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# Corrigendum: Hantavirus: an overview and advancements in therapeutic approaches for infection

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## KEYWORDS

hantavirus, HFRS, HPS, immunotherapy, siRNA

## A corrigendum on

## Hantavirus: an overview and advancements in therapeutic approaches for infection

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In the published article, there were errors in [Table 1](#), [Table 3](#), and [Table 4](#).

The caption for [Table 1](#) only listed North and South America, but [Table 1](#) contains countries from North, Central, and South America.

In [Table 1](#), the reference for the row “Canada” was incorrectly listed as “Jonsson et al. (2010)”. The correct reference is “[Warner et al. \(2020\)](#)”.

In [Table 1](#), the reference for the row “Panama” was incorrectly listed as “Martinez-Valdebenito et al. (2014)”. The correct reference is “[Armién et al. \(2023\)](#)”. The corrected [Table 1](#) and its caption “Reported HTNV cases across North, Central, and South America.” appear below.

In [Table 3](#), the reference for the row “Lactoferrin” was incorrectly listed as “Gorbunova et al. (2010) and Arikawa et al. (1989)”. The correct reference is “[Murphy et al. \(2000, 2001\)](#)”.

In [Table 3](#), the reference for the row “Ribavirin” was incorrectly listed as “Schmaljohn et al. (1990) and Liang et al. (1996)”. The correct reference is “[Chung et al. \(2013\)](#) and [Ogg et al. \(2013\)](#)”.

In [Table 3](#), the reference for the row “Favipiravir” was incorrectly listed as “Arikawa et al. (1992)”. The correct reference is “[Safronetz et al. \(2013\)](#)”.

In [Table 3](#), the reference for the row “Vandenatib” was incorrectly listed as “Garrido et al. (2018)”. The correct reference is “[Bird et al. \(2016\)](#)”.

In [Table 3](#), the reference for the row “ETAR” was incorrectly listed as “Golias et al. (2007)”. The correct reference is “[Chung et al. \(2008\)](#)”.

In **Table 3**, the reference for the row “Coriticosteroids” was incorrectly listed as “Mills et al. (1999) and Xu et al. (2009)”. The correct reference is “Vial et al. (2013) and Brocato and Hooper (2019)”.

In **Table 3**, the reference for the row “Human Immune Sera” was incorrectly listed as “Tian et al. (2021)”. The correct reference is “Vial et al. (2015)”.

In **Table 3**, the reference for the row “JL16 and MIB22” was incorrectly listed as “Weinberg and Arbutnot (2010)”. The correct reference is “Garrido et al. (2018)”.

In **Table 3**, the reference for the row “Domain III and Stem Peptides” was incorrectly listed as “Taylor et al. (2013)”. The correct reference is “Barriga et al. (2016)”.

In **Table 3**, the reference for the row “CLVRNLAWC and CQATTARNC” was incorrectly listed as “Cicardi et al. (2010)”. The correct reference is “Hall et al. (2008)”.

In **Table 3**, the reference for the row “Incatibant” was incorrectly listed as “Aviziniene et al. (2023) and Mittler et al. (2023)”. The correct reference is “Antonen et al. (2013) and Laine et al. (2015)”.

In **Table 3**, the reference for the row “TNF- $\alpha$ ” was incorrectly listed as “Brocato et al. (2012), Manigold and Vial (2014), and Vial et al. (2015)”. The correct reference is “Vilcek (1991), Sundstrom et al. (2001), and Maes et al. (2004)”.

In **Table 3**, the reference for the row “RANTES/IP-10/MCP-1” was incorrectly listed as “Manigold and Vial (2014), and Malley et al. (2004)”. The correct reference is “Sundstrom et al. (2001) and Glass et al. (2003)”. The corrected **Table 3** and its caption “Lists some examples of potential antiviral therapies against Hantavirus.” appear below.

In **Table 4**, the reference for the row “Inactivated Vaccine” was incorrectly listed as “Sroga et al. (2021)”. The correct reference is “Khan et al. (2019)”.

In **Table 4**, the reference for the row “Virus-like Particles 1” was incorrectly listed as “Jonsson et al. (2005)”. The correct reference is “Dong et al. (2019)”.

In **Table 4**, the reference for the row “Virus-like Particles 2” was incorrectly listed as “Wray et al. (1985)”. The correct reference is “Dong et al. (2019)”.

In **Table 4**, the reference for the row “Virus-Vector Vaccines 1” was incorrectly listed as “Hopper et al. (1999)”. The correct reference is “Warner et al. (2019)”.

In **Table 4**, the reference for the row “Virus-Vector Vaccines 2” was incorrectly listed as “Brocato et al. (2013)”. The correct reference is “Prescott et al. (2014)”.

In **Table 4**, the reference for the row “Virus-Vector Vaccines 3” was incorrectly listed as “Deng et al. (2020)”. The correct reference is “Safronetz et al. (2009)”.

In **Table 4**, the reference for the row “Recombinant Vaccines 1” was incorrectly listed as “Hopper et al. (2014)”. The correct reference is “Geldmacher et al. (2004)”.

In **Table 4**, the reference for the row “Recombinant Vaccines 2” was incorrectly listed as “Ogg et al. (2013)”. The correct reference is “de Carvalho et al. (2002)”.

In **Table 4**, the reference for the row “Recombinant Vaccines 3” was incorrectly listed as “Ogg et al. (2013)”. The correct reference is “Maes et al. (2006)”.

In **Table 4**, the reference for the row “DNA Vaccines 1” was incorrectly listed as “Vial et al. (2013)”. The correct reference is “Hooper et al. (2013)”.

In **Table 4**, the reference for the row “DNA Vaccines 2” was incorrectly listed as “Antonen et al. (2013)”. The correct reference is “Hooper et al. (2001)”.

In **Table 4**, the reference for the row “DNA Vaccines 3” was incorrectly listed as “Laine et al. (2015)”. The correct reference is “Hooper et al. (2006)”.

In **Table 4**, the reference for the row “DNA Vaccines 4” was incorrectly listed as “Vial et al. (2013)”. The correct reference is “Hooper et al. (2013)”.

In **Table 4**, the reference for the row “DNA Vaccines 5” was incorrectly listed as “Fire et al. (1998)”. The correct reference is “Brocato et al. (2013)”.

In **Table 4**, the reference for the row “DNA Vaccines 6” was incorrectly listed as “Safronetz et al. (2013)”. The correct reference is “Jiang et al. (2017)”.

In **Table 4**, the reference for the row “Subunit Vaccines” was incorrectly listed as “Ye et al. (2019)”. The correct reference is “Maes et al. (2008)”. The corrected **Table 4** and its caption “Describing evaluation of Hantavirus vaccines in various animal models and some vaccines currently undergoing clinical trials.” appear below.

The authors apologize for these errors and state that they do not change the scientific conclusions of the article in any way. The original article has been updated.

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## References

- Antonen, J., Leppänen, I., Tenhunen, J., Arvola, P., Mäkelä, S., Vaheri, A., et al. (2013). A severe case of Puumala Hantavirus infection successfully treated with bradykinin receptor antagonist icatibant. *Scand. J. Infect. Dis.* 45, 494–496. doi: 10.3109/00365548.2012.755268
- Armién, B., Muñoz, C., Cedeño, H., Salazar, J. R., Salinas, T. P., González, P., et al. (2023). Hantavirus in Panama: twenty years of epidemiological surveillance experience. *Viruses* 15:1395. doi: 10.3390/v15061395
- Barriga, G. P., Villalón-Letelier, F., Márquez, C. L., Bignon, E. A., Acuña, R., Ross, B. H., et al. (2016). Inhibition of the Hantavirus fusion process by predicted domain III and stem peptides from glycoprotein Gc. *PLoS Negl. Trop. Dis.* 10:e0004799. doi: 10.1371/journal.pntd.0004799
- Bird, B. H., Shrivastava-Ranjan, P., Dodd, K. A., Erickson, B. R., and Spiropoulou, C. F. (2016). Effect of Vandetanib on Andes virus survival in the

- hamster model of Hantavirus pulmonary syndrome. *Antivir. Res.* 132, 66–69. doi: 10.1016/j.antiviral.2016.05.014
- Brocato, R., Josleyn, M., Wahl-Jensen, V., Schmaljohn, C., and Hooper, J. (2013). Construction and nonclinical testing of a Puumala virus synthetic M gene-based DNA vaccine. *Clin. Vaccine Immunol.* 20, 218–226. doi: 10.1128/CVI.00546-12
- Brocato, R. L., and Hooper, J. W. (2019). Progress on the prevention and treatment of Hantavirus disease. *Viruses* 11:610. doi: 10.3390/v11070610
- Chung, D.-H., Kumarapperuma, S. C., Sun, Y., Li, Q., Chu, Y.-K., Arterburn, J. B., et al. (2008). Synthesis of 1- $\beta$ -D-ribofuranosyl-3-ethynyl-[1, 2, 4] triazole and its *in vitro* and *in vivo* efficacy against Hantavirus. *Antivir. Res.* 79, 19–27. doi: 10.1016/j.antiviral.2008.02.003
- Chung, D.-H., Västermark, Å., Camp, J. V., McAllister, R., Remold, S. K., Chu, Y.-K., et al. (2013). The murine model for Hantaan virus-induced lethal disease shows two distinct paths in viral evolutionary trajectory with and without ribavirin treatment. *J. Virol.* 87, 10997–11007. doi: 10.1128/JVI.01394-13
- de Carvalho, N., Gonzalez Delia Valle, M., Padula, P., Bjorling, E., Plyusnin, A., and Lundkvist, A. (2002). Cross-protection against challenge with Puumala virus after immunization with nucleocapsid proteins from different hantaviruses. *J. Virol.* 76, 6669–6677. doi: 10.1128/jvi.76.13.6669-6677.2002
- Dong, Y., Ma, T., Zhang, X., Ying, Q., Han, M., Zhang, M., et al. (2019). Incorporation of CD40 ligand or granulocyte-macrophage colony stimulating factor into Hantaan virus (HTNV) virus-like particles significantly enhances the long-term immunity potency against HTNV infection. *J. Med. Microbiol.* 68, 480–492. doi: 10.1099/jmm.0.000897
- Garrido, J. L., Prescott, J., Calvo, M., Bravo, F., Alvarez, R., Salas, A., et al. (2018). Two recombinant human monoclonal antibodies that protect against lethal Andes Hantavirus infection *in vivo*. *Sci. Transl. Med.* 10:eaat6420. doi: 10.1126/scitranslmed.aat6420
- Geldmacher, A., Skrastina, D., Petrovskis, I., Borisova, G., Berriman, J. A., Roseman, A. M., et al. (2004). An amino-terminal segment of Hantavirus nucleocapsid protein presented on hepatitis B virus core particles induces a strong and highly cross-reactive antibody response in mice. *Virology* 323, 108–119. doi: 10.1016/j.virol.2004.02.022
- Glass, W. G., Rosenberg, H. F., and Murphy, P. M. (2003). Chemokine regulation of inflammation during acute viral infection. *Curr. Opin. Allergy Clin. Immunol.* 3, 467–473. doi: 10.1097/00130832-200312000-00008
- Hall, P. R., Hjelle, B., Brown, D. C., Ye, C., Bondu-Hawkins, V., Kilpatrick, K. A., et al. (2008). Multivalent presentation of antihantavirus peptides on nanoparticles enhances infection blockade. *Antimicrob. Agents Chemother.* 52, 2079–2088. doi: 10.1128/AAC.01415-07
- Hooper, J., Custer, D., Thompson, E., and Schmaljohn, C. (2001). DNA vaccination with the Hantaan virus M gene protects hamsters against three of four HFRS hantaviruses and elicits a high-titer neutralizing antibody response in Rhesus monkeys. *J. Virol.* 75, 8469–8477. doi: 10.1128/JVI.75.18.8469-8477.2001
- Hooper, J. W., Custer, D. M., Smith, J., and Wahl-Jensen, V. (2006). Hantaan/Andes virus DNA vaccine elicits a broadly cross-reactive neutralizing antibody response in nonhuman primates. *Virology* 347, 208–216. doi: 10.1016/j.virol.2005.11.035
- Hooper, J. W., Josleyn, M., Ballantyne, J., and Brocato, R. (2013). A novel sin Nombre virus DNA vaccine and its inclusion in a candidate pan-Hantavirus vaccine against Hantavirus pulmonary syndrome (HPS) and hemorrhagic fever with renal syndrome (HFRS). *Vaccine* 31, 4314–4321. doi: 10.1016/j.vaccine.2013.07.025
- Jiang, D.-B., Sun, L.-J., Cheng, L.-F., Zhang, J.-P., Xiao, S.-B., Sun, Y.-J., et al. (2017). Recombinant DNA vaccine of Hantavirus Gn and LAMP1 induced long-term immune protection in mice. *Antivir. Res.* 138, 32–39. doi: 10.1016/j.antiviral.2016.12.001
- Khan, A., Shin, O. S., Na, J., Kim, J. K., Seong, R.-K., Park, M.-S., et al. (2019). A systems vaccinology approach reveals the mechanisms of immunogenic responses to hantavirus vaccination in humans. *Sci. Rep.* 9:4760. doi: 10.1038/s41598-019-41205-1
- Laine, O., Leppänen, I., Koskela, S., Antonen, J., Mäkelä, S., Sinisalo, M., et al. (2015). Severe Puumala virus infection in a patient with a lymphoproliferative disease treated with icanitab. *Infect. Dis.* 47, 107–111. doi: 10.3109/00365548.2014.969304
- Maes, P., Clement, J., Cauwe, B., Bonnet, V., Keyaerts, E., Robert, A., et al. (2008). Truncated recombinant puumala virus nucleocapsid proteins protect mice against challenge *in vivo*. *Viral Immunol.* 21, 49–60. doi: 10.1089/vim.2007.0059
- Maes, P., Clement, J., Gavrilovskaya, I., and Van Ranst, M. (2004). Hantaviruses: immunology, treatment, and prevention. *Viral Immunol.* 17, 481–497. doi: 10.1089/vim.2004.17.481
- Maes, P., Keyaerts, E., Bonnet, V., Clement, J., Avsic-Zupanc, T., Robert, A., et al. (2006). Truncated recombinant Dobrava Hantavirus nucleocapsid proteins induce strong, long-lasting immune responses in mice. *Intervirology* 49, 253–260. doi: 10.1159/000093454
- Murphy, M., Kariwa, H., Mizutani, T., Yoshimatsu, K., Arikawa, J., and Takashima, I. (2000). *In vitro* antiviral activity of lactoferrin and ribavirin upon Hantavirus. *Arch. Virol.* 145, 1571–1582. doi: 10.1007/s007050070077
- Murphy, M. E., Kariwa, H., Mizutani, T., Tanabe, H., Yoshimatsu, K., Arikawa, J., et al. (2001). Characterization of *in vitro* and *in vivo* antiviral activity of lactoferrin and ribavirin upon Hantavirus. *J. Vet. Med. Sci.* 63, 637–645. doi: 10.1292/jvms.63.637
- Ogg, M., Jonsson, C. B., Camp, J. V., and Hooper, J. W. (2013). Ribavirin protects Syrian hamsters against lethal Hantavirus pulmonary syndrome—after intranasal exposure to Andes virus. *Viruses* 5, 2704–2720. doi: 10.3390/v5112704
- Prescott, J., DeBuysscher, B. L., Brown, K. S., and Feldmann, H. (2014). Long-term single-dose efficacy of a vesicular stomatitis virus-based Andes virus vaccine in Syrian hamsters. *Viruses* 6, 516–523. doi: 10.3390/v6020516
- Safonetz, D., Falzarano, D., Scott, D. P., Furuta, Y., Feldmann, H., and Gowen, B. B. (2013). Antiviral efficacy of favipiravir against two prominent etiological agents of Hantavirus pulmonary syndrome. *Antimicrob. Agents Chemother.* 57, 4673–4680. doi: 10.1128/AAC.00886-13
- Safonetz, D., Hegde, N. R., Ebihara, H., Denton, M., Kobinger, G. P., St. Jeor, S., et al. (2009). Adenovirus vectors expressing Hantavirus proteins protect hamsters against lethal challenge with Andes virus. *J. Virol.* 83, 7285–7295. doi: 10.1128/JVI.00373-09
- Sundstrom, J. B., McMullan, L. K., Spiropoulou, C. F., Hooper, W. C., Ansari, A. A., Peters, C. J., et al. (2001). Hantavirus infection induces the expression of RANTES and IP-10 without causing increased permeability in human lung microvascular endothelial cells. *J. Virol.* 75, 6070–6085. doi: 10.1128/JVI.75.13.6070-6085.2001
- Vial, P., Valdivieso, F., Ferres, M., Riquelme, R., Rioseco, M., Calvo, M., et al. (2013). Hantavirus study Group in Chile High-dose intravenous methylprednisolone for Hantavirus cardiopulmonary syndrome in Chile: a double-blind, randomized controlled clinical trial. *Clin. Infect. Dis.* 57, 943–951. doi: 10.1093/cid/cit394
- Vial, P. A., Valdivieso, F., Calvo, M., Rioseco, M. L., Riquelme, R., Arnedo, A., et al. (2015). A non-randomized multicentre trial of human immune plasma for treatment of Hantavirus cardiopulmonary syndrome caused by Andes virus. *Antivir. Ther.* 20, 377–386. doi: 10.3851/IMP2875
- Vilcek, J. (1991). Tumor necrosis factor—new insights into the molecular mechanisms of its multiple actions. *J. Biol. Chem.* 266:7313. doi: 10.1016/S0021-9258(20)89445-9
- Warner, B. M., Dowhanik, S., Audet, J., Grolla, A., Dick, D., Strong, J. E., et al. (2020). Hantavirus cardiopulmonary syndrome in Canada. *Emerg. Infect. Dis.* 26:3020. doi: 10.3201/eid2612.202808
- Warner, B. M., Stein, D. R., Jangra, R. K., Slough, M. M., Sroga, P., Sloan, A., et al. (2019). Vesicular stomatitis virus-based vaccines provide cross-protection against Andes and sin nombre viruses. *Viruses* 11:645. doi: 10.3390/v11070645

TABLE 1 Reported HTNV cases across North, Central, and South America.

| Country       | Cases | Year       | Source                               |
|---------------|-------|------------|--------------------------------------|
| USA           | 850   | 1993–2021  | CDC                                  |
| Canada        | 143   | As of 2020 | <a href="#">Warner et al. (2020)</a> |
| Panama        | 712   | 1999–2019  | <a href="#">Armién et al. (2023)</a> |
| Costa Rica    | 3     | Till 2016  | PAHO                                 |
| Argentina     | 1,350 | As 2016    | PAHO                                 |
| Chile         | 1,028 | As of 2016 | PAHO                                 |
| Brazil        | 2,032 | Till 2017  | PAHO                                 |
| Paraguay      | 319   | Till 2016  | PAHO                                 |
| Uruguay       | 169   | Till 2016  | PAHO                                 |
| Bolivia       | 300   | Till 2016  | PAHO                                 |
| Ecuador       | 73    | As of 2016 | PAHO                                 |
| Peru          | 6     | As of 2016 | PAHO                                 |
| French Guiana | 3     | Till 2016  | PAHO                                 |

TABLE 3 Lists some examples of potential antiviral therapies against Hantavirus.

| Antiviral therapy            | Type                                       | Function                                 | Target                    | Disease       | References   |
|------------------------------|--|--|---------------------------|---------------|--|
| Lactoferrin                  | Lactoferrin                                | Block viral entry                        | Viral GP                  | HFRS          | <a href="#">Murphy et al. (2000, 2001)</a>   |
| Ribavirin                    | Nucleoside analogs                         | Inhibit viral replication                | RdRp                      | HCPS and HFRS | <a href="#">Chung et al. (2013)</a> and <a href="#">Ogg et al. (2013)</a>                                      |
| Favipiravir                  | Pyrazine derivatives                       | Block viral entry                        | RdRp                      | HCPS          | <a href="#">Safronetz et al. (2013)</a>  |
| Vandetanib                   | Tyrosine kinase inhibitor                  | Improve vascular function                | VEGF/Vascular function    | HCPS          | <a href="#">Bird et al. (2016)</a>   |
| ETAR                         | Nucleoside analog                          | Inhibit viral entry                      | RdRp                      | HCPS and HFRS | <a href="#">Chung et al. (2008)</a>  |
| Corticosteroids              | Hormone                                    | Rebuild immune homeostasis               | Immunotherapy             | HCPS and HFRS | <a href="#">Vial et al. (2013)</a> and <a href="#">Brocato and Hooper (2019)</a>                               |
| Human Immune Sera            | Human pAbs                                 | Block viral entry                        | Viral GP                  | HCPS          | <a href="#">Vial et al. (2015)</a>   |
| JL16 and MIB22               | Human mAbs                                 | Block viral entry                        | Viral GP                  | HCPS          | <a href="#">Garrido et al. (2018)</a>  |
| Domain III and stem peptides | Peptides                                   | Block viral entry                        | Gc glycoprotein           | HCPS and HFRS | <a href="#">Barriga et al. (2016)</a>  |
| CLVRNLAWC and CQATTARNC      | Cyclic nonapeptides                        | Block viral entry                        | Host receptor             | HCPS          | <a href="#">Hall et al. (2008)</a>   |
| Icatibant                    | Small molecule                             | Improve vascular function                | BK type 2 receptor        | HFRS          | <a href="#">Antonen et al. (2013)</a> and <a href="#">Laine et al. (2015)</a>                                  |
| TNF- $\alpha$                | Small proteins/Pro-inflammatory cytokines  | Increase systemic toxicity               | Vascular function         | HCPS and HFRS | <a href="#">Vilcek (1991)</a> , <a href="#">Sundstrom et al. (2001)</a> and <a href="#">Maes et al. (2004)</a> |
| RANTES/IP-10/MCP-1           | Small proteins/Pro-inflammatory chemokines | Immunomodulators/Inhibit viral infection | Microvascular endothelium | HFRS          | <a href="#">Sundstrom et al. (2001)</a> and <a href="#">Glass et al. (2003)</a>                                |

TABLE 4 Describing evaluation of Hantavirus vaccines in various animal models and some vaccines currently undergoing clinical trials.

| Vaccine type          | Antigen   | Animal model                          | Immunogenicity evaluation   | References                                |
|-----------------------|---|---------------------------------------|---|---|
| Inactivated vaccine   | Formalin inactivated HNTV   | Humans                                | Humoral response Neutralizing antibodies  | <a href="#">Khan et al. (2019)</a>        |
| Virus-like particles  | HTNV-VLP with CD40L or GM-CSF   | Mice                                  | Cytotoxic response Neutralization antibody Cytolytic activity                               | <a href="#">Dong et al. (2019)</a>        |
|                       | M   | DHFR-deficient CHO cells              | Antigen-specific IFN- $\gamma$ production Effective against HTNV Still in developing phases | <a href="#">Dong et al. (2019)</a>        |
| Virus-vector vaccines | Replication-competent VSV-vectored SNV or ANDV glycoproteins                  | Syrian Hamster                        | Cross-reactive IgG antibodies Neutralizing antibodies                                       | <a href="#">Warner et al. (2019)</a>      |
|                       | Replication-competent VSV-vectored ANDV glycoproteins                         | Syrian Hamsters                       | Neutralizing antibodies   | <a href="#">Prescott et al. (2014)</a>    |
|                       | Non-replicating Ad vector expressing N, Gn, Gc, or Gn/Gc                      | Syrian Hamsters                       | CD8+ cell response Neutralizing antibodies  | <a href="#">Safronetz et al. (2009)</a>   |
| Recombinant vaccines  | Yeast-expressed DOBV nucleoprotein  | Mice                                  | NP-specific IgG response Th1/Th2 response Cross-reactivity with HTNV and PUUV               | <a href="#">Geldmacher et al. (2004)</a>  |
|                       | Nucleoproteins from ANDV, TOPV, DOBV or PUUV                                  | Bank voles                            | Specific CD8+ cell production Cross-reactive response against PUUV                          | <a href="#">de Carvalho et al. (2002)</a> |
|                       | Truncated recombinant PUUV nucleoprotein linked to bacterial membrane protein | Mice                                  | CD8+ T-cell response NP IgG response  | <a href="#">Maes et al. (2006)</a>        |
| DNA vaccines          | HTNV/PUUV/SNV/ANDV M gene segment mix   | Rabbits                               | Neutralizing antibodies   | <a href="#">Hooper et al. (2013)</a>      |
|                       | HTNV M segment  | Rhesus macaques                       | Neutralizing antibodies Cross-reactivity with SEOV and DOBV                                 | <a href="#">Hooper et al. (2001)</a>      |
|                       | ANDV and HNTV M gene segments   | Rhesus macaques                       | Neutralizing antibodies   | <a href="#">Hooper et al. (2006)</a>      |
|                       | SNV M gene segment  | Syrian hamsters                       | Neutralizing antibodies   | <a href="#">Hooper et al. (2013)</a>      |
|                       | PUUV M gene segment   | Syrian hamsters                       | Protection against lethal ANDV infection, without nAbs Neutralizing antibodies              | <a href="#">Brocato et al. (2013)</a>     |
|                       | Gn glycoprotein   | BALB/c mice                           | Effective against HTNV Still in developing phases   | <a href="#">Jiang et al. (2017)</a>       |
| Subunit vaccines      | NP (nucleocapsid protein)   | <i>E. coli</i> mutant ICONE NMRI mice | Effective against PUUV In developing Phases   | <a href="#">Maes et al. (2008)</a>        |