genotype 2B isolates The genome of RV is a single molecule of positive-strand RNA of approximately 1 0 kb with a GC content of 69.5 %, by far the most of any RNA virus sequenced to date.[16] The 5' end of the RNA has a 7-methyl-guanosine cap.[17]

The5' proximal ORF (approximately 6,385 nucleotides) encodes the nonstructural proteins, while the 3' proximal ORF (3, 1 89 nucleotides) encodes the three structural proteins, capsid, E2, and E l .[19] The structural proteins are translated from a 5' capped and polyadenylated subgenomic RNA that is collinear with the 3' one-third of the 405 genome 166.[20] The complete nucleotide sequences have been determined for the genomes of several wild-type and vaccine strains of RV18 and are available in GenBank.[21] In addition, infectious complementary DNA (cDNA) clones of several strains have been produced and used to map genetic elements involved in viral replication and attenuation.[22]

The placement of rubella virus in the family Togaviridae implies a common genome structure and replication strategy. Complete nucleotide sequences are available for several strains of rubella virus.[23,24] The 9,762 nucleotide genome RNA contains a 5' terminal 7-methylguanosine and a 3' terminus that is polyadenylated.[25]

The togaviruses have nonstructural or replication proteins encoded at the 5' end of their genome RNA, whereas the 3' end encodes the proteins that comprise the virus particle, or virion.[26] In the togaviruses, these structural proteins are translated from a subgenomic messenger RNA (mRNA) that derives from, and is co-terminal with, the 3' end of the genome.[27]

p١٥٠ contributes to several domains which are conserved among other RNA virus-encoded proteins. A protease domain located in the carboxyl portion of p1٥٠ is responsible for cleavage of the nonstructural precursor protein p٢٠٠ and is critical for virus

replication.[28] Mutagenesis studies have shown the RV protease protein is a metalloprotease which requires divalent cations for activity.[29]

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