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Comparison of hematologic, biochemical, and coagulation parameters in α1,3-galactosyltransferase gene-knockout pigs, wild-type pigs, and 4 primate species

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Abstract

Background—The increasing availability of genetically-engineered pigs is steadily improving the results of pig organ and cell transplantation in nonhuman primates (NHPs). Current techniques offer knock-out of pig genes and/or knock-in of human genes. Knowledge of normal values of hematologic, biochemical, coagulation, and other parameters in healthy genetically-engineered pigs and NHPs is important, particularly following pig organ transplantation in NHPs. Furthermore, information on parameters in various NHP species may prove important in selecting the optimal NHP model for specific studies.

Methods—We have collected hematologic, biochemical, and coagulation data on 71 α1,3-galactosyltransferase gene-knockout (GTKO) pigs, 18 GTKO pigs additionally transgenic for human CD46 (GTKO.hCD46), 4 GTKO.hCD46 pigs additionally transgenic for human CD55 (GTKO.hCD46.hCD55), and 2 GTKO.hCD46 pigs additionally transgenic for human thrombomodulin (GTKO.hCD46.hTBM).

Results—We report these data and compare them with similar data from wild-type pigs, and the 3 major NHP species commonly used in biomedical research (baboons, cynomolgus, and rhesus monkeys) and humans, largely from previously published reports.

Conclusions—Genetic modification of the pig (e.g., deletion of the Gal antigen and/or the addition of a human transgene) (i) does not result in abnormalities in hematologic, biochemical, or coagulation parameters that might impact animal welfare, (ii) seems not to alter metabolic

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CONFLICT OF INTEREST

John Bianchi, Suyapa Ball, Anneke Walters, and David Ayares are employees of Revivicor Inc. No other author has a conflict of interest.

function of vital organs, though this needs to be confirmed after their xenotransplantation, and (iii) possibly (though by no means certainly) modifies the hematologic, biochemical, and coagulation parameters closer to human values. The present study may provide a good reference for those working with genetically-engineered pigs in xenotransplantation research and eventually in clinical xenotransplantation.

Keywords

α1,3-galactosyltransferase gene-knockout; Coagulation; Genetically-engineered; Hematology; Pig; Plasma biochemistry; Swine

INTRODUCTION

Pigs have provided a valuable and popular large animal model for biomedical research, especially during the last 3 to 4 decades (1), and are the source-animal of choice for xenotransplantation (2). Pigs offer many similarities to humans in terms of anatomy, physiology, biochemistry, pathology, and pharmacology (2,3) and therefore provide a large animal model to bridge the gap between rodents and humans. Knowledge of normal hematologic and biochemical values in any species used in biomedical research is important. Normal hematologic, biochemical, and physiologic values in several breeds of wild-type (WT, genetically-unmodifed) pigs, e.g., Yorkshire, Yucatan, Landrace, have been reported by several groups (1, 3–5).

With increasing numbers of genetically-engineered pigs becoming available (Table 1), research experience obtained from small animal models (e.g., gene-knockout and/or knock-in technology) can be translated to large animal models. Whereas the ultimate goal is clinical application of cells, tissues, and organs from genetically-engineered pigs for human therapeutic applications (6), it will be critical from a regulatory and safety perspective to have data available on hematologic, biochemical, and physiologic parameters in the source animals.

Measurement of these parameters essentially serves two aims, namely assessment of (i) the health status of the animals themselves, which includes the effect of the genetic modification (i.e., gene knockout or knock-in) on the respective parameter, and (ii) any molecular and/or physiologic incompatibilities following a xenogeneic transplant. While the first aim relates to safety, the second relates to the efficacy of a xenotransplantation “product”.

The genetic modification of pigs has been essential to progress in overcoming the barriers to xenotransplantation (7–10). Early experience in the 1990s using pigs transgenic for human decay-accelerating factor (hCD55) showed significantly extended survival of pig kidneys in NHPs (7). Expression of human complement-regulatory transgenes (e.g., CD46, CD55, CD59) is now common in pigs (7,8), as is knockout of the α1,3-galactosyltransferase gene (Table 1) (9). Islets obtained from pigs transgenic for human CD46 when transplanted into diabetic monkeys have demonstrated >1 year normalization of blood glucose and cure of diabetes (11). Casu et al. (12,13) and Graham et al. (14) have reported differences in glucose metabolism between pigs and NHPs; pigs differ from NHPs and humans by having a much lower C-peptide level, and a less rapid response to a glucose challenge and to arginine stimulation.

Extended survival was also achieved with the transplantation of organs from GTKO pigs (15,16). Recently, heart xenograft survival has been extended to 8 months using GTKO pigs expressing human CD46 (GTKO.hCD46) (17).

In our recent experience in liver xenotransplantation (18), we observed that pig alanine transaminase (ALT), but not aspartate transaminase (AST), in GTKO pigs is significantly lower than in WT pigs, but similar to human and baboon levels (19). We hypothesized that there would be other differences in hematologic, biochemical, and coagulation parameters between WT and GTKO pigs. To our knowledge, there is, hitherto, no published report of normal laboratory values of GTKO pigs in the literature.

In the present study, we report normal hematologic, biochemical, and coagulation values in healthy pigs with various genetic modifications. We compared these values with those of WT pigs and 4 primate species - (i) baboons (*Papio* species), (ii) cynomolgus monkeys (*Macaca fascicularis*), (iii) rhesus monkeys (*Macaca mulatta*), and (iv) humans, to identify possible differences and similarities.

MATERIALS AND METHODS

Animals

Genetically-engineered and WT pigs—Genetically-engineered pigs (on a Landrace large white WT background) were obtained from Revivicor Inc. (Blacksburg, VA, USA). There were a total of 71 GTKO pigs (49 females, 22 males), 18 GTKO pigs transgenic for human CD46 (GTKO.hCD46) (14 females, 4 males), 4 GTKO.hCD46 pigs additionally transgenic for human CD55 (GTKO.hCD46.hCD55) (2 females, 2 males), and 2 GTKO.hCD46 pigs transgenic for human thrombomodulin (GTKO.hCD46.hTBM) (2 males). The number of pigs with a GTKO or GTKO.hCD46 background was 95 and 24, respectively. Their mean ages and weights are shown in Table 2.

Wild-type (Landrace large white) pigs (n=19; 9 females, 10 males) were obtained from Country View Farm, Schellsburg, PA, USA. Their mean ages and weights are shown in Table 3.

Baboons—All baboons used in our own studies (n=45; 13 females and 32 males) were obtained from the University of Oklahoma Health Sciences Center (Oklahoma City, OK, USA). Their mean age was 2.7±0.5 (range 1.8–3.6) years and mean weight was 8.5±2.0 (range 5.6–15.9) kg, respectively.

All animal care was in accordance with the *Principles of Laboratory Animal Care* formulated by the National Society for Medical Research and the *Guide for the Care and Use of Laboratory Animals* prepared by the Institute of Laboratory Animal Resources and published by the National Institutes of Health (NIH publication No. 86-23, revised 1985). Protocols were approved by the University of Pittsburgh Institutional Animal Care and Use Committee.

Blood collection and tests

Blood was collected when the animals were surgically and immunologically naïve. Animals were sedated by an intramuscular injection of 5–10mg/kg of ketamine hydrochloride (Fort Dodge, IA USA). Blood samples were collected by venepuncture for hematologic (EDTA tube), biochemical (plain tube), and coagulation (sodium citrate tube) analysis using standard methods either in the Central Laboratory of Presbyterian Hospital of the University of Pittsburgh Medical Center, Pittsburgh, PA, USA or of Virginia-Maryland Regional College of Veterinary Medicine, Blacksburg, VA, USA.

Equipment used at the University of Pittsburgh and Virginia-Maryland Regional College were, respectively, Beckman LH750 (Fullerton, CA) and Siemens ADVIA 2120 (Tarrytown, NY) for hematologic values, Diagnostic Stago STAR Evolution (Parsippany, NJ) for coagulation parameters, and Beckman DXC 800 (Fullerton, CA) and Olympus America AU400 (Melville, NY) for biochemical parameters.

Literature search and collection of data

A literature search was carried out to identify significant reports on normal values of various parameters in healthy WT pigs, baboons, cynomolgus monkeys, and rhesus monkeys. Published reports detailed normal values in different species and considered factors such as (i) gender, (ii) age, (iii) weight, and (iv) diet. We have not subdivided the data by age, etc., as we wished to compare our data with a large number of animals from each species, as this is how normal human ranges are reported. We have included data from the literature on various parameters from a large number of WT pigs or NHPs. Normal human values and ranges were obtained from the Central Laboratory of Presbyterian Hospital of the University of Pittsburgh Medical Center, Pittsburgh, PA, USA.

Data and statistical analyses

Data analyses were conducted with GraphPad Prism v5.01 (La Jolla, CA, USA). Mean values of sample subsets were calculated and compared using the Student t-test, with a p value of <0.05 being considered statistically significant.

RESULTS

Normal values obtained from healthy GTKO pigs with or without added transgenes from our own study are shown in Table 2. Table 3 shows normal values in different breeds of WT pigs, such as Landrace, Yucatan, and Yorkshire, from our own center and from published studies. Healthy naïve baboon normal values from our own center and from the literature are shown in Table 4. Normal values for healthy cynomolgus and rhesus monkeys from the literature are shown in Tables 5 and 6, respectively. Table 7 compares data on GTKO and WT pigs and from baboons and monkeys with normal human values.

Hematologic parameters

White blood cell (WBC) count—GTKO pigs had a significantly lower mean WBC than WT pigs (p<0.01) (Table 7). Pigs with a GTKO background appeared to have a lower WBC when young (Table 2). Mean WBC count was significantly higher in GTKO and WT pigs than in humans or NHPs (p<0.01) (Table 7). All NHP species tested showed a similar WBC to humans, except in cynomolgus monkeys where the WBC count was significantly higher (p<0.01), though cynomolgus monkeys from Mauritius exhibited similar WBC counts to humans (Tables 5 and 7).

With regard to WBC subsets, GTKO pigs had significantly fewer neutrophils than WT pigs, humans, baboons, and rhesus monkeys (p<0.01). Cynomolgus monkeys had the lowest neutrophil counts among all species tested (p<0.01 vs all other species) (Table 7), but had the highest lymphocyte counts (p<0.01 vs all other species). Monocyte counts were significantly higher in pigs (GTKO and WT) in comparison to other species (p<0.01). Eosinophil and basophil counts were similar in all species (Table 7).

Red blood cell (RBC) parameters—RBC counts were significantly higher in GTKO and WT pigs than in humans and NHP species (p<0.01). Hemoglobin values were comparable in all species, except WT pigs in which the hemoglobin was significantly lower (p<0.01 vs all other species). GTKO and WT pig hematocrits were significantly lower than in NHPs (p<0.01), but were within the human range (Table 7). GTKO and WT pigs exhibited a significantly lower mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) than seen in human and NHP species (p<0.01). Mean corpuscular hemoglobin concentration (MCHC) in all species, except WT pigs, was comparable to that in humans. Percentage RBC distribution width (RDW) was significantly higher in pigs (GTKO and WT) than in primate species (p<0.01) (Table 7).

Renal function and electrolytes

Pigs (GTKO and WT) exhibited higher potassium, calcium, and phosphorus values than humans, baboons, and rhesus monkeys (p<0.01 in all comparisons) (Table 7). Cynomolgus monkeys showed the highest potassium, calcium, and chloride values in comparison to other species (p<0.01) (Table 7). Sodium values were comparable in all species, except in cynomolgus monkeys, which had significantly higher values (p<0.01) (Table 7). Cynomolgus monkeys showed significantly higher urea values than other species (p<0.01) (Table 7). Serum creatinine values were comparable in all species. Carbon dioxide (CO_2)levels were significantly lower in rhesus monkeys (p<0.01). GTKO and WT pigs and baboons exhibited CO_2 levels within the human range (Table 7).

Hepatic function

AST and ALT values were comparable in all species, except that WT pig ALT was significantly higher than in other species (p<0.01) (Table 7). Alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) were higher in pigs and NHPs than in humans (Table 7). ALP was highest in cynomolgus monkeys (10-fold more than in humans) and baboons (5-fold more than in humans). WT pigs exhibited the highest LDH values (5-fold higher than in humans, and 2-fold higher than in GTKO pigs) (Table 7). Total, direct, and indirect bilirubin values were comparable in all species. Total protein and albumin levels were significantly lower in pigs than in NHPs and humans (p<0.01) (Table 7). Levels of total protein and albumin appeared to be lower in younger than in older GTKO pigs (p<0.01) (Table 2). In contrast, WT pigs did not show significantly different total protein and albumin levels between low (young) and high (older) weight pigs (Table 3). Total cholesterol, triglyceride, and glucose levels were comparable in all species (Table 7), except in rhesus monkeys, which exhibited higher cholesterol and triglyceride and lower glucose levels (p<0.01) (Table 7).

Coagulation profiles

WT pigs and cynomolgus monkeys had significantly lower prothrombin times (PT) and partial thromboplastin times (PTT) than GTKO pigs, baboons, rhesus monkeys, and humans (p<0.01 in all comparisons). GTKO pigs exhibited similar PT and PTT to humans. Rhesus monkeys had significantly prolonged PTT compared with other species (p<0.01) (Table 7). While GTKO pigs had international normalized ratio (INR) and d-dimer comparable to humans, baboons showed significantly increased INR and d-dimer (p<0.01). GTKO pigs showed positive fibrinogen degradation products (FDP). Fibrinogen levels were comparable in GTKO pigs, cynomolgus monkeys, and humans, but baboons had significantly lower fibrinogen levels than other species (p<0.01) (Table 7).

Other parameters

Although lipase levels were comparable in humans, GTKO pigs and baboons, amylase levels were significantly lower in humans than in other species (p<0.01). GTKO pigs showed a 13-to-45-fold increase in amylase in comparison to humans and baboons, but only a 4-fold increase in comparison to cynomolgus monkeys (Table 7). Younger GTKO pigs showed significantly higher levels of amylase in comparison to older GTKO pigs (p<0.01) (Table 2). In contrast, amylase levels were higher in older baboons (p<0.01) (Table 4). Iron levels were comparable in all species.

The cardiac enzymes, total creatine kinase (CPK), myocardial band of CPK (CPK-MB) and its relative index, and troponin I were measured only in pigs of GTKO.hCD46 background (Table 2). Total CPK and CPK-MB were significantly higher in GTKO.hCD46 pigs than in humans ($p<0.01$). However, the CPK-MB relative index and troponin I values were comparable in GTKO.hCD46 pigs to humans (Table 7).

DISCUSSION

In biomedical research, it is essential to compare pre-treatment values (i.e., in a surgically and immunologically naïve animal) with post-treatment values. Therefore, knowledge of normal hematologic, biochemical, and coagulation parameters is important. The present study reports, for the first time, the mean values in genetically-engineered pigs important to xenotransplantation research, all on a GTKO background. Moreover, the study compares these values with those in WT pigs and 4 species of primate, including humans.

We report differences in certain parameters between GTKO and WT pigs and/or pigs between primates and/or between NHPs and humans, which may prove important in xenotransplantation research and, ultimately, in clinical xenotransplantation. It should be kept in mind that the health status of the animals may affect a specific parameter. For example, designated pathogen-free pigs may have lower white blood cell counts than pigs housed under routine circumstances. Differences in normal levels of potassium or other electrolyte may be problematic after pig kidney xenotransplantation. After the transplantation of a pig kidney or liver into a NHP, the level of a parameter may reflect the normal level in the NHP (e.g., WBC count), or the normal level in the pig (e.g., serum potassium or albumin). In fact, prominent proteinuria has been underlined by several groups after pig-to-NHP kidney xenotransplantation (16,20). The loss of protein may reflect the physiologic ability of the pig kidney to reduce the albumin levels of the NHP to the normal pig albumin level, which is significantly lower (Table 7). Alternatively, it could reflect an inability of pig kidneys to retain NHP albumin, or reduced synthesis of albumin in the pig liver. Soin et al previously reported severe hypophosphatemia and persistent hypoalbuminemia due to increased proteinuria after pig-to-NHP renal xenotransplantation (21). Whether this was related to a physiologic incompatibility between pig and primate or was the result of a low-grade immune response remains unknown. In our experience, healthy pigs do not have proteinuria (Hara H, personal observation). The topic of physiologic incompatibilities has been reviewed elsewhere (22).

After pig liver xenotransplantation, a great number of parameters may reflect those in the pig, since the liver is the major site of production of many proteins. After pig heart xenotransplantation, the knowledge of normal values of CPK and troponin I is important to monitor damage to the transplanted heart.

GTKO pigs had significantly lower WBC counts than WT pigs, which may be related to the cleanliness of the housing in which they are reared (though GTKO pig values fell within the range of published normal values for WT pigs). Pigs (both GTKO and WT) have higher WBC counts than the primates we tested (Table 7). As important as high WBC count could be, the higher percentage of lymphocytes in the recipient NHPs may also be important with regard to successful lymphocyte depletion. Cynomolgus monkeys have the highest lymphocyte count among four primate species and pigs (Table 7). This high lymphocyte count may result in an increased need for of lymphocyte-depleting agents to achieve the desired outcome.

It should be kept in mind that the health status of the animals may affect a specific parameter. For example, designated pathogen-free pigs may have lower white blood cell counts than pigs housed under routine circumstances.

Cynomolgus monkeys are also special in respect to RBC. It is well known that CD52 is expressed on erythrocytes of most NHP species. As a result, alemtuzumab (anti-CD52 monoclonal antibody) can be used only in cynomolgus monkeys of Indonesian origin, which do not express CD52 on their RBCs (23). The RBC MCV in humans is almost 30–50% greater than that in GTKO pigs, and the MCV of baboon RBC is 30–40% greater than in pigs. Theoretically, this discrepancy could well adversely impact the perfusion of a pig organ after transplantation into a primate. However, evidence from numerous pig-to-NHP organ transplantation studies suggests that this is not the case, and that organ perfusion is satisfactory (unless affected by rejection, etc.). Furthermore, biopsies obtained after pig-to-NHP kidney, heart, and liver xenotransplantation have not shown unequivocal defects in the microcirculation (except when thrombosis occurs following fibrin and platelet aggregation) (15–18,20).

These observations illustrate how baseline (pre-treatment) knowledge of parameters is key to success in biomedical research. Attention has been drawn to the importance of knowing normal parameters in NHP by recent publications by the Emory Group (24,25) with particular regard to MHC typing as a key to successful outcome.

Although our study did not detect any significant difference in total, direct, or indirect bilirubin levels among the species tested (Table 7), the relevance of these data should be interpreted cautiously. Kobayashi et al reported that hepatic bile was significantly less viscous in baboons compared with that in humans and pigs, with pig and human hepatic bile viscosity being similar (26). In our experience of GTKO pig-to-baboon liver xenotransplantation, we observed cholestatic damage on liver histopathology without structural obstruction of the bile ducts, but with the presence of viscous bile (18,27). However, bile stasis may not be a significant problem after pig liver Tx into humans (25).

The lower values for PT and PTT in WT pigs and in cynomolgus monkeys need particular attention as they may impact a coagulopathic state and related complications. A significantly shorter PTT in WT pigs could be related to intrinsic pathway coagulation factors, such as FXII, FXI, and FIX. We have previously reported data suggesting that FXII (initiator of the intrinsic coagulation pathway) in WT pigs is significantly higher (2-fold) than in GTKO pigs (27,28). We have also documented the production of pig coagulation factors after GTKO pig liver xenotransplantation in baboons (27). Knowledge of baseline coagulation values in both organ-source pig and recipient NHP is of importance when monitoring post-transplantation changes. We previously reported the baseline extended coagulation profile in nine healthy baboons (29).

There are other observations from our data that cannot be explained. For example, in GTKO pigs with added transgenes, serum amylase was high when compared with GTKO pigs (Table 2). However, at necropsy, no features suggestive of pancreatitis were observed in these pigs. Similarly, serum cholesterol was particularly low in these pigs. Larger numbers of pigs will need to be studied to confirm, and possibly explain, these observations.

While differences have been observed in various parameters between WT and genetically-engineered pigs, there is no evidence that such differences would lead to an increased risk profile, as compared to the significant benefits that genetically-engineered pigs may provide in overcoming the challenges for human clinical application.

A minor weakness of our comparative study is that data from different centers may have been obtained using different laboratory equipment. However, our own and most other studies have been carried out in hospital laboratories in which standard equipment is used. We suggest there are unlikely to be wide or significant differences in the data obtained. Furthermore, our own data, and we strongly suspect the vast majority of data in the literature, were obtained using equipment equilibrated and validated with respect to human material, not to nonhuman primate material. We do not see this as a major problem. If data from various centers are to be compared, it could be argued that this provides some uniformity to the data as they will all have been obtained on equipment validated to human material.

In conclusion, it appears that genetic modification of the pig (e.g., deletion of the Gal antigen and/or the addition of a human transgene) (i) does not result in abnormalities in hematologic, biochemical, or coagulation parameters that might impact animal welfare, (ii) seems not to alter metabolic function of vital organs, though this needs to be confirmed after their xenotransplantation, and (iii) possibly (though by no means certainly) modifies the hematologic, biochemical, and coagulation parameters closer to human values. The present study may provide a good reference for those working with genetically-engineered pigs in xenotransplantation research and eventually in clinical xenotransplantation.

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Abbreviations (in text and tables)

ALP	alkaline phosphatase
ALT	alanine transaminase
AST	aspartate transaminase
GGT	gamma-glutamyl transferase
GTKO	α1,3-galactosyltransferase gene-knockout
INR	international normalized ratio
LDH	lactate dehydrogenase
MCH	mean corpuscular hemoglobin
MCV	mean corpuscular volume
MCHC	mean corpuscular hemoglobin concentration
MPV	mean platelet volume
NHP	nonhuman primate
PT	prothrombin time
PTT	partial thromboplastin time
RBC	red blood cells
RDW	red blood cell distribution width

WBC	white blood cells
WT	wild-type

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Table 1

Common genetically-engineered pigs currently available for biomedical research

Knock-out technology for deletion of antigen expression
- GTKO (α1,3-galactosyltransferase gene-knockout)
Knock-in technology for human complement regulation
- human CD46
- human CD55
- human CD59
Knock-in technology for human thromboregulation
- human CD39
- human thrombomodulin (TBM)
- human endothelial protein c receptor (EPCR)

Pigs with multiple gene modifications exist (e.g., GTKO.hCD46.hCD55 or GTKO.hCD46.hTBM or GTKO.hCD55.hCD59.hCD39.hTBM)

Table 2

Normal hematologic, biochemical and coagulation values in healthy GTKO pigs

	Test	Unit	GTKO	N	GTKO.hCD46	N	GTKO.hCD46.hCD55	N	GTKO.hCD46.hTBM	N	Mean	SD	Total N
Age/Weight			154 days (range 10-647) / 79kg (range 3-247)		72 days (range 18–390) / 8kg (range 3-29)		45 days (range 40-54) / 9kg (range 8-10)		38 days (range 34-41) / 7.5kg (6.4-8.7)		**132 days (range 10-647) / 69kg (range 3-247)**		
Hematology	WBC	/mm^3	15.9	71	14.8	17	13.3	4	10.7	2	**15.5**	**1.0**	**94**
	RBC	$\times10^6$/mm^3	6.5	71	5.9	17	4.2	4	5.1	2	**6.3**	**1.4**	**94**
	Hemoglobin	g/dL	12.8	71	11.0	17	6.7	4	9.1	2	**12.2**	**2.5**	**94**
	Hematocrit	%	40.3	71	33.3	17	21.9	4	26.4	2	**37.9**	**8.0**	**94**
	Platelets	$\times10^3$/mm^3	432	71	406	17	444	4	310	2	**425**	**210**	**94**
	MCV	fL	63	71	56	17	53	4	52	2	**61.3**	**9.0**	**94**
	MCH	pg	20	71	19	17	18	4	18	2	**19.7**	**2.3**	**94**
	MCHC	g/dL	32	71	33	17	34	4	34	2	**32.3**	**1.9**	**94**
	RDW	%	18.2	2	21.4	10	22.9	4	21.2	2	**21.4**	**3.7**	**18**
	MPV	fL	9.7	2	9.1	7	9.1	4	9.1	2	**9.1**	**0.8**	**15**
	Neutrophil	%	40.0	71	48.4	17	43.5	4	46.0	2	**41.8**	**13.8**	**94**
	Lymphocyte	%	51.7	71	40.9	17	38.5	4	46.0	2	**49.1**	**15.5**	**94**
	Monocyte	%	5.1	71	4.6	17	4.3	4	2.5	2	**4.9**	**3.1**	**94**
	Eosinophil	%	2.6	71	1.5	17	0.8	4	1.0	2	**2.3**	**2.5**	**94**
	Basophil	%	0.1	71	0.0	17	0.5	4	0.0	2	**0.1**	**0.3**	**94**
Renal Function and Electrolytes	Sodium	mmol/L	146	61	140	18	136	4	140	2	**144**	**7**	**85**
	Potassium	mmol/L	5.6	61	5.1	18	3.3	4	3.8	2	**5.3**	**1.1**	**85**
	Chloride	mmol/L	104	61	101	18	99	4	106	2	**103.0**	**8.0**	**85**
	Calcium	mg/dL	11.0	61	10.4	18	10.0	4	9.7	2	**10.8**	**0.8**	**85**
	Phosphorus	mg/dL	8.9	61	8.5	16	9.2	4	8.5	2	**8.8**	**1.8**	**83**
	CO_2	mmol/L	28	61	28	11	30	4	26	2	**28**	**5**	**78**
	Urea	mg/dL	14.6	61	8.8	17	5.8	4	5.5	2	**12.8**	**9.9**	**84**
	Creatinine	mg/dL	1.2	61	0.9	17	0.5	4	0.7	2	**1.1**	**0.5**	**84**

	Test	Unit	GTKO	N	GTKO.hCD46	N	GTKO.hCD46.hCD55	N	GTKO.hCD46.hTBM	N	Mean	SD	Total N
Liver Function	AST	IU/L	38	71	36	18	30	4	36	2	**37**	**29**	**95**
	ALT	IU/L	55	2	40	18	47	4	40	2	**42**	**15**	**26**
	ALP	IU/L	145	2	249	18	409	4	324	2	**272**	**146**	**26**
	LDH	IU/L	559	2	471	9	433	4	468	2	**472**	**109**	**17**
	GGT	IU/L	78	61	65	16	58	4	47	2	**74**	**16**	**83**
	Tot Bilirubin	mg/dL	0.2	61	0.1	9	0.2	4	0.2	2	**0.2**	**0.2**	**76**
	Dir Bilirubin	mg/dL	0.1	61	0.1	9	0.1	4	0.1	2	**0.1**	**0.1**	**76**
	Indir Bilirubin	mg/dL	0.1	61	0.1	9	0.1	4	0.1	2	**0.1**	**0.1**	**76**
	Tot Protein	g/dL	6.2	61	5.5	18	3.9	4	3.8	2	**5.9**	**1.4**	**85**
	Albumin	g/dL	3.8	61	2.8	18	1.3	4	1.3	2	**3.4**	**1.1**	**85**
	Cholesterol	mg/dL	98	2	85	16	62	3	59	2	**81**	**22**	**23**
	Triglyceride	mg/dL	14	2	39	16	14	3	11	2	**31**	**22**	**23**
	Glucose	mg/dL	90	71	93	18	75	4	66	2	**89**	**27**	**95**
Coaulation Profile	PT	sec	14.4	2	13.6	9	13.9	4	13.2	2	**13.6**	**0.5**	**17**
	PTT	sec	32.5	2	34.8	9	35.8	4	29.3	2	**34.1**	**14.0**	**17**
	INR		1.1	2	1.1	9	1.1	4	1.1	2	**1.1**	**0.1**	**17**
	D-Dimer	µg/mL	0.22	2	0.22	9	0.22	4	0.14	2	**0.20**	**0.05**	**17**
	FDP	µg/mL	5to20	2	<5	9	5to20	4			**5to20**		**15**
	Fibrinogen	mg/dL	265	71	197	9	156	4	143	2	**250**	**121**	**86**
Others	Amylase	IU/L	459	2	1292	16	2941	4	2780	2	**1622**	**1130**	**24**
	Lipase	IU/L			14	14	10	4	11	2	**13.1**	**13.2**	**20**
	Iron	µg/dL			110	9	79	3	121	2	**104.0**	**48.0**	**14**
	Total CPK	IU/L	1209	59	1228	8	510	4	652	2	**1166**	**2305**	**73**
	CPK-MB isoenzyme	ng/mL			1.2	1	5.1	4	4.8	1	**4.4**	**4.0**	**6**
	CPK-MB relative index				0.1	1	0.9	4	0.6	1	**0.7**	**0.5**	**6**
	Troponin I	ng/mL			0.10	1	0.10	4	0.10	1	**0.11**	**0.02**	**6**

Table 3

Normal hematologic, biochemical and coagulation values in healthy WT pigs

	Test	Unit	Ekser (2012)	N	Klem* (2010)	N	Egeli* (1998)	N	Rispat* (1993)	N	Hannon* (1990)	N	Mean	SD	Total N
Type /Weight			*Landrace*		*Landrace*		*Landrace*		*Yucatan*		*Yorkshire*				
			12.7 kg		30-50 kg		12.2 kg		13.8 kg		21.3 kg				
Hematology	WBC	/mm^3	16.0	19	27.3	99	13.4	60	14.9	135			**18.6**	**6.4**	**313**
	RBC	×10^6/mm^3	5.1	19	7.4	99	5.8	60	7.34	135			**6.9**	**1.1**	**313**
	Hemoglobin	g/dL	9.3	19	12.0	99	10.1	60	8.9	135	8.5	26	**10.0**	**1.4**	**339**
	Hematocrit	%	26.3	19	39.0	99	32.0	60	47.0	135	27.0	69	**37.9**	**8.7**	**382**
	Platelets	×10^3/mm^3	261	19	549	99			510	135			**507**	**156**	**253**
	MCV	fL	51	19	54	99	57	60	64	135			**59**	**6**	**313**
	MCH	pg	18	19			18	60	17	135			**17**	**1**	**214**
	MCHC	g/dL			31	99	31	60	19	135			**25**	**7**	**294**
	RDW	%			18	99	20.6	60					**19.0**	**1.8**	**159**
	MPV	fL													
	Neutrophil	%			37	99	41	60	54	135			**45.6**	**8.9**	**294**
	Lymphocyte	%			51	99	51	60	39	135			**45.5**	**6.9**	**294**
	Monocyte	%			6.5	99	1.6	60	4.7	135			**4.7**	**2.5**	**294**
	Eosinophil	%			2.6	99	1.6	60	1.6	135			**1.9**	**0.6**	**294**
	Basophil	%			0.7	99	0.9	60	0.06	135			**0.4**	**0.4**	**294**
Renal Function and Electrolytes	Sodium	mmol/L	139	19	149	101	143	60	140	127	138	35	**143**	**4**	**342**
	Potassium	mmol/L	3.9	19	6.3	101	4.3	60	5.5	127	4.4	35	**5.3**	**1.0**	**342**
	Chloride	mmol/L	103	19	106	101	107	60	103	127	106	17	**104.8**	**1.9**	**324**
	Calcium	mg/dL			11.2	101	11.2	60	10.9	127	9.6	15	**11.0**	**0.8**	**303**
	Phosphorus	mg/dL			10.8	101	10.2	60	6.7	127	4.0	17	**8.6**	**3.2**	**305**
	CO_2	mmol/L	29	19									**29**	**4**	**19**
	Urea	mg/dL	10	19	8.7	101	5.9	60	19.2	127	8.9	17	**12.4**	**5.1**	**324**
	Creatinine	mg/dL	1.0	19	1.2	101	1.0	60	0.9	127	1.0	17	**1.0**	**0.1**	**324**
Liver Function	AST	IU/L	41	19	46	101	32	60	39	127			**40**	**6**	**307**

	Test	Unit	Ekser (2012)	N	Klem* (2010)	N	Egeli* (1998)	N	Rispat* (1993)	N	Hannon* (1990)	N	Mean	SD	Total N
	ALT	IU/L	79	19	68	101	39	60	57	127			**58**	**17**	**307**
	ALP	IU/L	140	19	211	101	824	60	58	127			**263**	**349**	**307**
	LDH	IU/L	140	19	795	101	1207	60	773	127			**826**	**440**	**307**
	GGT	IU/L	50	19	50	101	29	60					**43**	**12**	**180**
	Tot Bilirubin	mg/dL	0.1	19	1.0	101	0.1	60	0.3	127			**0.5**	**0.4**	**307**
	Dir Bilirubin	mg/dL	0.1	19									**0.1**	**0.0**	**19**
	Indir Bilirubin	mg/dL	0.1	19									**0.1**	**0.0**	**19**
	Tot Protein	g/dL	3.7	19	5.8	101	4.8	60					**5.2**	**1.1**	**180**
	Albumin	g/dL	1.6	19	2.5	101	3.0	60			2.5	40	**2.6**	**0.6**	**220**
	Cholesterol	mg/dL			120	101	116	60	78	127			**101**	**23**	**288**
	Triglyceride	mg/dL			80	101	80	60	29	127			**58**	**29**	**288**
	Glucose	mg/dL	62	19	115	101	121	60	67	127	83	33	**92**	**27**	**340**
Coaulation Profile	PT	sec							11.7	135			**11.7**	**0.6**	**135**
	PTT	sec							15.5	135			**15.5**	**1.2**	**135**
	INR														
	D-Dimer	μg/mL													
	FDP	μg/mL													
	Fibrinogen	mg/dL													
Others	Amylase	IU/L													
	Lipase	IU/L													
	Iron	μg/dL			173	101	179	60					**175.2**	**4.2**	**161**

* Klem et al (4), Egeli et al (5), Rispat et al (3), Hannon et al (1).

Table 4

Normal hematologic, biochemical and coagulation values in healthy baboons (*Papio species*)

	Test	Unit	Ekser (2012)	N	Schuurman* (2004)	N	Havill* (2003)	N	Harewood* (1999)	N	Hainsey* (1993)	N	Mean	SD	Total N
Age / Weight			2.7 years (8.5 kg)		7.7-8.9 kg		0-12 Months		not available		4.4 years				
Hematology	WBC	/mm^3	7.5	45	7.9	85	11.6	109	10.2	1024	9.6	89	**10.0**	**1.7**	**1352**
	RBC	×10^6/mm^3	5.0	45	5.1	85	5.2	110	5.1	1024	5.0	90	**5.1**	**0.1**	**1354**
	Hemoglobin	g/dL	12.4	45	13.0	85	13.2	109	12.6	1023	12.6	89	**12.7**	**0.3**	**1351**
	Hematocrit	%	37.7	45	40.2	85	40.8	109	40	1024	38.2	89	**39.9**	**1.3**	**1352**
	Platelets	×10^3/mm^3	295	45	368	85	410	110	439	1020	316	89	**419**	**61**	**1349**
	MCV	fL	76	44	79	85	78	110	77	1024	77	90	**77**	**1**	**1353**
	MCH	pg	25	44	26	85	25	110	25	1023	25	90	**25**	**0**	**1352**
	MCHC	g/dL	33	44	32	85	33	110			33	90	**33**	**0**	**329**
	RDW	%	12.7	37			13.5	110			12.8	90	**13.1**	**0.4**	**237**
	MPV	fL	8.6	37			8.7	60			8.3	89	**8.5**	**0.2**	**186**
	Neutrophil	%	54	45	40	85	52	91			62	90	**52.0**	**9.1**	**311**
	Lymphocyte	%	38	45	56	85	45	110			36	90	**44.4**	**9.0**	**330**
	Monocyte	%	5	45	3	85	3	103			2	90	**3.2**	**1.1**	**323**
	Eosinophil	%	1	44	1	85	1	97			1	90	**0.9**	**0.1**	**316**
	Basophil	%	1	44	0	85	1	88			0	90	**0.3**	**0.5**	**307**
Renal Function and Electrolytes	Sodium	mmol/L	146	40	150	67	144	103	146	1044	149	25	**146**	**2**	**1279**
	Potassium	mmol/L	3.7	40	5.0	67	4.3	104	3.7	1045	3.9	25	**3.8**	**0.5**	**1281**
	Chloride	mmol/L	107	40	108	67	110	104	108	1042	99	24	**108**	**4**	**1277**
	Calcium	mg/dL	10.0	39	10.2	67			9.5	1034	9.0	25	**9.5**	**0.5**	**1165**
	Phosphorus	mg/dL	5.2	35	7.2	67			4.1	1034	2.9	25	**4.3**	**1.8**	**1161**
	CO_2	mmol/L	27	35			20	103	23	1040	24	25	**23**	**3**	**1203**
	Urea	mg/dL	15	40	22	67	12	103	14	1042	14	25	**14**	**4**	**1277**
	Creatinine	mg/dL	0.7	40	0.93	67	0.7	104	0.7	1046	1	25	**0.7**	**0.1**	**1282**
Liver Function	AST	IU/L	37	40	31	67	46	106	36	1037	39	25	**37**	**6**	**1275**
	ALT	IU/L	31	40	39	67	33	106	40	1042	45	25	**39**	**6**	**1280**

	Test	Unit	Ekser (2012)	N	Schuurman* (2004)	N	Havill* (2003)	N	Harewood* (1999)	N	Hainsey* (1993)	N	Mean	SD	Total N
	ALP	IU/L	832	40			1221	104	581	1036	248	25	**638**	**411**	**1205**
	LDH	IU/L	287	35	287	37					276	25	**284**	**6**	**97**
	GGT	IU/L	59	38	74	67			36	1043	39	25	**39**	**18**	**1173**
	Tot Bilirubin	mg/dL	0.2	40	0.23	67			0.11	1023	0.2	25	**0.1**	**0.1**	**1155**
	Dir Bilirubin	mg/dL	0.1	36									**0.1**	**0.1**	**36**
	Indir Bilirubin	mg/dL	0.1	36									**0.1**	**0.1**	**36**
	Tot Protein	g/dL	6.5	40	7.02	67	6.3	106	6.9	1043	7.1	25	**6.8**	**0.3**	**1281**
	Albumin	g/dL	3.8	40	4.39	67	3.8	103	4.1	1042	3.5	25	**4.1**	**0.3**	**1277**
	Cholesterol	mg/dL	122	36	133	67	134	106	97	948	99	25	**103**	**18**	**1182**
	Triglyceride	mg/dL	50	35	51	67			61	933	66	25	**60**	**8**	**1060**
	Glucose	mg/dL	86	40	88	67	83	106	99	1046	83	24	**96**	**7**	**1283**
Coaulation Profile	PT	sec	16	34	12	6					13	32	**14.3**	**1.9**	**72**
	PTT	sec	34	34	28	6					32	32	**32.6**	**3.1**	**72**
	INR		1.3	34									**1.3**	**0.1**	**34**
	D-Dimer	μg/mL	0.7	22									**0.7**	**0.8**	**22**
	FDP	μg/mL	<5	16									**<5**	**n.a**	**16**
	Fibrinogen	mg/dL	213	32							166	32	**190**	**33**	**64**
Others	Amylase	IU/L	153	35	178	37					243	25	**186**	**46**	**97**
	Lipase	IU/L	38	13							25	22	**30**	**9**	**35**
	Iron	μg/dL	122	13					162	849	68	24	**159**	**47**	**886**

* Schuurman et al (30), Havill et al (31), Harewood et al (32), Hainsey et al (33).

Table 5

Normal hematologic, biochemical and coagulation values in healthy Cynomolgus monkeys (*Macaca fascicularis*)

	Test	Unit	Bonfanti* (2009)	N	Schuurman* (2005)	N	Koga* (2005)	N	Mean	SD	Total N
Type / Age			*Mauritius*		*not available*		*Chinese*				
			not available		3.5 years		3-7 years				
Hematology	WBC	/mm^3	8.6	60	11.9	106	12.4	440	**11.9**	**2.1**	**606**
	RBC	×10^6/mm^3	6.9	60	6.5	106	5.5	440	**5.8**	**0.7**	**606**
	Hemoglobin	g/dL	13.8	60	12.2	106	13.1	440	**13.0**	**0.8**	**606**
	Hematocrit	%	49	60	40	106	43	440	**43**	**5**	**606**
	Platelets	×10^3/mm^3	359	60	430	106	442	440	**432**	**45**	**606**
	MCV	fL	72	60	62	106	78	440	**75**	**8**	**606**
	MCH	pg	20	60	19	106	24	440	**23**	**3**	**606**
	MCHC	g/dL	29	60	31	106	31	440	**31**	**1**	**606**
	RDW	%	13.7	60					**13.7**	**0.9**	**60**
	MPV	fL	9	60					**9.0**	**1.1**	**60**
	Neutrophil	%	27	60	42	106	32	440	**33.2**	**7.8**	**606**
	Lymphocyte	%	65	60	48	106	60	440	**58.4**	**8.7**	**606**
	Monocyte	%	5.7	60	6.8	106	3.6	440	**4.4**	**1.6**	**606**
	Eosinophil	%	1.6	60	2.8	106	2.7	440	**2.6**	**0.7**	**606**
	Basophil	%	0.4	60	0.3	106	0.8	440	**0.7**	**0.3**	**606**
Renal Function and Electrolytes	Sodium	mmol/L	158	60	159	106			**158**	**0**	**166**
	Potassium	mmol/L	6.3	60	5.5	106			**5.8**	**0.6**	**166**
	Chloride	mmol/L			113	106			**113**	**4**	**106**
	Calcium	mg/dL	12.3	60	10.5	106			**11.1**	**1.2**	**166**
	Phosphorus	mg/dL	6.3	60	5.4	106	5.6	304	**5.6**	**0.5**	**470**
	CO_2	mmol/L									
	Urea	mg/dL	44.5	60	19.1	106	20.5	328	**23.1**	**14.3**	**494**
	Creatinine	mg/dL	0.92	60	1.1	106	0.6	328	**0.8**	**0.3**	**494**
Liver Function	AST	IU/L	43	60	31	106	32	328	**33.1**	**6.5**	**494**

	Test	Unit	Bonfanti* (2009)	N	Schuurman* (2005)	N	Koga* (2005)	N	Mean	SD	Total N
	ALT	IU/L	45	60	61	106	43	328	**47.1**	**9.9**	**494**
	ALP	IU/L	2046	60			964	312	**1139**	**765**	**372**
	LDH	IU/L	789	60	340	106	653	296	**599**	**230**	**462**
	GGT	IU/L	153	60	108	106			**124.1**	**31.5**	**166**
	Tot Bilirubin	mg/dL	0.3	60	0.4	106	0.2	328	**0.3**	**0.1**	**494**
	Dir Bilirubin	mg/dL	0.1	60					**0.1**	**0.0**	**60**
	Indir Bilirubin	mg/dL									
	Tot Protein	g/dL	8.1	60	8.9	106	7.5	304	**7.9**	**0.7**	**470**
	Albumin	g/dL	4.9	60	4.7	106	4.0	288	**4.3**	**0.5**	**454**
	Cholesterol	mg/dL	127	60	144	106	128	304	**132**	**9**	**470**
	Triglyceride	mg/dL	64	60	56	106	37	304	**45**	**14**	**470**
	Glucose	mg/dL	79	60	79	106	82	304	**81**	**2**	**470**
Coaulation Profile	PT	sec					9.4	616	**9.4**	**0.5**	**616**
	PTT	sec					21.6	616	**21.6**	**2.2**	**616**
	INR										
	D-Dimer	µg/mL									
	FDP	µg/mL									
	Fibrinogen	mg/dL	236	60					**236**	**28**	**60**
Others	Amylase	IU/L			440	106			**440**	**150**	**106**
	Lipase	IU/L									
	Iron	µg/dL	156	60					**156**	**36**	**60**

*Bonfanti et al (34), Schuurman et al (35), Koga et al (36).

Table 6

Normal hematologic, biochemical and coagulation values in healthy Rhesus monkeys (*Macaca mulatta*)

	Test	Unit	Chen* (2009)	N	Smucny* (2004)	N	Buchl* (1997)	N	Mean	SD	Total N
Age / Weight			3.6 years		8.6 ± 2.6 kg		3.6 years				
Hematology	WBC	/mm^3	15.7	35	7.6	3086	10.1	476	**8.0**	**4.1**	**3597**
	RBC	×10^6/mm^3	5.3	35	5.6	3093	5.8	476	**5.6**	**0.3**	**3604**
	Hemoglobin	g/dL	12.8	35	13.3	2974	12.9	476	**13.2**	**0.3**	**3485**
	Hematocrit	%	41.8	35	41.0	3023	40.0	476	**40.9**	**0.9**	**3534**
	Platelets	×10^3/mm^3	359	35					**359**	**71**	**35**
	MCV	fL	79	35	75	2952	70	476	**74**	**5**	**3463**
	MCH	pg	24	35	24	3068	22	476	**24**	**1**	**3579**
	MCHC	g/dL	31	35	32	3062	32	476	**32**	**1**	**3573**
	RDW	%	13	35					**13.0**	**0.7**	**35**
	MPV	fL									
	Neutrophil	%	39	35	52	1611	63	476	**54.3**	**12.0**	**2122**
	Lymphocyte	%	57	35	39	2977	32	476	**38.2**	**12.9**	**3488**
	Monocyte	%	2.3	35	3.7	1436	3	476	**3.5**	**0.7**	**1947**
	Eosinophil	%	0.1	35	3.9	1419	0.8	476	**3.1**	**2.0**	**1930**
	Basophil	%	0.0	35			0.2	476	**0.2**	**0.1**	**511**
Renal Function and Electrolytes	Sodium	mmol/L	151	36			147	476	**147**	**3**	**512**
	Potassium	mmol/L	4.8	36	4.0	1558	4.0	476	**4.0**	**0.5**	**2070**
	Chloride	mmol/L	107	36			113	476	**113**	**4**	**512**
	Calcium	mg/dL	10.7	36	9.2	2476	10.3	476	**9.4**	**0.8**	**2988**
	Phosphorus	mg/dL			4.0	2465	4.9	476	**4.1**	**0.6**	**2941**
	CO_2	mmol/L	13.9	36					**13.9**	**3.9**	**36**
	Urea	mg/dL	21.9	36	16.9	2594	19.0	476	**17.3**	**2.5**	**3106**
	Creatinine	mg/dL	0.8	36	1.1	2492	0.8	476	**1.0**	**0.2**	**3004**
Liver Function	AST	IU/L	39	36	33	2464	36	476	**33.6**	**3.0**	**2976**
	ALT	IU/L	53	36	45	2259	42	476	**44.6**	**5.7**	**2771**

	Test	Unit	Chen* (2009)	N	Smucny* (2004)	N	Buchl* (1997)	N	Mean	SD	Total N
	ALP	IU/L	546	36	131	2474	430	476	**184**	**214**	**2986**
	LDH	IU/L	514	36	276	1553	410	476	**311**	**119**	**2065**
	GGT	IU/L	74	36			60	476	**61.0**	**9.9**	**512**
	Tot Bilirubin	mg/dL	2.8	36			0.2	476	**0.4**	**1.8**	**512**
	Dir Bilirubin	mg/dL	0.7	36					**0.7**	**0.2**	**36**
	Indir Bilirubin	mg/dL	2.1	36					**2.1**	**0.7**	**36**
	Tot Protein	g/dL	7.8	36	7.1	2773	7.3	476	**7.1**	**0.4**	**3285**
	Albumin	g/dL	5.4	36	3.9	1864	4.4	476	**4.0**	**0.8**	**2376**
	Cholesterol	mg/dL	114	36	142	2482	142	476	**142**	**16**	**2994**
	Triglyceride	mg/dL	74	36	93	818	45	476	**75**	**24**	**1330**
	Glucose	mg/dL	103	36	66	2516	70	476	**67**	**20**	**3028**
Coaulation Profile	PT	sec	14.2	24					**14.2**	**0.9**	**24**
	PTT	sec	43	24					**43.0**	**5.4**	**24**
	INR										
	D-Dimer	μg/mL									
	FDP	μg/mL									
	Fibrinogen	mg/dL									
Others	Amylase	IU/L									
	Lipase	IU/L									
	Iron	μg/dL	156	36					**156**	**30**	**36**

*Chen et al (37), Smucny et al (38), Buchl et al (39).

Table 7

Comparison of normal GTKO and WT pig mean values with 4 primate species

	Test	Unit	GTKO*	WT*	Baboon	Cyno*	Rhesus*	Human
Hematology	WBC	/mm^3	**15.5**	18.6	10.0	11.9	8.0	3.8 – 10.6
	RBC	×10^6/mm^3	6.3	6.9	5.1	5.8	5.6	3.73 – 4.89
	Hemoglobin	g/dL	12.2	10.0	12.7	13.0	13.2	11.6 – 14.6
	Hematocrit	%	37.9	37.9	39.9	43.1	40.9	34.1 – 43.3
	Platelets	×10^3/mm^3	425.0	506.6	419.2	431.7	359.0	156 – 369
	MCV	fL	**61.3**	58.7	77.2	74.6	74.4	82.6 – 97.4
	MCH	pg	**19.7**	17.4	25.1	22.7	23.7	27.8 – 33.4
	MCHC	g/dL	32.3	25.5	32.6	30.7	32.0	32.7 – 35.5
	RDW	%	**21.4**	19.0	13.1	13.7	13.0	11.8 – 15.2
	MPV	fL	9.1	n.a.	8.5	9.0	n.a.	6.8 – 10.4
	Neutrophil	%	41.8	45.6	52.0	33.2	54.3	44 – 77
	Lymphocyte	%	49.1	45.5	44.4	58.4	38.2	13 – 44
	Monocyte	%	4.9	4.7	3.2	4.4	3.5	4 – 13*
	Eosinophil	%	2.3	1.9	0.9	2.6	3.1	0 – 6
	Basophil	%	0.1	0.4	0.3	0.7	0.2	0 – 1
Renal Function and Electrolytes	Sodium	mmol/L	144.0	142.9	146.1	158.4	147.3	136 – 146
	Potassium	mmol/L	**5.3**	5.3	3.8	5.8	4.0	3.5 – 5.0
	Chloride	mmol/L	103.0	104.8	108.0	113.4	112.6	95 – 110
	Calcium	mg/dL	**10.8**	11.0	9.5	11.1	9.4	8.4 – 10.2
	Phosphorus	mg/dL	8.8	8.6	4.3	5.6	4.1	2.5 – 4.5
	CO2	mmol/L	28.1	29.0	22.9	n.a.	13.9	21–32
	Urea	mg/dL	12.8	12.4	14.3	23.1	17.3	5.0 – 20.0
	Creatinine	mg/dL	1.1	1.0	0.7	0.8	1.0	0.6 – 1.1
Liver Function	AST	IU/L	37.0	40.1	36.6	33.1	33.6	< 40
	ALT	IU/L	42.0	58.5	39.2	47.1	44.6	< 40
	ALP	IU/L	**272.0**	263.1	637.7	1138.6	183.7	38 – 126

	Test	Unit	GTKO*	WT*	Baboon	Cyno*	Rhesus*	Human
	LDH	IU/L	**472.0**	825.9	284.2	598.8	311.0	< 170
	GGT	IU/L	**74.0**	43.0	39.0	124.1	61.0	< 40
	Tot Bilirubin	mg/dL	0.2	0.5	0.1	0.3	0.4	0.3 – 1.5
	Dir Bilirubin	mg/dL	0.1	0.1	0.1	0.1	0.7	0.1 – 0.4
	Indir Bilirubin	mg/dL	0.1	0.1	0.1	n.a.	2.1	0.2 – 1.1
	Tot Protein	g/dL	5.9	5.2	6.8	7.9	7.1	6.3 – 7.7
	Albumin	g/dL	3.4	2.6	4.1	4.3	4.0	3.4 – 5.0
	Cholesterol	mg/dL	81.0	100.6	103.2	131.5	141.7	<200
	Triglyceride	mg/dL	31.0	57.5	60.1	44.8	75.3	<150
	Glucose	mg/dL	89.0	92.1	96.4	81.0	67.1	70 – 99
Coaulation Profile	PT	sec	13.6	11.7	14.3	9.4	14.2	11.3 – 14.5
	PTT	sec	34.1	15.5	32.6	21.6	43.0	22.7 – 35.6
	INR		1.1	n.a.	1.3	n.a.	n.a.	0.8 – 1.2
	D-Dimer	μg/mL	0.2	n.a.	0.7	n.a.	n.a.	<0.45
	FDP	μg/mL	5to20	n.a.	<5	n.a.	n.a.	<5 neg, >20 pos
	Fibrinogen	mg/dL	250.0	n.a.	189.5	235.8	n.a.	200 – 400
Others	Amylase	IU/L	**1622.0**	n.a.	185.7	440.0	n.a.	35 – 118
	Lipase	IU/L	13.1	n.a.	29.8	n.a.	n.a.	22 – 51
	Iron	μg/dL	104.0	175.2	158.9	156.3	156.0	28 – 170
	Total CPK	IU/L	**1166.0**	n.a.	n.a.	n.a.	n.a.	60 – 400
	CPK-MB isoenzyme	ng/mL	4.4	n.a.	n.a.	n.a.	n.a.	0 – 3
	CPK-MB relative index		0.7	n.a.	n.a.	n.a.	n.a.	0 – 3
	Troponin I	ng/mL	0.1	n.a.	n.a.	n.a.	n.a.	< 0.4

*GTKO = α1,3-galactosyltransferase gene-knockout pigs; WT = wild-type pigs; Cyno = cynomolgus monkeys; Rhesus = rhesus monkeys. n.a. = not available. GTKO values indicated in bold are statistically different from human values.