Hemagglutinin (HA) and Neuraminidase (NA) [[1](https://www.sciencedirect.com/topics/immunology-and-microbiology/hemagglutinin-neuraminidase#:~:text=We%20define%20the%20HA%E2%80%93NA%20balance%20as%20the,decoy%20receptors%20present%20on%20cells%20and%20mucus.), [2](https://www.sciencedirect.com/topics/immunology-and-microbiology/virus-hemagglutinin#:~:text=Hemagglutination%20inhibition%20(HI)%20assay%0A%0ASome%20viruses%20such%20as,(RBCs)%20and%20agglutinate%20them%20termed%20hemagglutination%20(HA).), [3](https://pmc.ncbi.nlm.nih.gov/articles/PMC10549826/#:~:text=Abstract.%20Influenza%20virus%20neuraminidase%20(NA)%20can%20act,hemagglutination:%20T148%2C%20D151%2C%20and%20more%20recently%2C%20H150.)]

HA and NA are **two glycoproteins found on the surface of influenza viruses**. They play crucial roles in the virus life cycle, facilitating attachment to host cells and release of new viruses. [[4](https://www.cancer.gov/publications/dictionaries/cancer-terms/def/hemagglutinin-neuraminidase), [5](https://pmc.ncbi.nlm.nih.gov/articles/PMC6520700/), [6](https://pmc.ncbi.nlm.nih.gov/articles/PMC136693/#:~:text=Hemagglutinin%2Dneuraminidase%20(HN)%20protein%2C%20which%20is%20responsible%20for,type%2Dspecific%20manner%20to%20induce%20efficient%20membrane%20fusion.), [7](https://www.nature.com/articles/srep45043)]

**Functions: [**[**8**](https://www.sciencedirect.com/topics/medicine-and-dentistry/hemagglutinin#:~:text=Hemagglutinin%20antigen%20(H)%20is%20a%20glycoprotein%20that,and%20fuse%20with%20the%20host%20cell%20membrane.)**,** [**9**](https://www.sciencedirect.com/topics/neuroscience/neuraminidase)**,** [**10**](https://pmc.ncbi.nlm.nih.gov/articles/PMC3169259/#:~:text=Hemagglutinin%20(HA)%20and%20neuraminidase%20(NA)%20are%20two,and%20the%20induction%20of%20protective%20immune%20responses1%2C2.)**]**

* **HA:** Binds the virus to sialic acid receptors on host cell membranes, initiating infection. [[5](https://pmc.ncbi.nlm.nih.gov/articles/PMC6520700/), [11](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/hemagglutinin-neuraminidase#:~:text=The%20surface%20glycoprotein%2C%20hemagglutinin%20neuraminidase%20(HN)%2C%20is,viral%20envelope%20and%20host%20cell%20plasma%20membrane.)]
* **NA:** Cleaves sialic acid receptors, allowing the virus to detach from infected cells and release new viruses. [[5](https://pmc.ncbi.nlm.nih.gov/articles/PMC6520700/), [12](https://www.sciencedirect.com/topics/immunology-and-microbiology/hemagglutinin-neuraminidase#:~:text=Haemagglutinin%2Dneuraminidase%20(HN)%20is%20one%20of%20two%20hPIV,the%20past%20few%20decades%20with%20variable%20success.), [13](https://pubmed.ncbi.nlm.nih.gov/31137516/)]

**Role in Infection: [**[**14**](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/hemagglutinin-neuraminidase#:~:text=The%20surface%20glycoprotein%2C%20hemagglutinin%20neuraminidase%20(HN)%2C%20is,viral%20envelope%20and%20host%20cell%20plasma%20membrane.)**]**

1. **Attachment:** HA binds to sialic acid receptors on the host cell surface. [[7](https://www.nature.com/articles/srep45043), [15](https://pmc.ncbi.nlm.nih.gov/articles/PMC2937864/), [16](https://www.youtube.com/watch?v=caMne7nQUL8), [17](https://pmc.ncbi.nlm.nih.gov/articles/PMC3410141/#:~:text=(i)%20HA%20spikes%20on%20the%20viral%20envelope,acid%2Dcontaining%20receptors%20on%20the%20host%20cell%20membrane.)]
2. **Entry:** The virus enters the host cell through fusion or endocytosis. [[18](https://pmc.ncbi.nlm.nih.gov/articles/PMC8830744/#:~:text=It%20involves%20virus%20internalisation%20through%20endocytosis%20and,and%20Wiley%2C%202000;%20Hamilton%20et%20al.%2C%202012).)]
3. **Replication:** The virus replicates inside the host cell. [[19](https://pmc.ncbi.nlm.nih.gov/articles/PMC4162146/#:~:text=Influenza%20viruses%20exploit%20these%20fundamental%20processes%20within,an%20epithelial%20cell%20surface%20sialic%20acid%20moiety.), [20](https://pmc.ncbi.nlm.nih.gov/articles/PMC7149683/#:~:text=After%20gaining%20entry%20into%20the%20body%2C%20a,upon%20the%20type%20of%20viral%20nucleic%20acid.)]
4. **Release:** NA cleaves sialic acid receptors, allowing the newly produced viruses to detach from the host cell and infect new ones. [[15](https://pmc.ncbi.nlm.nih.gov/articles/PMC2937864/), [21](https://pubmed.ncbi.nlm.nih.gov/37754760/)]

Importance in Antiviral Therapy: [[22](https://synapse.patsnap.com/article/what-are-hemagglutinin-inhibitors-and-how-do-they-work#:~:text=By%20understanding%20how%20hemagglutinin%20interacts%20with%20host,critical%20component%20in%20the%20fight%20against%20influenza.)]

HA and NA are important targets for antiviral drugs. Neuraminidase inhibitors (NAIs), such as oseltamivir (Tamiflu), prevent NA from cleaving sialic acid receptors, blocking virus release and inhibiting infection. [[23](https://pmc.ncbi.nlm.nih.gov/articles/PMC6362415/#:~:text=While%20the%20NA%20is%20the%20main%20target,monoclonal%20antibodies%20(%20Nachbagauer%20and%20Krammer%2C%202017).), [24](https://pmc.ncbi.nlm.nih.gov/articles/PMC374304/), [25](https://pmc.ncbi.nlm.nih.gov/articles/PMC7172302/), [26](https://wwwnc.cdc.gov/eid/article/24/10/et-2410_article), [27](https://pmc.ncbi.nlm.nih.gov/articles/PMC4074938/), [28](https://www.cdc.gov/flu/hcp/antivirals/index.html#:~:text=The%20neuraminidase%20inhibitors%20include:%20Oseltamivir%20(available%20as,influenza%20in%20people%20one%20year%20and%20older.)]

**Additional Notes: [**[**29**](https://pmc.ncbi.nlm.nih.gov/articles/PMC136693/#:~:text=In%20contrast%2C%20paramyxoviruses%20have%20two%20glycoproteins%20that,the%20fusion%20(F)%20protein%20induces%20fusion%20(16).)**,** [**30**](https://www.sciencedirect.com/science/article/pii/S0969212605001310#:~:text=For%20many%20of%20the%20paramyxoviruses%20(e.g.%2C%20parainfluenza,(HN)%20has%20hemagglutinating%20and%20neuraminidase%20(NA)%20activities.)**,** [**31**](https://www.sciencedirect.com/topics/medicine-and-dentistry/paramyxoviridae#:~:text=3.2%20Paramyxoviruses%0A%0AThe%20Paramyxoviridae%20are%20a%20family%20of,and%20mumps%20virus%20(Lamb%20and%20Kolakofsky%2C%202001).)**]**

* HA and NA are also found in other viruses, such as paramyxoviruses. [[29](https://pmc.ncbi.nlm.nih.gov/articles/PMC136693/#:~:text=In%20contrast%2C%20paramyxoviruses%20have%20two%20glycoproteins%20that,the%20fusion%20(F)%20protein%20induces%20fusion%20(16).), [30](https://www.sciencedirect.com/science/article/pii/S0969212605001310#:~:text=For%20many%20of%20the%20paramyxoviruses%20(e.g.%2C%20parainfluenza,(HN)%20has%20hemagglutinating%20and%20neuraminidase%20(NA)%20activities.), [31](https://www.sciencedirect.com/topics/medicine-and-dentistry/paramyxoviridae#:~:text=3.2%20Paramyxoviruses%0A%0AThe%20Paramyxoviridae%20are%20a%20family%20of,and%20mumps%20virus%20(Lamb%20and%20Kolakofsky%2C%202001).)]
* The subtypes of HA and NA determine the host specificity and virulence of influenza viruses. [[7](https://www.nature.com/articles/srep45043), [32](https://pubmed.ncbi.nlm.nih.gov/2915381/)]
* Mutations in HA and NA can lead to changes in virus infectivity and resistance to antiviral drugs. [[33](https://virologyj.biomedcentral.com/articles/10.1186/1743-422X-6-74#:~:text=The%20viruses%20resistant%20to%20these%20drugs%20emerge,infected%20cells%20without%20the%20need%20of%20NA.), [34](https://pmc.ncbi.nlm.nih.gov/articles/PMC7798331/#:~:text=According%20to%20the%20above%20results%2C%20HA%20and,contribute%20to%20virulence%20alteration%20during%20serial%20passaging.)]

Conclusion: [[35](https://www.tandfonline.com/doi/pdf/10.1038/s41426-018-0182-2#:~:text=(NA)%2C%20which%20are%20responsible%20for%20viral%20recognition%2C,H7N9%20infection%20in%20clinical%20settings%2010%2C%2011.)]

Hemagglutinin (HA) and neuraminidase (NA) are essential viral glycoproteins that play critical roles in influenza virus infection. They facilitate attachment to host cells, entry, and release of new viruses. Understanding their functions and interactions is crucial for developing effective antiviral therapies and vaccines. [[16](https://www.youtube.com/watch?v=caMne7nQUL8), [36](https://pmc.ncbi.nlm.nih.gov/articles/PMC112098/#:~:text=Balanced%20Hemagglutinin%20and%20Neuraminidase%20Activities%20Are%20Critical,Replication%20of%20Influenza%20A%20Virus%20%2D%20PMC.), [37](https://pubs.acs.org/doi/10.1021/acscentsci.8b00666), [38](https://www.sciencedirect.com/science/article/pii/S1198743X16302312#:~:text=The%20HA%20initiates%20the%20virus%20entry%20by,host%20specificity%20and%20resistance%20to%20antiviral%20treatment.), [39](https://pmc.ncbi.nlm.nih.gov/articles/PMC7397844/#:~:text=Influenza%20A%20and%20B%20viruses%20have%20two,A%20viruses%20are%20further%20classified%20into%20subtypes.), [40](https://pmc.ncbi.nlm.nih.gov/articles/PMC5536029/), [41](https://pubmed.ncbi.nlm.nih.gov/31629602/), [42](https://pmc.ncbi.nlm.nih.gov/articles/PMC6563287/), [43](https://www.sinobiological.com/research/virus/influenza-hemagglutinin-function#:~:text=Hemagglutinin%20(HA)%20or%20Haemagglutinin%20(BE)%20is%20an,to%20the%20cell%20that%20is%20being%20infected.)]

*Generative AI is experimental.*

[1] [https://www.sciencedirect.com/topics/immunology-and-microbiology/hemagglutinin-neuraminidase](https://www.sciencedirect.com/topics/immunology-and-microbiology/hemagglutinin-neuraminidase#:~:text=We%20define%20the%20HA%E2%80%93NA%20balance%20as%20the,decoy%20receptors%20present%20on%20cells%20and%20mucus.)

[2] [https://www.sciencedirect.com/topics/immunology-and-microbiology/virus-hemagglutinin](https://www.sciencedirect.com/topics/immunology-and-microbiology/virus-hemagglutinin#:~:text=Hemagglutination%20inhibition%20(HI)%20assay%0A%0ASome%20viruses%20such%20as,(RBCs)%20and%20agglutinate%20them%20termed%20hemagglutination%20(HA).)

[3] [https://pmc.ncbi.nlm.nih.gov/articles/PMC10549826/](https://pmc.ncbi.nlm.nih.gov/articles/PMC10549826/#:~:text=Abstract.%20Influenza%20virus%20neuraminidase%20(NA)%20can%20act,hemagglutination:%20T148%2C%20D151%2C%20and%20more%20recently%2C%20H150.)

[4] <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/hemagglutinin-neuraminidase>

[5] <https://pmc.ncbi.nlm.nih.gov/articles/PMC6520700/>

[6] [https://pmc.ncbi.nlm.nih.gov/articles/PMC136693/](https://pmc.ncbi.nlm.nih.gov/articles/PMC136693/#:~:text=Hemagglutinin%2Dneuraminidase%20(HN)%20protein%2C%20which%20is%20responsible%20for,type%2Dspecific%20manner%20to%20induce%20efficient%20membrane%20fusion.)

[7] <https://www.nature.com/articles/srep45043>

[8] [https://www.sciencedirect.com/topics/medicine-and-dentistry/hemagglutinin](https://www.sciencedirect.com/topics/medicine-and-dentistry/hemagglutinin#:~:text=Hemagglutinin%20antigen%20(H)%20is%20a%20glycoprotein%20that,and%20fuse%20with%20the%20host%20cell%20membrane.)

[9] <https://www.sciencedirect.com/topics/neuroscience/neuraminidase>

[10] [https://pmc.ncbi.nlm.nih.gov/articles/PMC3169259/](https://pmc.ncbi.nlm.nih.gov/articles/PMC3169259/#:~:text=Hemagglutinin%20(HA)%20and%20neuraminidase%20(NA)%20are%20two,and%20the%20induction%20of%20protective%20immune%20responses1%2C2.)

[11] [https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/hemagglutinin-neuraminidase](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/hemagglutinin-neuraminidase#:~:text=The%20surface%20glycoprotein%2C%20hemagglutinin%20neuraminidase%20(HN)%2C%20is,viral%20envelope%20and%20host%20cell%20plasma%20membrane.)

[12] [https://www.sciencedirect.com/topics/immunology-and-microbiology/hemagglutinin-neuraminidase](https://www.sciencedirect.com/topics/immunology-and-microbiology/hemagglutinin-neuraminidase#:~:text=Haemagglutinin%2Dneuraminidase%20(HN)%20is%20one%20of%20two%20hPIV,the%20past%20few%20decades%20with%20variable%20success.)

[13] <https://pubmed.ncbi.nlm.nih.gov/31137516/>

[14] [https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/hemagglutinin-neuraminidase](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/hemagglutinin-neuraminidase#:~:text=The%20surface%20glycoprotein%2C%20hemagglutinin%20neuraminidase%20(HN)%2C%20is,viral%20envelope%20and%20host%20cell%20plasma%20membrane.)

[15] <https://pmc.ncbi.nlm.nih.gov/articles/PMC2937864/>

[16] <https://www.youtube.com/watch?v=caMne7nQUL8>

[17] [https://pmc.ncbi.nlm.nih.gov/articles/PMC3410141/](https://pmc.ncbi.nlm.nih.gov/articles/PMC3410141/#:~:text=(i)%20HA%20spikes%20on%20the%20viral%20envelope,acid%2Dcontaining%20receptors%20on%20the%20host%20cell%20membrane.)

[18] [https://pmc.ncbi.nlm.nih.gov/articles/PMC8830744/](https://pmc.ncbi.nlm.nih.gov/articles/PMC8830744/#:~:text=It%20involves%20virus%20internalisation%20through%20endocytosis%20and,and%20Wiley%2C%202000;%20Hamilton%20et%20al.%2C%202012).)

[19] [https://pmc.ncbi.nlm.nih.gov/articles/PMC4162146/](https://pmc.ncbi.nlm.nih.gov/articles/PMC4162146/#:~:text=Influenza%20viruses%20exploit%20these%20fundamental%20processes%20within,an%20epithelial%20cell%20surface%20sialic%20acid%20moiety.)

[20] [https://pmc.ncbi.nlm.nih.gov/articles/PMC7149683/](https://pmc.ncbi.nlm.nih.gov/articles/PMC7149683/#:~:text=After%20gaining%20entry%20into%20the%20body%2C%20a,upon%20the%20type%20of%20viral%20nucleic%20acid.)

[21] <https://pubmed.ncbi.nlm.nih.gov/37754760/>

[22] [https://synapse.patsnap.com/article/what-are-hemagglutinin-inhibitors-and-how-do-they-work](https://synapse.patsnap.com/article/what-are-hemagglutinin-inhibitors-and-how-do-they-work#:~:text=By%20understanding%20how%20hemagglutinin%20interacts%20with%20host,critical%20component%20in%20the%20fight%20against%20influenza.)

[23] [https://pmc.ncbi.nlm.nih.gov/articles/PMC6362415/](https://pmc.ncbi.nlm.nih.gov/articles/PMC6362415/#:~:text=While%20the%20NA%20is%20the%20main%20target,monoclonal%20antibodies%20(%20Nachbagauer%20and%20Krammer%2C%202017).)

[24] <https://pmc.ncbi.nlm.nih.gov/articles/PMC374304/>

[25] <https://pmc.ncbi.nlm.nih.gov/articles/PMC7172302/>

[26] <https://wwwnc.cdc.gov/eid/article/24/10/et-2410_article>

[27] <https://pmc.ncbi.nlm.nih.gov/articles/PMC4074938/>

[28] [https://www.cdc.gov/flu/hcp/antivirals/index.html](https://www.cdc.gov/flu/hcp/antivirals/index.html#:~:text=The%20neuraminidase%20inhibitors%20include:%20Oseltamivir%20(available%20as,influenza%20in%20people%20one%20year%20and%20older.)

[29] [https://pmc.ncbi.nlm.nih.gov/articles/PMC136693/](https://pmc.ncbi.nlm.nih.gov/articles/PMC136693/#:~:text=In%20contrast%2C%20paramyxoviruses%20have%20two%20glycoproteins%20that,the%20fusion%20(F)%20protein%20induces%20fusion%20(16).)

[30] [https://www.sciencedirect.com/science/article/pii/S0969212605001310](https://www.sciencedirect.com/science/article/pii/S0969212605001310#:~:text=For%20many%20of%20the%20paramyxoviruses%20(e.g.%2C%20parainfluenza,(HN)%20has%20hemagglutinating%20and%20neuraminidase%20(NA)%20activities.)

[31] [https://www.sciencedirect.com/topics/medicine-and-dentistry/paramyxoviridae](https://www.sciencedirect.com/topics/medicine-and-dentistry/paramyxoviridae#:~:text=3.2%20Paramyxoviruses%0A%0AThe%20Paramyxoviridae%20are%20a%20family%20of,and%20mumps%20virus%20(Lamb%20and%20Kolakofsky%2C%202001).)

[32] <https://pubmed.ncbi.nlm.nih.gov/2915381/>

[33] [https://virologyj.biomedcentral.com/articles/10.1186/1743-422X-6-74](https://virologyj.biomedcentral.com/articles/10.1186/1743-422X-6-74#:~:text=The%20viruses%20resistant%20to%20these%20drugs%20emerge,infected%20cells%20without%20the%20need%20of%20NA.)

[34] [https://pmc.ncbi.nlm.nih.gov/articles/PMC7798331/](https://pmc.ncbi.nlm.nih.gov/articles/PMC7798331/#:~:text=According%20to%20the%20above%20results%2C%20HA%20and,contribute%20to%20virulence%20alteration%20during%20serial%20passaging.)

[35] [https://www.tandfonline.com/doi/pdf/10.1038/s41426-018-0182-2](https://www.tandfonline.com/doi/pdf/10.1038/s41426-018-0182-2#:~:text=(NA)%2C%20which%20are%20responsible%20for%20viral%20recognition%2C,H7N9%20infection%20in%20clinical%20settings%2010%2C%2011.)

[36] [https://pmc.ncbi.nlm.nih.gov/articles/PMC112098/](https://pmc.ncbi.nlm.nih.gov/articles/PMC112098/#:~:text=Balanced%20Hemagglutinin%20and%20Neuraminidase%20Activities%20Are%20Critical,Replication%20of%20Influenza%20A%20Virus%20%2D%20PMC.)

[37] <https://pubs.acs.org/doi/10.1021/acscentsci.8b00666>

[38] [https://www.sciencedirect.com/science/article/pii/S1198743X16302312](https://www.sciencedirect.com/science/article/pii/S1198743X16302312#:~:text=The%20HA%20initiates%20the%20virus%20entry%20by,host%20specificity%20and%20resistance%20to%20antiviral%20treatment.)

[39] [https://pmc.ncbi.nlm.nih.gov/articles/PMC7397844/](https://pmc.ncbi.nlm.nih.gov/articles/PMC7397844/#:~:text=Influenza%20A%20and%20B%20viruses%20have%20two,A%20viruses%20are%20further%20classified%20into%20subtypes.)

[40] <https://pmc.ncbi.nlm.nih.gov/articles/PMC5536029/>

[41] <https://pubmed.ncbi.nlm.nih.gov/31629602/>

[42] <https://pmc.ncbi.nlm.nih.gov/articles/PMC6563287/>

[43] [https://www.sinobiological.com/research/virus/influenza-hemagglutinin-function](https://www.sinobiological.com/research/virus/influenza-hemagglutinin-function#:~:text=Hemagglutinin%20(HA)%20or%20Haemagglutinin%20(BE)%20is%20an,to%20the%20cell%20that%20is%20being%20infected.)