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A ÐÍÍÁ÷¸Ð²¡¶¾ NS1 µ°×½á¹¹Ñ§¾¿½ÓÕ¹

¹ùÓ¨Ó¨ , ÍõÓ¾¸É *

(ÖÐ¹úÅ©Òµ¿ÆÑ§Ô°¹ú¶¯Ö¦ÊÕÒ½ÑÐ¿ÉÙÊÒ½ÚÎÌ¼ÊÕ¹ú¼ÒÖØµãÊµÑéÒ£¬ ¹ú¶¯Ö¦ õ 150001)

Õª Òª£º½ÜÄÉÀ´ A ÐÍÍÁ÷¸ÑÏÏÖØÍµÐ²×ÅÈÈÀà°ÍÐóÇÝµÄ½¿µ£¬ Ëæ×ÅÑÐ¿µÄÉíÈëÉ£¬ ÈÉÃÇÒÑ¾·¢ÏÖ A ÐÍÍÁ÷¸Ð²¡¶¾Ä NS1 µ°×¶Ô²¡¶¾¼ÁÄ¦ÓÐÖØÒªÓ°Ïì£¬ ÊÇÒ»¸ö¶à¹¦Ä¦ÈÃÜ¶¾Ä¦Òò×Ó¡¢ ËüÖ÷Ï¸°û¿¹²¡¶¾ÃâÒßÌØÖÖÄ×Ó£ ¸ù¾ÝÄã¹¦ÄÜµÄ²»Í¬·ÖÎªÁ½¸ö¦¶¾ÃâÒßÌØÖÖÄ×Ó£¬ ÊÇÒ»¸ö¶à¹¦Ä¦ÈÃÜ¶¾Ä¦Òò×Ó¡¢ ÄÃ°ÆÄ NS1 µ°×½á¹¹ÒÑ¼¹½áÍÖ£¬ Ê¹ÈÉÃÇ¿ÉÔÔÖ±¹ÛµÄÈÏÊ¶ÄãÄ¸÷¸ö¹¦Ä¦ÈÃÜ¶¾ÄÃÎÎ»µã¡µÄ×÷ÓÃ»ÚÓÄ£¡ ¸ÃÍÃ×ÛÉÏÄÉ NS1 µ°×µÄ½á¹¹ÌØÕ÷¡¢ ÒÑÖªµÄ¹¦Ä¦ÄÜÎ»µã¼°ÄãÄ¹¦ÄÜ£¬ ÎªÕÓ½á¹¹Ë®Æ½ÉÏÑÐ ¾¿NS1 µ°×µÄ¹¦Ä¦ÄÜÌá¹©²Î¿¼¡£

¹Ø¼üÊ £ºA ÐÍÍÁ÷¸Ð²¡¶¾ ; ·Ç¸½á¹¹µ°× ; ½á¹ ; ¹ÃÜ
ÖÐÍ¼·ÖÀàºÅ £ºQ852.659.5£»Q511 ¡¡¡¡ ÎÄÏ×±êÊ¶Âë £ºA

Progresses in structure studies of influenza A virus NS1 protein

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Abstract: Nonstructural protein 1(NS1)have been reported as one of the major virulence factors of Influenza A virus. The protein is a small, dimeric, multi-functional protein which takes part in both protein-protein and protein-RNA interactions, and has a crucial role in the ability of the virus to evade the antiviral response of the infected cells. According to its multiple functions, NS1A protein is made up of two domains: an N-terminal RNA-binding domain (RBD) (residues 1–73) and a C-terminal effector domain (ED) (residues 84–230/237). The structures of the two domains have been crystallized. In this review, we described the current understanding of NS1A structure and function as well as the relationship between them.

Key words: Influenza A virus; nonstructural protein; structure; function

A ÐÍÍÁ÷¸Ð²¡¶¾ÊÇÒ»ÖÖÑÏÏÖØÍ£°|ÈÉÃàÒÔ¼°ÐóÇÝ½¡ ¿µÄ²¡¶¾£¬ ÊôÓÚÕýÐ§²¡¶¾¿ÆÆ£¬ ÆäµÄ»ùÒò×é°ü°¬ 8 ¸öÕ ½Ú¶ÎµÄµ¥¸¹°¹É RNA£¬ÆäÖÐµÚºÚ¶Ó½¶¶Î¡µÄÄæ¸¹»ò¸ïÄ¶Ô·Ö ×ÓÕÃ¿Î² 26 kµÄµ°×³ÆÆ×÷·Ç¸½á¹¹µ°× 1(Nonstructural protein 1, NS1)¡£A ÐÍÍÁ÷¸Ð²¡¶¾Â²¡ÐÓÓë°Ü¶àÒòÈØ ÓÐ¾ØÆ£¬ µ«NS1 µ°×ÎÞÒÈÉÇÆäÖÐÒ»¸öÓÒª¹µÄÓ°ÏìÒò ÈØ£ ÑÐ¿±ÍÃ÷£¬ NS1 µ°×ÄÜ¹»ÔÚ¶àÖÖ¶¯ÎïÄÆÐÍÍÈÐÓº° Ïì²¡¶¾µÄ¶Á|£¬ ÊÇÒ»ÖÖ¿¹²¡¶¾ÃâÒßÌØÖÖÄ×Ó£¬ ¿ÉÖÔÍ" ¹ý¶àÖÖ»ÚÖÄµ½½ÉÈÐÖ÷ÌåÄÚÃâÒßÌ·´Ó| ¡£ ËüµÄÔÔÍ"¹ý×è Ö¹IÐÍ¸ÉÈÅÄÜÊÍ·ÅÀ´ÖÖÖÄ»ùÌåµÄÄÈÌìÐÔÃâÒßÌ£¬ ²¢Ò Í"¹ý¾ÞÉÙÌåÄÚÊ÷Í»×´Ï¸°û³ÉÊì¡¢ ¼µµÍÉ÷Í»Ï¸°ûÒÝÄÖ TÏ¸°û·´Ó|À´ÖÖÖÄ»ñµÃÐÔÃâÒßÌ [1] ¡£

NS1 µ°×ÊÇÒ»¸ö¶à¹¦Ä¦ÄÜµ°×£¬ ÄÜ¹»²ÎÓëµ°× ÖÊ- µ°×ÊÊ¡¢ µ°×ÊÊ -RNA µÄ½á¹¹¡£ ¸ù¾ÝÄã¹¦ÄÜ¿É ¶"ÒåÎªÁ½¸ö¼¹½áÓò £ºN- ¶ËRNA ½á°ïÖò (RNA-binding domain, RBD)(°±»ùËá²Ð»ù 1-73)£»C- ¶ËÐÞÓ|Çø (Effector domain, ED)(°±»ùËá²Ð»ù 84-230/237)£¬Á½ ¸ö½á¹ÓòÖ®¼ÄÉ loop ÇøÁ¬½Ó¡£ NS1 µ°×Ö®ÄÚÊÊÇÒ» ¸ö¶à¹¦ÄÜµ°×ÊÇÒòÎªµ°×ÉÏ´æÔÚ¶à¸ö¹¦Ä¦ÄÜÎ»µã£¬ ¶ø ÕâÐ©¹¦ÄÜÎ»µãÓÖÓë½á¹¹Ïà¶ÔÓ|£¬ ¼½á¹ÊÇ¹¦ÄÜµÄ» ù´¡£ Ä¿Ç°ÑÐ¾¿½ÎªªÇåªµµÄÖ÷ªµÄ¹¦ÄÜ»µãÓÐ RBD É Ï

ÊÕ¸åÈÕÆÚ £º2009-10-20£»ÐÞ»ØÈÕÆÚ £º2009-11-19
»ù½ðÏîÄ¿ £ºÖÐ¹úÅ©Òµ¿ÆÑ§Ô°¹ú¶¯Ö¦ÊÕÒ½ÑÐ¿ÉÙÔ°Ëù³¤ »ù½ðÖ§Ö§ (2008-17)

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µÄRNA½á°ïÃæ¿Ú´ü°Í EDÖÐCPSF30½á°Ï¿Ú´ü¡£ NS1 µ°°×Í"¹ýÕâÐ©¹|ÄÜÞÔÎ»µãÊµïÖÆäÒÖÖÆÈÞÖ÷¿¹²¡¶¾·´ Ó|µÄ¹|ÄÜ¡£ Ä¿Ç°ÖÑ¾-Í"¹ý´Å¹²Õñ¡¢ X ÉäÏ³§ÌåÑÜÉä µÈ·½·"²â¶"ÁÈÖ»Ð© A ÐÍÁ÷¸Ð²¡¶¾¾ÓêµÄ NS1 µ°°×§Ì åá½¹£¬ ÆäÖÐºüÄ" NS1 ×ÓÉ ×Ì RBD °ÍED µÄ¥ Ìæ¢ ¶¾¾ÌåÁ§Ìåá½¹¡¢ RBD ÓëdsRNA ¸´°ïÎïÌ³§Ìå ½á¹¡¢ EDÓëCPSF30 F2F3 ¸´°ïÎïÌ½á¹ÓÔ¼ÈÉ«³¤ NS1 µ°°×µ¥Ìå§Ìåá½¹¡£ ÕâÐ©½á¹µÄ½âÎöÓÚ½á¹Ë®Æ½ÉÏ ½ÉÊ¼ö NS1 µ°°×·¢»Ó¹|ÄÜµÄ»ùÖÆ¡£

1¡ ¡RNA½á°ïÓÒ½á¹

Ä¿° PDB §Ìåá½¹ÊÿÁ¿âÐ¹²ÓÐ 5 ÌõA ÐÍÁ÷¸Ð ²¶¼ NS1 µ°× RBD §Ìåá½¹¼ÇÂ¼ (PDB ID£°1NS1¡¢1AIL¡¢2ZKO¡¢2ZOA ÕÒ 3F5T ÖÐRBD ½á¹)£¬Ê¹ ÓÃDiscoveryStudio2.1È¼½µ¶ÓÉÌÓÉ½á¹ÖÐ RBDµ¥Ìå½ø ÐÐ½á¹µµ°Ï·¢ïÖ α È¡ÔÓ RMSD ÕÒÔ 0.54µ½1.26Ö® ¼ä¬ µ°°×ÓÉÊ¶¾¾½á¹ÓÛµµ·½Ê½»ù¾ÌåÍ¬£¬ ½ÓÚ loop ÇøºÍ¸ö¹°»ùÉä²âÁ´ÓÐÇø¹ð¡£ RBD µ¥Ìå½á¹ÄÉÊ½ïà Í£¬ ¾ÓÉ 3 ¸ö²»Í¬½ïÌçµÄ α- ÃÝÐý×é³ÉÉ¬ ÃÝÐýÖ®¼ä ÓÉloop ÇøÁ¬½Ó¡£

Í"¹ý½á¹·ÖÎö½ÊÊ¾ö NS1 RBD½á¹ÓõÊÇÍ"¹ýÕÛ µµÐÎ³É¾ÓÐ 6 ¸öÃÝÐýµÄÍ¬Ô´¶¾¾ÌåÀ´Ê¶¹ð dsRNA µÄ[2, 3]£¬¶¾ NS1 RBD ÓëdsRNA µÄÏà»¥×÷ÓÃÊÊÒ² ÖÑ¾¹»½ïÖ¡£ NS1 RBD ÊÇÉ 6 ¸öÃÝÐýÐÎ³ÉµÄ¶ÀÌØ½á ¹£¬ Ã¿¸ö¾¹Ìå¶¼ÓÃ" 3 ¸öα- ÃÝÝ £°α1¡¢α2¡¢α3 [4]¡£ ÔÚRBD ±íÃæÓÐÒ»¸ö½ÉÊµÄ¿Ú´ü£¬ ¿Ú´ü¹ÃæÉÉ 2 ¸ö´ ÏòÃÝÐýµÄ α- ÃÝÝ α1¡¢α1' ÐÎ³É£¬ ÉÄ±ÚÉÉ·´ÏòÃÝÐý α- ÃÝÝ α2¡¢α2' ÐÎ³É¡£

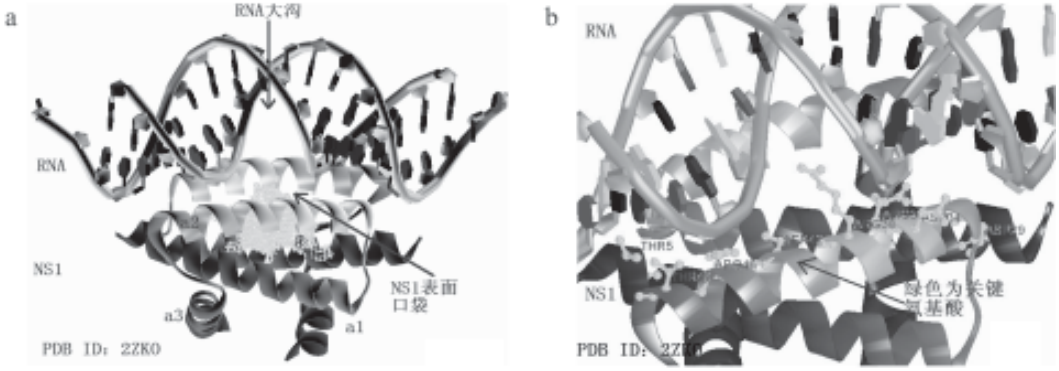
1.1¡ ¡RNA½á°ïÓõÉ dsRNA ¸´°ïÎïµÄ§Ìåá½¹

ChengµÈ[1]²â¶"ÆÉ RBD ÓëdsRNA ¸´°ïÎïÌ³§Ìåá ¹¹(PDB ID£°2ZKO)£¬ÖÖÊµÕýÊÇÇ°ÃæèùÌâá¼°µÄ½á°Ï ¿Ú´ü´|Óë dsRNA ½á°Ï¡£ ÕÙ½á°Ï°ó dsRNA µÄ´ó¹µ¸² ¸ÇÕÙ½á°Ï¿Ú´ü¹µÄ±íÃæéÏ£¬ dsRNA Ë«ÃÝÐýµÄÓáÏïßÓë NS1A ÖÐ·´ïòÃÝÐýµÄÁÁ½¸ö α- ÃÝÝ α2¡¢α2' µÄÓáïßù ±¾ÃÝÐý (Í¼1a)¡£ÊÇÉ dsRNA Ê¶±ðµÄ¹Ø¼ü°±»ùÈá²Ð»ù ÓÐArg38¡¢Arg35¡¢Arg46 ¡¢Thr5¡¢Asp29¡¢Asp34¡¢ Ser42 °ÍThr49 µÈÎ»ÓÚ·´ïòÃÝÐý α- ÃÝÝ α2¡¢α2' ÉÏ µÄÒÐÐ©°±»ùÈá (Í¼1b)£¬ÕÙ½á°Ï¹ý³ÌÖÐÕâ¼¸Î»°±»ùÈá Í"¹ýÐÎ³ÉÇâ¼ÍÓë RNA Ë«ÃÝÐý²ûÉÍ×î³õµÄ½á°Ï¡£ Ôò½á¹ÓõÉÍ"¹ýÍ»±ãÊµÑéµÄ¼¼Ä NS1RBD ¹Ø¼ü°±»ùÈá½á ¹ûÒ»ÓÃ [1]¡£

ÁíÍâ¬ ÑÐ¼¿ÕÓ»¹·¢ïÖ NS1 RBD Ö®ÄÚÒÔÃÜ¹»Çø ·ÖdsRNA¡¢dsDNA ÕÒ dsRNA-DNA ²¢ÇÓÎÐÒÒÃÐÒÀ ÀµÐÊ¶±ð dsRNA ÊÇÒòÎªÁ½¸ö·Ö×ÓÖ®¼ä½ÉÚÓµÄÏà»¥×÷ ÓÃ¾ÖÒ½ÓÖ¸Ïò RNA ÁíÓÒÇ -Á×ÈÄ¹Ç¼ÍÓë 2'- ôÇ»ù»ù ÊÊ¢ Arg35 °ÍThr49 ¿ÉÒÖÖ±½ÓÊ¶±ð RNA µÄ2' ôÇ»ù»ù ÊÆ¬ ÁíÍâ»¹Ó Thr5¡¢Asp29 °ÍAsp34 ¶¼ÉÒÖÍ"¹ýÑÎ ÇÅÊ¶±ð RNA µÄ2'- ôÇ»ù»ùÍÅ [1]¡£

1.2¡ ¡RNA½á°ïÓò¹|ÄÜ

ÔÚÁíÍÁ÷¸Ð²¡¶¾¾Ê¾¼¹ý³ÌÖÐ NS1 RBDµÄRNA½á °ïµÄ¹|ÄÜÓÁ½ñÈÔÎ ÑÐ¼¿Í¸³¹£¬ Ä¿Ç°ÁÕ±êÈÏÎª RBD Í" ¹ýÓê²¡¶¾ dsRNA½á°Ï¸ÕÄë dsRNA£¬ Ê¹Ö®ÎÞ·"Óëµ¥ Ï¸°ûÁÚ¼¾ÉÐ¼Ø»î I ÐÍ¸ÉÈÅÈØ×÷ÓÃµµ°°×²ûÉúÏà»¥×÷ ÓÃ¬ Ê¹ÈÐÖ÷Ï¸°ûÎÞ·"²ûÉú β ¸ÉÈÅØÓ¬ ´Ó¶¾Ñµ½ÒÖÖÆ ÉÐÖ÷ÃâÒ©¡¢ ÔöÇ¿²¡¶¾¶Á|µÄ×÷ÓÃ¡£ Ö®Ç°µÄÖ»ÐÐ©½ÉÚÏÖ ÔÚÓÑ¾-±»ÖÓÃ÷ÊÇ´´íÎóµÄ¡£ ÀýÈçÔÚÔçÁÚµÄÑÐ¼¿ÖÐÈÏÎª NS1 ¿ÉÒÖÖ"¹ý RBD ÕÆ dsRNA ¶¾ÖÖÓÁÚ RNA µÄ° °½¶Ã (PKR)µÄ»ÎÔ¬ µ«Ëæ°óÖ°ÊµÊÇ NS1 ED ÓëPKR µÄ½á°Ï²ûÉúÒÖÖÆ×÷ÓÃ [5]¡£ÁíÎâ NS1 µ°°×»¹¾ÓÐÖÖÆ RNA ³ÁÄ-ìØÔ (¼´RNA ¸ÉÈÅ»ÎÔ)£¬ÀàÈÆÁÓÑÑ°µÄ RNA ³ÁÄ-ÒÖÖ×Ó¡£ Ô¬ÒÇ NS1 ÓëRNA ½á°Ï¶¾ÖÖÆ RNA ¸ÉÈÅ¡£ ²»Í¬µÄ ÐÍÁ÷¸Ð²¡¶¾¾Ê¾¼¾ÓÐ²»Í¬µÄÖÖ



Í¼1¡ ¡NS1ÓëdsRNA ¸´°ïÎïµÄ§Ìåá½¹ (a)ÕÒ¾ºá½á°Ï¹Ø¼ü°±»ùÈá (b)

ÖÆRNA ³ÁÄ¬»îÐÔ [1, 6]¡£

NS1µº°×Óë°ÎÖÖ RNA½á°ïÖ±½Ó½ô¶" NS1µº°×µÄ ¹|ÄÜ¡£ NS1 µº°×¿ÉÖÔÍ"¹ÿÎÃÃÐ»ÚÖÃÓ°ïÌÉÐÖ÷µº°×·–Ò¢£ °Í"¹ýÓë mRNA µÄ3' ¶à¾ÍÜÙÜÖÉáÎ²½á°ÏÀ´ÖÖÖÆ³É ÊïÏ¸°ûµÄ mRNA ¹ÉÊ¾ö [7]£»½áÏ U6snRNA¡¢U6atac snRNA ÖÖÖÆ°Ìà mRNA µÄ¼ô¼ [8, 9]£»NS1 µº°×¿ÉÖÔ ÓëÄÁ RNA(dsRNA)½á°ïÉ¬ ÖÖÆ 2'-5' ¹ÑÏÙÜÖÉá°Ï³É Ã¸/RNA Ã¸L ÅÖÃ·¶¾Ø½ÓÓ»ëÖ¹ α/β ¸ÉÐÄÈÖµÄ²¹ÉÍ£¬ ½µµÍÉÐÖ÷Ï¸°ûµÄ¿¹²¡¶¾»îÐÔ £»ÁÍÃ NS1 Óë²¡¶¾ RNA½á °Ï°óÍ"¹ýÓë ED½á°ïµÄ eIF4GI Áª°Ï×÷ÓÃÉ¹µÃ²¡¶¾µÄ ·–ÖëÉ®Æ¾Ðò¼Ó¡£ ÖÖÉ NS1 Óë²»Í–ÖÖÀµÄ RNA(RNA µÄÐÒÁÐ½á¹¹¶¼¿ÉÄÜ²»Í¬)½á°ïÁó¶" NS1 µº°×µÄ¹|ÄÜ¡£

2 ¡¡ÐÒÓ|Çº½á¹¹

Ä¿°ÒÐ© A ÐÍÁ÷¸Ð²¡¶¼¾ÓêµÄ NS1 µª× ED½á ¹¹ÑÑ¼±»½ÃÏÖ³ÖÖ£¬ PDB ¾ÝÌâ½á¹¹ÉÿÁÝ¿ãÓÐ¹²ÓÐ 7 Ìõ A ÐÍÁ÷¸Ð²¡¶¼ NS1 ED ¾ÝÌâ½á¹¹¼ÇÃ¼ (PDB ID£° 2KKZ¡¢3EE8¡¢3EE9¡¢3D6R¡¢2RHK¡¢2GX9¡¢ 3F5T ÖÐED½á¹)£¬ÊÃ Discovery Studio2.1 ÈÍ¼pÑ Ã¿¸öÍ¼½á¹¹ÖÐµÄµ¥ÌåÌ¬¡³ÖÀ´Í"¹ýµº°×ÓÊ½á¹¹µp °Ï·¢ÏÖ α Ì¼Ô»Ó RMSD ÖÃÚ 0.92 µ½2.05 Ö®ä¿¬¶p ¼¶½á¹¼°ïÌáÍ–£¬ ½ÃÚ loop ÇøÖÎ¼ÇÈ»ù¶ÈÄ©Î²´|ÓÐ ËÙ²»Í¬¡£ °µÊ¼ÄÈÈÙÓÐ A ÐÍÁ÷¸Ð²¡¶¼ NS1 ED µ¥ÌåÁ´ ÕÛµpÄÉÊ½»ù±¼ÌâÍ–£¬ µ«ÊÇ¶p¾ÜÌåÏà»¥×÷ÓÃ¿ÇæÆ½á°Ï ÄÉÊ½î±ð"Ü ÕÊ¡ ÕÃ¿ÉÄÜÓë¶¼ÈÌÒÌ±ÐÕÐ¹Ø»ò¶Ã¿ÉÄÜÇ ÓÉ¾ÀÑ¼ Á|ÒÌ³ÉµÄÉ¬ ¾ÌâÔ·Ò»¹ÓÉ´ÑÑ¼¡ÈÓ±µÄÉÍÈë ÑÑ¼ [10, 11, 12]¡£

2.1 ¡¡NS1 µº°×ÐÒÓ|Çº¾ÌâÌ½á¹¹ÌØÕ÷

ÑÑ¼¿±ÍÃ÷ NS1 ÐÒÓ|ÇºÃ¿¸öµ¥ÌåÌ¾¼°ü°¬ 7¸öβ-ÕÛ µpÉ¡¢ 3¸öα-ÃÝÐÝ£¬ ÕÃ¸öá¹¹±»³ÆÎª α-ÃÝý β-ÐÂ ÕÃÕÛµp£¬ ÊÇÒ»ÖÖÉµÄÕÛµp½á¹¹¡£ Ö®ÄÚÔÒ³ÆÎªÐÂÕÃÕÛ µpÊÇÒòÎªÕÛ½á¹¹Ó 6¸öβ-ÕÛµpÉÐ³É 1¸öÐÂÕÃ×´µÄ ÍäÇú¹ç¢ÇÒÒÔ 1¸ö α-ÃÝÐýÎªÖÉÄ¡£ Õâ6¸öβ-ÕÛp ÉÐ¼ÓÕ α-ÃÝÐýµÄÒ»²à£¬ ÐÍ³ÉÍøÂç×´ÊÈ®ÐÔÍà»¥×÷ÓÃ ÖÉÄ¡£ ÈçÓë 2a ÉÍÊ¾¬ µÍÕ»¸ö β-ÕÛµpÉ (a)ÕÉÃÕÕÃ×´ ½á¹¹Í»ÆÐÒ»²à£¬ ÓÉÕ»¸ö¶Ì α-ÃÝý (A)Á¼Ó β-ÕÛµpÉ b ÉÍ¡£ ÕÕÕâÖ®°óÉÇ 5¸öβ-ÕÛµp¹É (b¡¢c¡¢d¡¢e¡¢ f)ÒÀ´ÎÊ×Î²ÏàÁóÐÎ³É·´ÏòÃ¼ÐÐµÄ βÕÛµpÉ-º°üÎß»ÅÖÉÉÄ µÄÃÝý B¡£ÕÂ¸öÃÝý B ÊÇ½á¹¹Ó×î³¤µÄ α-ÃÝý£¬ Ö® °óÁ½ÓÅ f¡¢g ÕÛµp¹ÉÓë d ÕÛµp¹ÉÅµÁÚÇÒ·´ÏòÃ¼ÐÐ¡£ ÕÛµpÉ g °óÃæ¼Ó<Î°óÒ»¸ö¶p¼¶½á¹¹ÊÇ α-ÃÝý C£¬ÐÎ ³ÉÐÂÕÃ×´½á¹¹µÄÁÍÈÈ®ÐÔ½á°Ï²Û [10-14]¡£ÁÍÍâ£¬ ÑÐ¼ÓÓ»¹·¢ ÏÖÐßÓ|ÇºµÄÌåµÄÊÉ®ÐÔ½á°Ï²Û (ÈçÄ¼ 2b ÖÐÃÍÉ«µÄ½á°Ï ²Û)¡£ÕâÁ¸ö½á°Ï¿ÚÜÉÇÓÉ Gly183~Asn188 °±»ÜÉáµÄÖ÷ ÁÔÒ¼ Lys108¡¢Lys110¡¢Ile117¡¢Gln121¡¢Val180 °±»ÜÉáµÄ²ãÁ´ÐÎ³É¡£ Ä¿°ÒÑ¼ÖÉµÄÚ¿ÚÜÉÇ ÇÐ¸ÍÖë ¶à¾ÍÜÙÑÑ®¯ÌÒÌÒÒ¿µÄ 30 kDaÑù (subunit CPSF30) F2F3 Ð¿Ö¸»ÜÐµÄ½á°ÏÎ»ã¡£ Das[12]µÈ¾ÍÐÓÉÉ NS1 ED ÓëCPSF30 F2F3 Ð¿Ö¸»ÜÐÏà½á°Ï¸´°ÏÎï¾ÝÌâ½á¹¹£¬ ·¢ÏÖÄæ½á°Ï·ÊÉ¼Î²ÉÄ¾ÌÌåµ°°×¸´°ÏÎï£¬ ²¢ÇÒÓë½á°Ï F2F3 Ð¿Ö¸»ÜÐÓ ED ¶p¾ÜÌåÏà»¥×÷ÓÃ¿ÇæÓÐ½Ï´ó±ä »¯£ ´ÉÍâ£¬ ÁíÒ»¸ö¼¥ÌåµÄ Trp187 Ò²¿ÉÓÔ½á°ïµ½ÕÂ ¸ö¿Ú"ÜÖÐ¡£

¾Ý±¨µÀÐÒÓ|Çº¶p¾ÜÌåÏà»¥×÷ÓÃ¿ÇæÓæ´æÔÚ 2 Ö»Í¬µÄÄÉÊ½ £°ÃÝý -ÃÝÐýÏà»¥×÷ÓÃæ (Í¼2c)ÕÕ¼ºÕÛµp ¹É-ÕÛµp¹ÉÏà»¥×÷ÓÃæ (Í¼2b)¡£ÄÇ°¾¾¾ NS1 ÐÒÓ| ÇºÐÎ³É¶p¾ÜÌåÉ±ÊÊÉÇÄÄÖÖ·½Ê½»¹Ã»ÓÐ¶¨ÂÛ£¬ µ«ÑÐ¼ºÕß ÆÕ±éÇãÏòÓÚ°óÕß¡£

2.2 ¡¡ÐÒÓ|Çº½á¹¹|ÄÜ

NS1 µª× C ¶ÉÐÒÓ|ÇºÖÁÉÙ½á°ïÉÄÖÖ²»Í¬µº°× £° ÑÓÉÏÆÐÊ¿Ò»Ó (eIF4GI)¡¢ÉÄÁ RNA ÒÀµµÄµº°×¼¼ÃÃ¸ (PKR)¡¢¶à¾ÍÜÙÜÖÉá½á°ïµº°× II (PAB II)ÕÕ¼ÇÐ¸î ¶à¾ÍÜÙÜÖÉáµÄÌØòìÉÕÒ»Ó 30 kDa Ñù (subunit CPSF30)£¬ÌåïÖÄÉÄä¶à¹|ÄÜµº°×ÓÊµÄ¼¼¼ÕÉ¡£ NS1 Óë eIF4GI µÄ½á°ïÄÜ¹»¸¨ÖÚÉÚÍá¸ß²¡¶¾ mRNA µÄ·–Ò£»ÓëCPSF30¡¢PABII½á°Ï°óÍ"¹ýÓ°ïïÏ¸°ûÄÚÇºÌà RNA 3'-Ä©¶¶¼¼¹¹ÄÜ¹»ÖÖÓÄÏ¸°ûµÄ¹ú²úÉú mRNA£¬ÌØ¾ÊÇ IFN-β µÄmRNA£»ÓëPABII µÄ½á°ïÄÜ¹»»èÖ¹ PABII ÕÕÞ Ö÷Ï¸°ûºÉÄÚÑÓ³ÇºÌà mRNA µÄpoly-A ÎÊ² ²¢»èÖ¹Ã mRNA µÄºÉÄ³ö¡£ Ä¿°³ÝÉÉ NS1-CPSF30¸´

Í¼2¡¡NS1 ÐÒÓ|Çº¼ÌâÌ½á¹¹ (a)ÕÕ¼°¶p¾ÜÌåµÄÄ¼ÖÖÌà»¥×÷ÓÃÄÉÊ½ (b¡¢c)

[illegible] NS1 [illegible] [illegible] NS1 [illegible] [illegible] NS1 [illegible] [illegible] [11] [illegible]

3 [illegible] NS1 [illegible]

Bornholdt [illegible] Prasad [illegible] [10] [illegible] X [illegible] H5N1(A/Vietnam/1203/2004)A [illegible] NS1 [illegible] (PDB ID [illegible] 3F5T) [illegible] NS1 [illegible] RBD [illegible] NS1 [illegible] 3 [illegible] ED [illegible] NS1 [illegible] (RBD [illegible] ED) [illegible] 2 [illegible] NS1 [illegible] dsRNA [illegible] 3 [illegible] NS1 [illegible] dsRNA [illegible] NS1 [illegible] dsRNA [illegible] dsRNA [illegible] NS1 [illegible] RNA [illegible] NS1 [illegible] A [illegible] NS1 [illegible] [15] [illegible] NS1 [illegible] [16] [illegible] NS1 [illegible] [17] [illegible] NS1 [illegible] NS1 [illegible] A [illegible]

[illegible]

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