Texas Biomedical Research Institute, San Antonio, TX: NHP research services

1. Research services offered (including specialized techniques and expertise)

Texas Biomed offers research services for NHP at ABSL4 and ABSL3.

The ABSL4 at Texas Biomed is heavily involved in testing vaccines and therapeutics for efficacy against high containment pathogens. Typically, the NHP is the only model that sufficiently replicates human disease and immune responses to allow therapy testing. The pathogens include Ebola virus, Marburg virus and Lassa fever virus. We have also performed work for some ABSL3 pathogens in the ABSL4 because of the available personnel and infrastructure that has been developed to support these studies. These include treatments for Equine encephalitis viruses. The vaccines range from attenuated viruses, virus-vector based, recombinant protein-based or DNA-based. The therapies are either small molecule or recombinant antibody-based. Several of the vaccines have been advanced to phase 1 clinical trials and one has been tested in phase 2 trials.

Five faculty have key roles in performing ABSL4 NHP work. These faculty are nationally recognized for developing approaches for performing 2 animal rule studies that can be sent to the FDA and move treatments toward the clinic. Each PI incorporates this knowledge in study protocols and are a fundamental resource for these studies.

The ABSL3 at Texas Biomed is focused on *M. tuberculosis* research, with a current focus on vaccine development in juvenile macaques. The NHP is currently the only model that accurately recapitulates TB latency and disease pathogenesis in humans. The ABSL3 NHP capabilities are poised to expand in 2018 with an intended recruitment of faculty that work with NHP species in the context of *M. tuberculosis* infection. Study capabilities will include disease pathogenesis, vaccine and drug testing.

2. Veterinary and other research support services offered

The SNPRC Veterinary Resources provides support for the high containment programs at Texas Biomed. This group includes 12 veterinarians three of which are board certified in experimental medicine (DACLAM) and two are board certified in veterinary pathology (DVACP). A behavioral staff includes nine members that are supervised by a Ph.D. level behaviorist. Over 70% of the 76 veterinarian technicians in SNPRC are AALAS Certified. A robust training program assist each member of the team in training for certification. The Veterinary Resources group has 1000 years of experience in NHP research due to the long tenure of a highly dedicated team. The Texas Biomed animal care program receives oversight from the IACUC, OLAW and USDA. The animal care program and facilities are AAALAC accredited.

3. Specialized facilities (e.g., ABSL-4 laboratories)

The ABSL4 laboratory (1,200 sq.ft) can accommodate 24 NHP at one time.

The ABSL3 laboratory has 5 animal bays that can accommodate 12 macaques for a total of 60 animals at a time. Alternatively, the space can accommodate 18 marmosets. The facility includes a pathology suite for necropsies, procedures room and other support space.

4. Specialized major equipment (e.g., fMRI, confocal microscopy, etc.)

Redacted by agreement has developed aerosol exposure models for filoviruses and Equine encephalitis viruses. A full complement of Vetscan equipment is present in the ABSL4 to provide clinical blood chemistry and hematology analysis.

5. Unique or unusual resources (e.g., databases, models, etc.)

The SNPRC has a breeding colony of marmosets. Redacted by agreement has evaluated marmosets as small NHP models of Ebola virus, Marburg virus disease (PMID 21959017) and Lassa Fever disease (PMID 17409137). These models offer an important and alternative second NHP model for each of these lethal diseases Redacted by agreement has collaborated successfully to use the Lassa Fever disease model for NIH funded research for a new vaccine candidate (PMID 18692539).

6. NHP species currently used, species maintained as breeding colonies, and housing capacity

Species	Availability/current use	ABSL4 housing capacity
Cynomolgus macaques	80% of all studies obtained from outside sources with a census of 20-100 at any time	24
Rhesus macaques	SPF breeding colony of ~900 animals	24
Marmosets	Breeding colony of ~320 animals	36

Over the past 4 years and for the foreseeable future it is expected that 9 studies will be performed per year in the current BSL4 facility. Each study involves on average 20-24 animals and therefore uses up to 216 animals per year. The funding for this facility primarily using NHPs is listed below:

Source	2013	2014	2015	2016
HHS/NIH	4.30	5.67	9.42	6.98
HHS/BARDA	-	-	1.60	1.53
DOD/DTRA	0.98	0.54	0.30	0.03
DOD/JPEO-CBD	2.77	4.85	2.80	1.45
For Profit	-	0.11	2.27	0.22
Non-Federal Grants and Contracts	0.05	0.15	0.20	0.24
Total	8.11	11.32	16.59	10.46

Species	ABSL3 housing capacity
Cynomolgus macaques	60
Rhesus Macaques	60
Marmosets	90
Baboon	20 adults

1. **Compared to current usage, is the usage of certain NHP species anticipated to increase or decrease over the coming 5 years, and if changing, for which species and what factors are thought to be responsible for the expected changes?**

The ABSL4 has operated at maximum capacity for many years, with studies running throughout the year, except during annual shutdown of the lab for decontamination, repairs and recertification (typically 1 month). Given that the projected need for these studies is unlikely to change over the next 5 years, the number of studies will remain constant. For ABSL4 studies the cynomolgus macaque is the model of choice for vaccine work and the rhesus macaque is usually used for drug therapies. However, the choice is based purely on poor historical data that is not supported by current data. Due to the lack of difference between the two models the cynomolgus macaque will likely become more predominant as more modern data on disease progression is available for the cynomolgus macaque due to extensive efforts to develop a vaccine.

The use of NHP in high containment will increase at ABSL3 through strategic recruitment and facility expansions. This will primarily be rhesus and cynomolgous macaques and will primarily be for TB vaccine programs. The Rhesus model is also being used for metabolomics studies to address how drug resistant *M. tuberculosis* [multi (MDR), extensive (XDR) and extreme (XXDR)] adapts to the host at different stages of the infection (pending funding). We anticipate operating at maximum capacity in 2018.

The baboon model of pertussis vaccines is a rapidly expanding area at Texas Biomed. The baboon is the only animal that accurately mimics whooping cough following exposure to Bordetella pertussis. We currently have six scheduled vaccine trials of 16-20 animals each and four large multi-year contracts pending. Although these studies do not require ABSL3, they will be conducted in biobubbles at ABSL2+ during the challenge phase.

2. Are there significant new capabilities (e.g., technologies or techniques) that are likely to become more important in NHP research in the coming 5 years, or conversely, are there capabilities that are currently in use that are expected to be of diminished importance?
Infectious disease work is expected to expand with additional pathogens and novel therapeutics and vaccines that are expected to provide suppression of disease and often cures. The area of antibiotic resistance will likely be a major focus in high containment. Development of small molecule-based therapeutics toward clinical use will require pharma-like development of drug formulations. For this work there will be a greater need for PK, ADME-tox and testing of tissue distribution of small molecules and metabolic products, including advanced imaging capabilities such as high resolution PET CT and MALDI imaging.