Baboons (Papio sp.) have played a critical role in basic and translational research. Their large size and close genetic relationship to humans models many normative aspects of human biology. This makes baboons an excellent species to study reproductive biology, infectious diseases (including SARS-CoV-2), physiology, neuroscience, psychology, transplantation, skeletal biology, and evolution.

**Natural history**

Baboons are native to much of Sub-Saharan Africa. While baboon taxonomy is continually revised, most researchers accept six groupings of baboons, genus *Papio*, that are classified as separate at either the subspecies¹ or species level.² ³ These include olive (anubis), yellow (cynocephalus), hamadryas (hamadryas), Kinda (kindae), Guinea (papio), and chacma (ursinus) baboons.⁴ There are extensive hybrid zones in areas where the assorted baboons overlap in their natural ranges—baboon varieties can produce fertile offspring with all others—reflecting an interesting and complicated evolutionary history.

Social organization generally involves multi-male, multi-female groups with males usually leaving their natal group near puberty (male-biased dispersal). The predominate exceptions are hamadrayas and Guinea baboons, where basic social organization usually involves single-male, multi-female units that travel together in bands made up of many such units, with female-biased dispersal.⁵ Baboons are largely terrestrial or ground-living, and partly due to this are excellent models to study locomotion, skeletal disorders such as osteoporosis, and development of devices aiding human mobility such as artificial vertebral discs.⁶ Baboons are extraordinarily generalist animals, among the most ecologically flexible of all primates,⁷ inhabiting a wide range of environments and having a diverse diet—including fruits and seeds, tubers, leaves, flowers, invertebrate and vertebrate animals, and fungi. Indeed, they have been described as “eclectic omnivores,”⁸ making them an ideal model for research in which dietary interventions are needed or where the microbiome is involved; for example, to examine the effects of diet on obesity or gut health, or to contrast dietary-related health outcomes for particular diseases, such as diabetes.
Reproduction

Baboons differ from rhesus macaques in that they breed continuously throughout the year. This facet of baboon reproductive physiology and behavior facilitated the first major theoretical accounting for the origins of primate and human sociality. It is also a striking advantage in research requiring a consistent supply of new pregnancies or infants. Female baboons exhibit a prominent, colorful anogenital swelling that reaches peak tumescence near the time of ovulation; this allows reliable, non-invasive, and low-cost daily assessment of ovarian status and pregnancy. Baboons can develop spontaneous endometriosis and provide a natural model for investigating this condition, which can also be experimentally induced. They also have reproductive anatomy that closely approximates the human condition and the larger size and extended gestation is useful for studying pregnancy. For these reasons, baboons are an excellent model for investigations involving contraception, the physiology of ovulation, pregnancy and placentation, fetal development, developmental programming, gynecologic procedures and maternal-fetal transfer.

Immunology and Infectious Disease

Like humans, baboons have four immunoglobulin G (IgG 1-4) subclasses with close genetic identity to their human counterparts. As IgG is the only antibody class to show marked crossing of the placenta, providing fetal protection—and given the similarities in baboon-human reproductive physiology mentioned above—baboons are an ideal animal model for evaluating methods to enhance maternal-fetal transfer of IgG, including during vaccine administration. It is beneficial that baboons do not carry the herpes B virus, an occupational hazard. Furthermore, the ontogeny of the baboon immune system is similar to that of humans, including age-associated but individually-variable immune senescence.

Not surprisingly, baboons are superb models for many infectious diseases and for vaccine development. In particular baboons have been used extensively to study respiratory diseases like pneumonia, whooping cough, and most recently COVID-19. Infant baboons were shown to be infectable with respiratory syncytial virus (RSV) and develop pneumonia. This model has been used to test whether pregnant baboons could transfer maternal RSV antibodies to infants for protection against severe respiratory disease. Baboons have become the primary animal model to study pertussis, the bacteria that causes whooping cough. Baboons are the only research animal that faithfully recapitulates all major elements of human infection, including paroxysmal cough and transmission. Baboons have proved vital in the development and production of more potent acellular pertussis vaccines. Recently, it was found that baboons are susceptible to infection with SARS-CoV-2, and that they develop more severe COVID-19 disease than macaques or marmosets. Baboons harbor higher viral titers, have longer viremia, and have more pronounced lung pathology than macaques infected with SARS-CoV-2. These results indicate that baboons, which develop moderate-to-severe COVID-19, will be very useful for the assessment of antivirals and host-directed therapeutics against this important public health issue.

Like several other nonhuman primate species, baboons are susceptible to T. cruzi infection which causes Chagas disease. Ineffective translation of treatments to human clinical trials based on rodent data has resulted in the need for a better preclinical animal model for Chagas disease. Baboon response to these same treatments has since been shown to predict human response.
suggesting future studies of promising therapies in baboons will likely predict effective therapies in clinical trials.

Left: Olive baboon at the Southwest National Primate Research Center, Texas Biomedical Research Institute, San Antonio, Texas.

**Physiology**

The baboon has long been an important model for human physiology, including genetic, epigenetic, and environmental contributors to conditions such as obesity, cardiovascular disease, and diabetes, and their correlates with various health outcomes. One comprehensive study explored the genetic variants affecting response to high fat, high protein diets in over 3,000 pedigreed baboons. This has led to follow up studies on associated liver pathology like non-alcoholic steatohepatitis (NASH), non-alcoholic fatty liver disease (NAFLD), and liver cancer – all of which have alarming increasing rates in the United States. Other recent work has utilized baboons to assess novel methods for assessing resting energy expenditure and body temperature, as well as deploying tissue-specific ultrasound-targeted microbubble destruction gene-based therapy for aids in weight loss and to improve immunometabolism.

**Transplant Biology**

The large size and human-like anatomy of baboons has been useful in the field of transplant biology and the testing of medical devices. Pig to baboon heart xenotransplants are being used to determine both the immunomodulatory regimens humans will need and genetic modification pigs will need to make pig to human transplants a viable possibility. Toward this end, successful pig heart transplant into baboons has now been sustained for more than 900 days. Similar transplant studies are also allowing for research into methods of prolonging the survival of the organ between harvest and transplant. In addition to live organ transplants, there is increasing interest in studying decellularized tissue and organ grafts. For these studies, the comparable sizes of human and baboon organs and vasculature is being utilized.

**Neuroscience and psychology**

Baboons have brains with extensive cortical folding. They are flexible in behavior and frequently manipulate objects with their hands. As a stand-in for humans, they are excellent models for studies of brain function, brain physiology, and cognitive and social behaviors, including the investigation and treatment of neurocognitive-related disorders including Alzheimer’s and Parkinson’s diseases. Baboons have been instrumental in elucidating genetic contributions to brain architecture, in studying hemispheric brain specialization and novelty detection, in evaluating psychotropic drugs, and in many related areas of research.
Biological anthropology

The use of nonhuman primates, including baboons, in human-relevant research is predicated on our close evolutionary relationship with these animals—greater than 90% overall DNA sequence conservation. Thus, describing such relationships and understanding the similarities and differences between nonhuman primates and humans is a tantamount topic in evolutionary medicine. Baboons have been a predominate player in these types of investigations, and have shed light on aspects of anatomy, physiology, ecology, and behavior that are homologous, shared due to common descent, or analogous, shared due to common function, with humans. Baboons, for reasons described above, were the initial model used to closely describe normative anthropoid, including human, reproductive physiology and its influences on the evolution of social relationships.\(^3\) In recent years, baboons have been utilized to describe the evolution and genetic development of primate, including human, teeth,\(^3\) have provided insights on genetic and epigenetic contributors to skeletal joint formation, with key application to pathology such as osteoporosis,\(^3\) and proved a key comparator for interpretation of the locomotion of the 4.4 million-year-old hominid *Ardipithecus ramidus*. *Ardipithecus ramidus* is a crucial fossil form in early human evolution, especially relevant to the appearance and modification of obligate bipedal or two-footed posture and movement—the uniquely human form of locomotion that is unfortunately associated with many potential health risks, such as back, hip, knee, and foot problems.\(^3\)

Other models and considerations

This article gives only a broad overview of research areas where baboon models have proved influential. For example, among the many topics yet uncovered are many medical devices for human use that were first developed with baboons, such as high-frequency ventilators now used all over the world to treat infant respiratory distress syndrome.\(^3\) Some baboons are naturally afflicted with congenital epilepsy and can be studied with regards to treatments in that area.\(^3\) And there are established or emerging baboon applications to other pathologies such as cancer. Among all nonhuman primate models, baboons are especially notable for being appropriate for an exceptionally broad spectrum of research, including novel and exploratory investigations. If you are a researcher interested in human biology or health, baboons may very well be the optimal model for your area of interest. This overview provides some basic information on the model; for additional information please consider reviewing some of the literature (e.g., ref 3).

We believe that the African-origin baboon is an underutilized nonhuman primate model that can recapitulate the conditions of human life-span at the intersection of infectious diseases, inflammation and human diseases of the brain, central organs and metabolism.

References and notes.

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In the subspecies perspective, for example, olive baboons would be designated as *Papio hamadrayas anubis* and hamadrayas baboons would be *Papio hamadryas hamadryas*. In the “separate species” perspective these same forms would receive the names *Papio anubis* and *Papio hamadryas*.


