Nonhuman primate models for SARS-CoV-2 Research: Managing demand for specific-pathogen-free (SPF) animals

The SARS-CoV-2/COVID-19 pandemic has significantly increased the demand for specific-pathogen-free (SPF) nonhuman primates (NHPs) for development of vaccines and therapeutics, thus straining the supply of these animals for biomedical research studies. Non-SPF animals, which are available in greater numbers and include well-characterized primate species, should be considered in lieu of limited SPF animals for appropriate research studies.

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Ongoing shortages of nonhuman primates (NHPs) for use in biomedical research studies, as well as the high demand for biocontainment and research laboratory spaces adjacent to facilities housing the animals, have been exacerbated by the continuing need for these resources in SARS-CoV-2 studies.[1,2] SARS-CoV-2 vaccine and antiviral therapy research increased the demand for critical NHP animal models because they are anatomically and physiologically similar to humans and, therefore, are needed to provide the investigational new data required by the U.S. Food and Drug Administration to approve and license a vaccine or antiviral therapy for human use.[3] The NHP model data allow a complete preclinical visualization of disease and show how humans may respond to therapeutic interventions aimed at treating and preventing viral infections.

The continuing, rapid development of vaccines and therapeutics to control the global COVID-19 pandemic has led not only to a high demand for general NHP resources, but also to an unprecedented number of requests for SPF NHPs. SPF animals are made free of specific pathogens (e.g., viruses, bacteria, parasites) through pathogen testing and segregation strategies. In general, the term SPF implies a more defined health status in breeding colonies and research animals than what is characterized in non-SPF colonies. The list of pathogens monitored for exclusion by routine testing varies for different NHP species and among different colonies, facilities, laboratories, and research priorities.[4,5]

SPF NHPs are important for many biomedical research studies because they are free of indigenous pathogens that can influence and confound study results or pose an occupational zoonotic risk to caretakers and research staff. For example, in SPF rhesus and pig-tailed macaque colonies supported by the National Institutes of Health (NIH) Office of Research Infrastructure Programs (ORIP) and Office of AIDS Research, at least three viruses that interfere with AIDS research study results are selected for targeted screening and exclusion: simian immunodeficiency virus, simian betaretrovirus, and simian T- cell lymphotropic virus type 1.[4] Macacine alphaherpesvirus 1 (monkey B virus) also is targeted for screening and exclusion in these colonies because this virus poses a significant health risk to humans.[6] As another example, an SPF baboon resource supported by ORIP is free of at least 18 recommended pathogens,[5] including herpesviruses, retroviruses, polyomavirus (simian virus 40), paramyxovirus (measles virus), arterivirus (Southwest baboon virus), and monkeypox virus. However, SPF NHP breeding colonies require extensive application of state-of-the-art diagnostic technologies and barrier facility management, as well as enhanced animal husbandry, care, and biosafety practices.

Although SPF NHPs are a critical resource for studies on vaccine development for infectious diseases, non-SPF animals are valuable for many preclinical investigations that require NHPs. For example, non-SPF NHPs can be used to test therapeutics that do not depend on a cell-mediated immune response and for the titration of challenge viral stocks for disease recapitulation. Non-SPF baboons offer an alternative to SPF macaques for evaluating antiviral or immunomodulator classes of therapeutics for COVID-19 research.[7] Non-SPF animals also can be used in noninfectious disease studies, such as neuroscience and cardiometabolic research. For these reasons, biomedical researchers should consider non-SPF animals in lieu of limited SPF animal resources for appropriate research studies to reduce the pressure on SPF NHP resources, particularly at a time when SPF NHPs and the specialized resources required to care for them are in high demand.

SPF NHP colonies will continue to be essential for future preclinical studies, especially studies to understand SARS-CoV-2 cellular immune responses in vulnerable populations (e.g., elderly individuals, pregnant women, children) and studies of SARS-CoV-2 post-acute sequelae (i.e., long-term COVID).[3] High-quality, well-cared for non-SPF NHPs, however, are available in large numbers and offer a viable alternative to SPF NHPs for many biomedical research studies for which SPF status is not an essential requirement. These non-SPF primate species are well characterized with respect to country of origin, pedigree, genetic profile, and health status.

NIH supports multiple NHP colonies, including SPF macaque colonies housed at the National Primate Research Centers (NPRCs), SPF and non-SPF macaque colonies at the Caribbean Primate Research Center, and SPF baboon colonies at Keeling Center for Comparative Medicine and Research. These centers and facilities are supported through grants administered by ORIP within the NIH Office of the Director. ORIP-supported SPF and non-SPF NHP resources provide primates for use in diverse areas of biomedical research.

Scientists vested in answering questions about current or future pandemic threats and developing treatment modalities, including vaccines that protect against infections or disease, should collaborate with NHP colony managers to address NHP supply and infrastructure needs.[1,2] A workshop aimed at reviewing the shortage of research NHPs—spearheaded by the U.S. National Academies of Sciences/Institute of Laboratory Animal Research—is planned for the future. This workshop will offer the opportunity to begin a dialogue on ways to respond to the increased demand for SPF NHPs for COVID-19 and other types of biomedical research. ❐

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