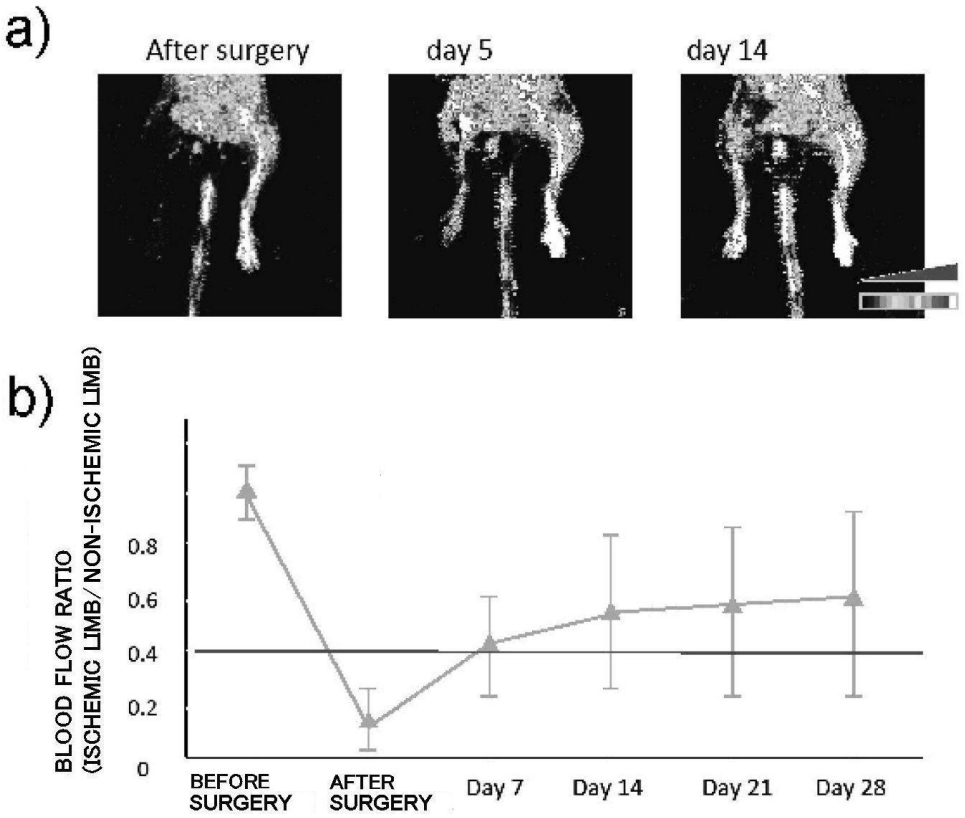
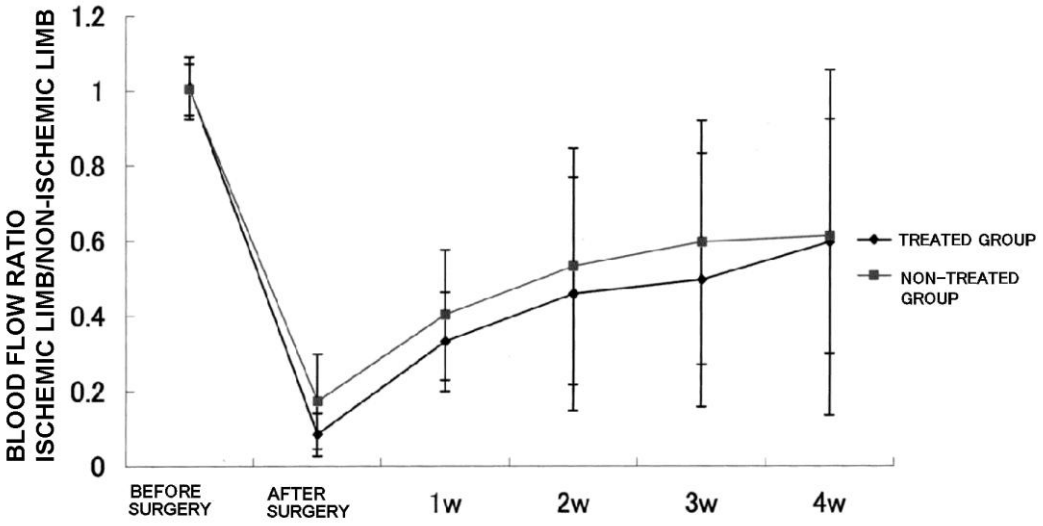
[Fig. 1]

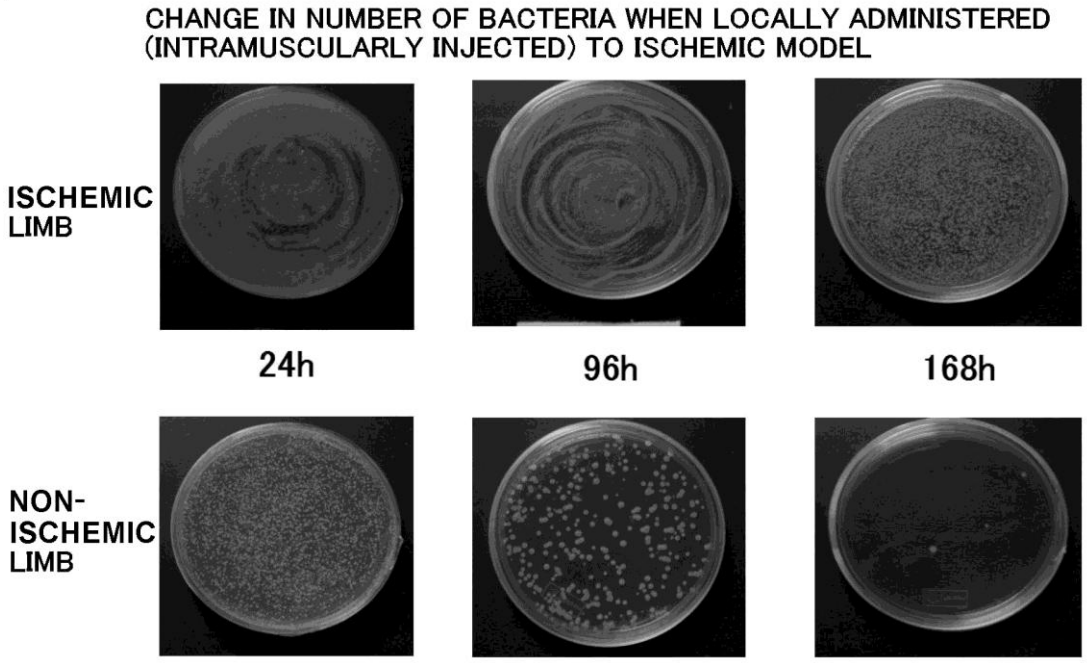


[Fig. 2]

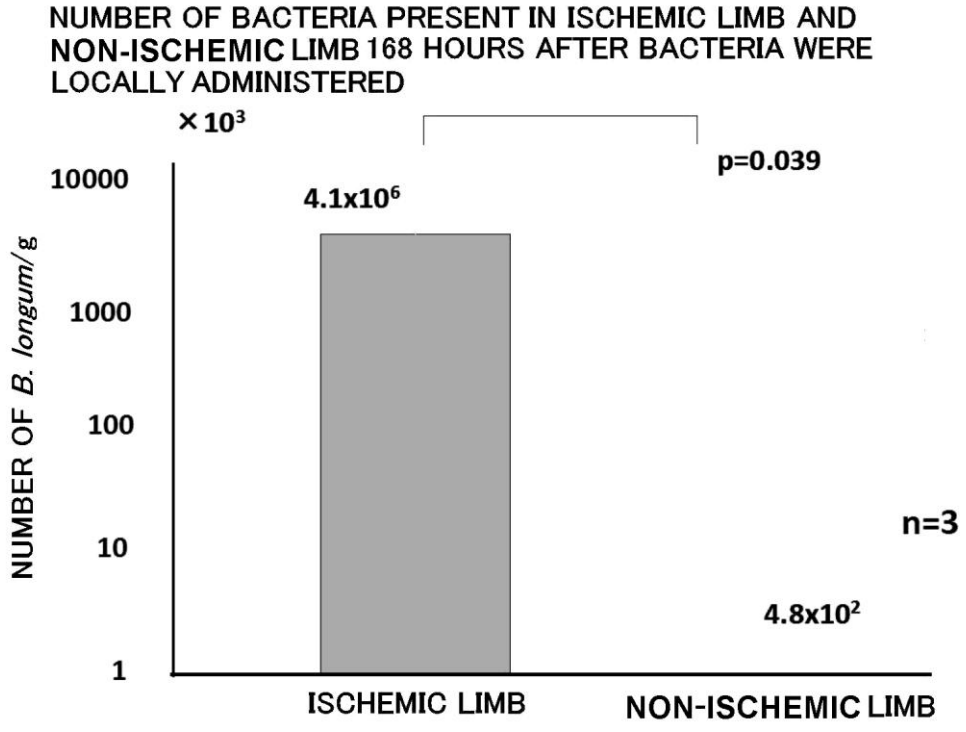


ADMINISTRATION OF *B. longum* DID NOT AFFECT THE ISCHEMIC STATE OF THE LOWER LIMB.

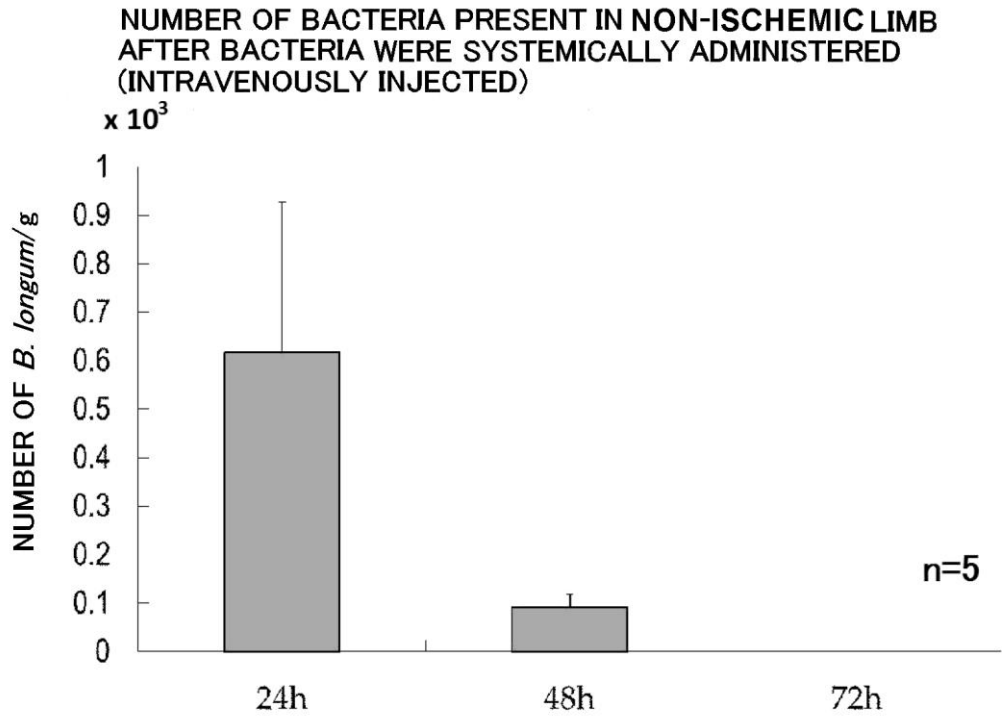
[Fig. 3]


CHANGE IN NUMBER OF BACTERIA WHEN LOCALLY ADMINISTERED (INTRAMUSCULARLY INJECTED) TO ISCHEMIC MODEL
ISCHEMIC LIMB
NON-ISCHEMIC LIMB
24h
96h
168h

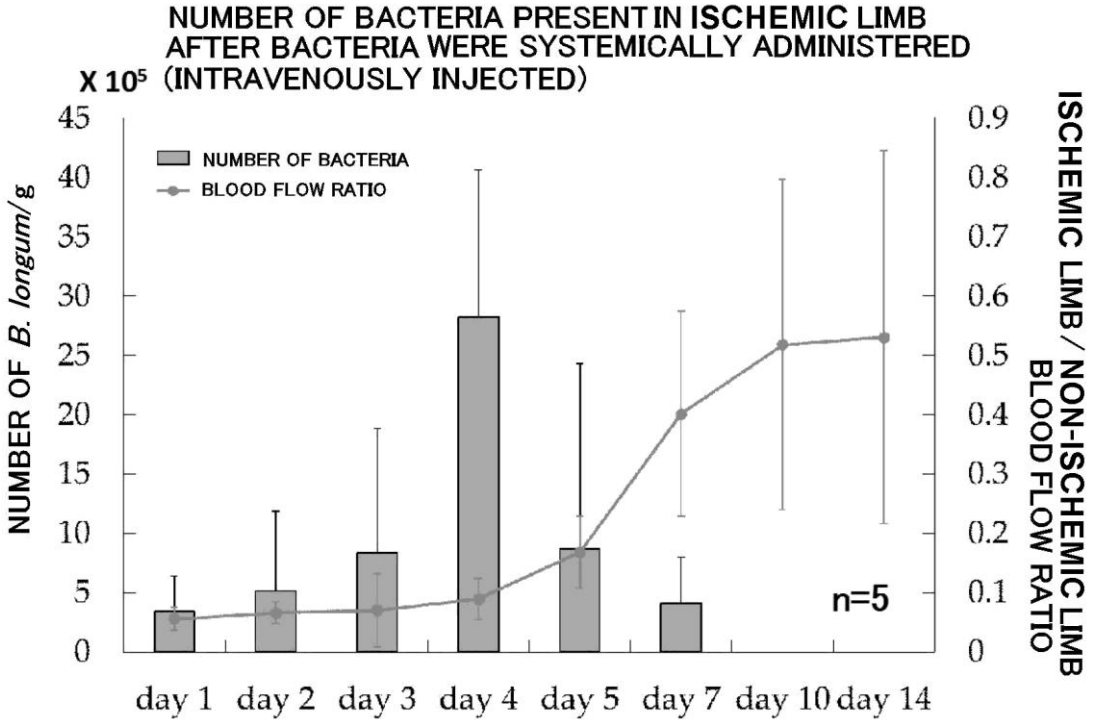
[Fig. 4]


NUMBER OF BACTERIA PRESENT IN ISCHEMIC LIMB AND NON-ISCHEMIC LIMB 168 HOURS AFTER BACTERIA WERE LOCALLY ADMINISTERED
×10³
NUMBER OF B. longum/g
10000
1000
100
10
1
4.1x10⁶
4.8x10²
p=0.039
n=3
ISCHEMIC LIMB
NON-ISCHEMIC LIMB

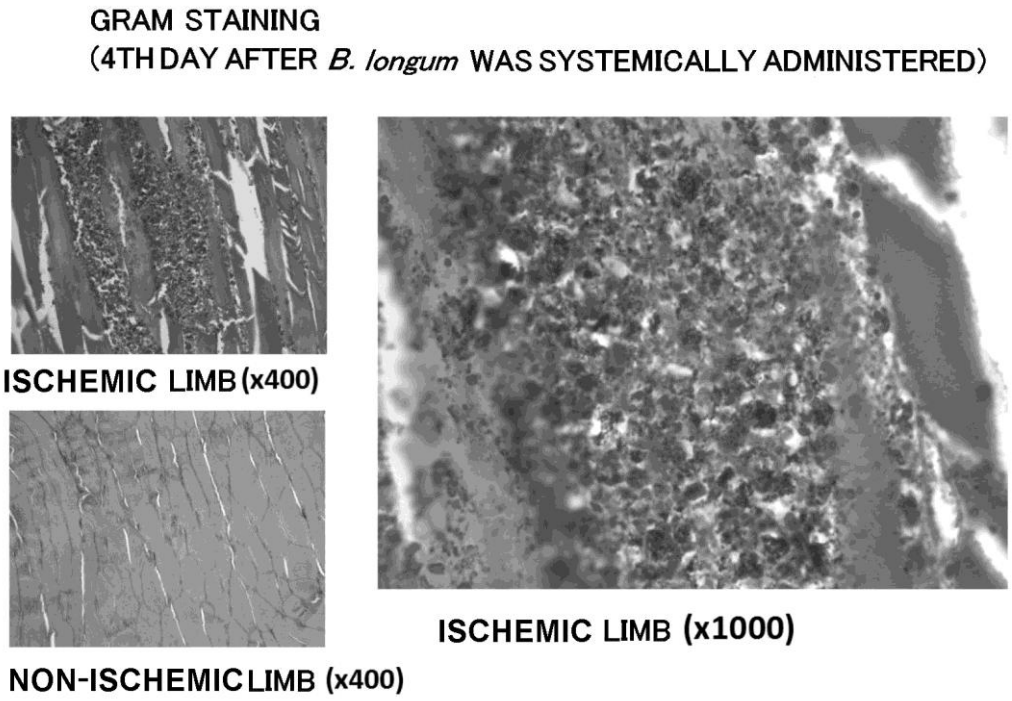
[Fig. 5]


NUMBER OF BACTERIA PRESENT IN NON-ISCHEMIC LIMB
AFTER BACTERIA WERE SYSTEMICALLY ADMINISTERED
(INTRAVENOUSLY INJECTED)
x 10^3
NUMBER OF B. longum/g
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
n=5
24h
48h
72h

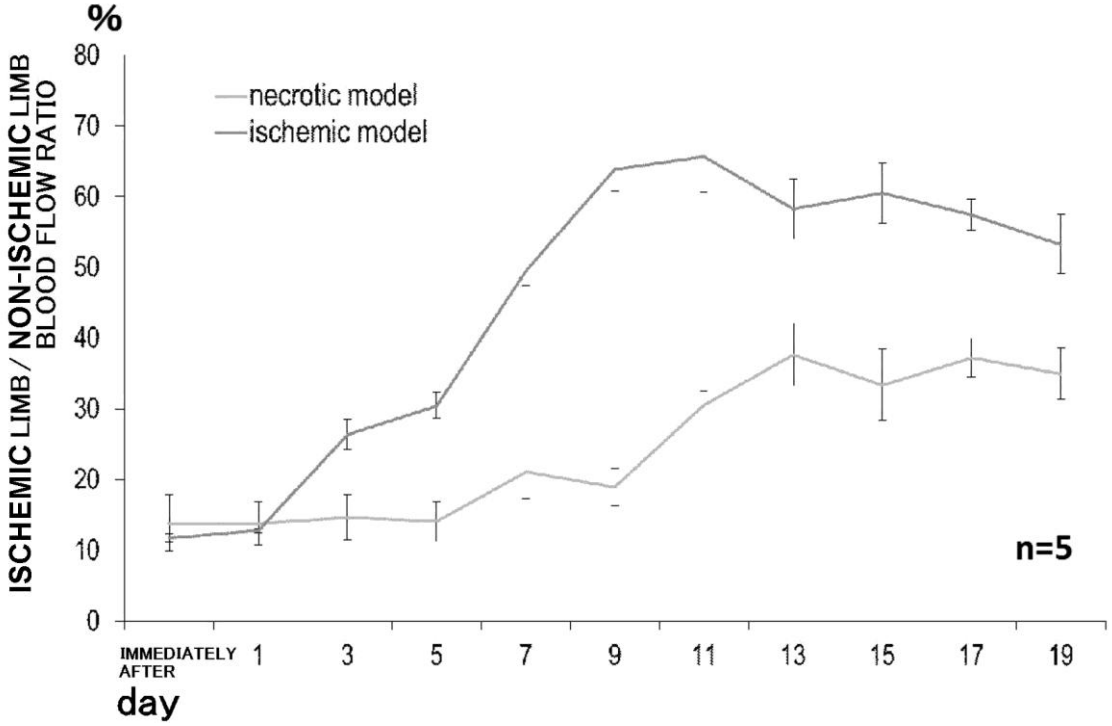
[Fig. 6]


NUMBER OF BACTERIA PRESENT IN ISCHEMIC LIMB
AFTER BACTERIA WERE SYSTEMICALLY ADMINISTERED
X 10^5 (INTRAVENOUSLY INJECTED)
NUMBER OF B. longum/g
NUMBER OF BACTERIA
BLOOD FLOW RATIO
ISCHEMIC LIMB / NON-ISCHEMIC LIMB
BLOOD FLOW RATIO
45
40
35
30
25
20
15
10
5
0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
n=5
day 1
day 2
day 3
day 4
day 5
day 7
day 10
day 14

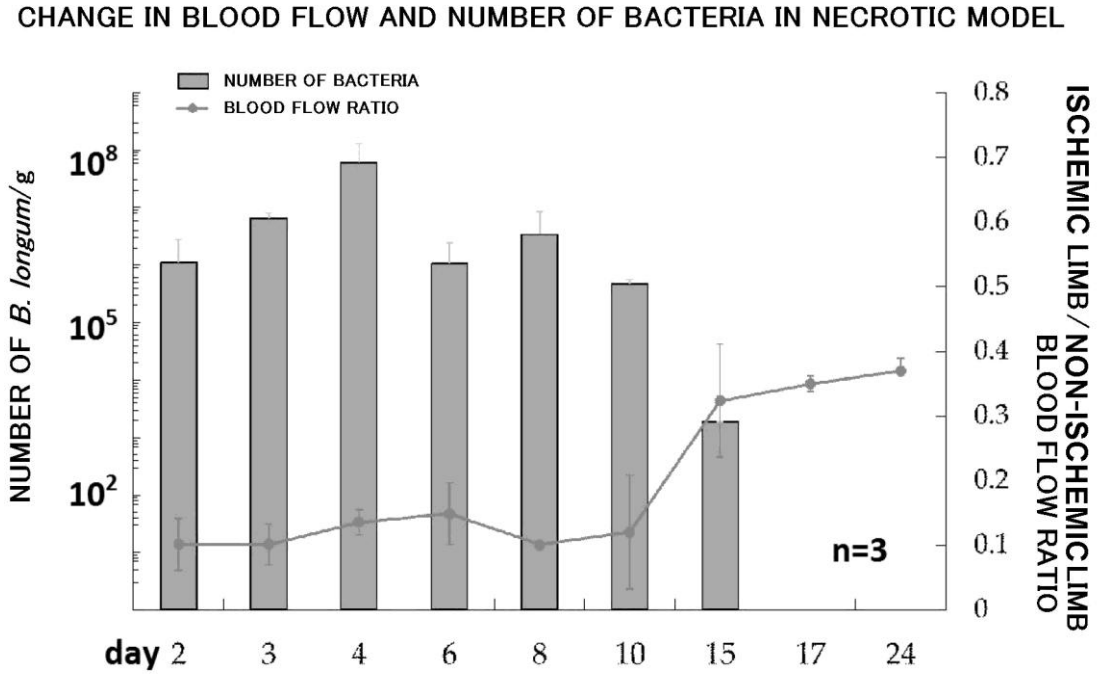
[Fig. 7]


GRAM STAINING
(4TH DAY AFTER B. longum WAS SYSTEMICALLY ADMINISTERED)
ISCHEMIC LIMB (x400)
ISCHEMIC LIMB (x1000)
NON-ISCHEMIC LIMB (x400)

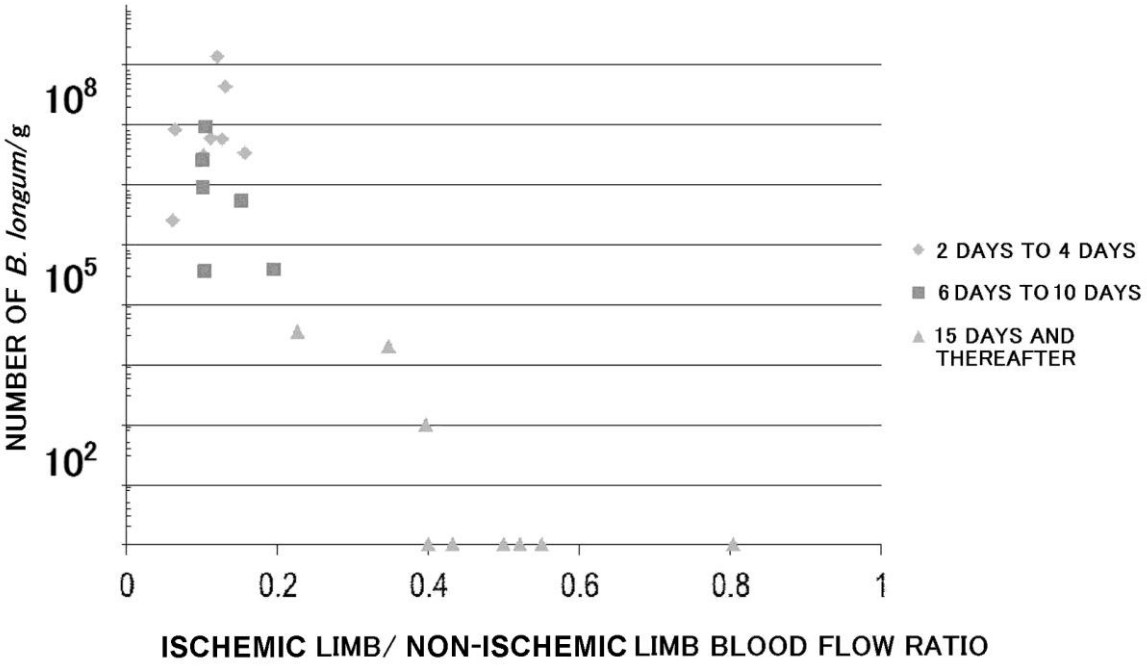
[Fig. 8]


%
ISCHEMIC LIMB / NON-ISCHEMIC LIMB BLOOD FLOW RATIO
necrotic model
ischemic model
n=5
0
10
20
30
40
50
60
70
80
IMMEDIATELY AFTER
1
3
5
7
9
11
13
15
17
19
day

[Fig. 9]

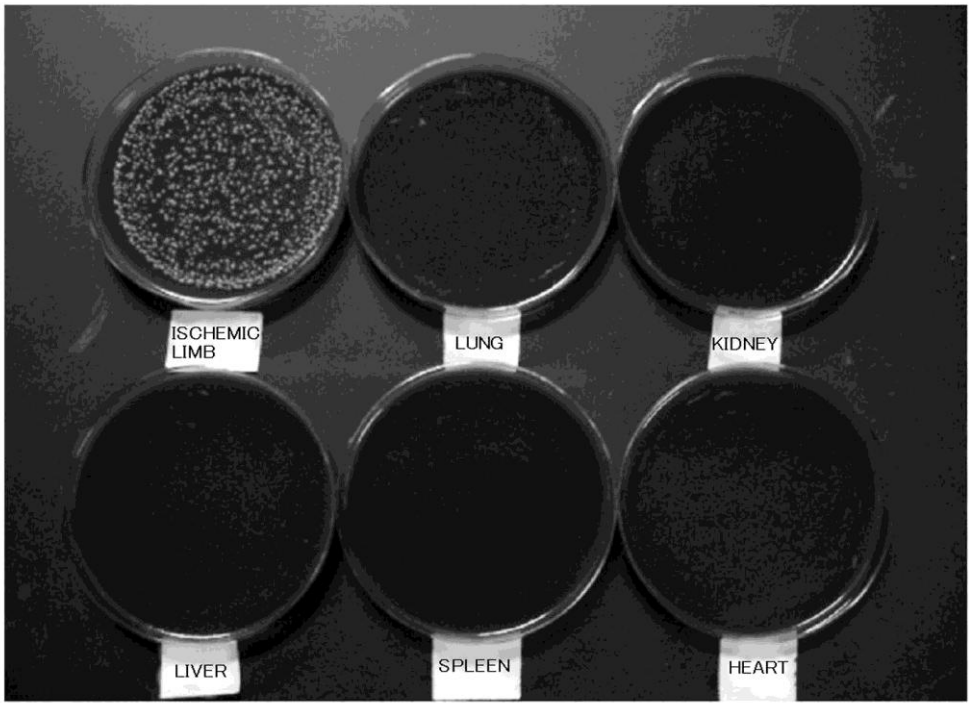

CHANGE IN BLOOD FLOW AND NUMBER OF BACTERIA IN NECROTIC MODEL
NUMBER OF BACTERIA
BLOOD FLOW RATIO
NUMBER OF B. longum/g
10^8
10^5
10^2
n=3
ISCHEMIC LIMB / NON-ISCHEMIC LIMB BLOOD FLOW RATIO
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
day 2
3
4
6
8
10
15
17
24

[Fig. 10]


NUMBER OF B. longum/g
10^8
10^5
10^2
2 DAYS TO 4 DAYS
6 DAYS TO 10 DAYS
15 DAYS AND THEREAFTER
0
0.2
0.4
0.6
0.8
1
ISCHEMIC LIMB/ NON-ISCHEMIC LIMB BLOOD FLOW RATIO

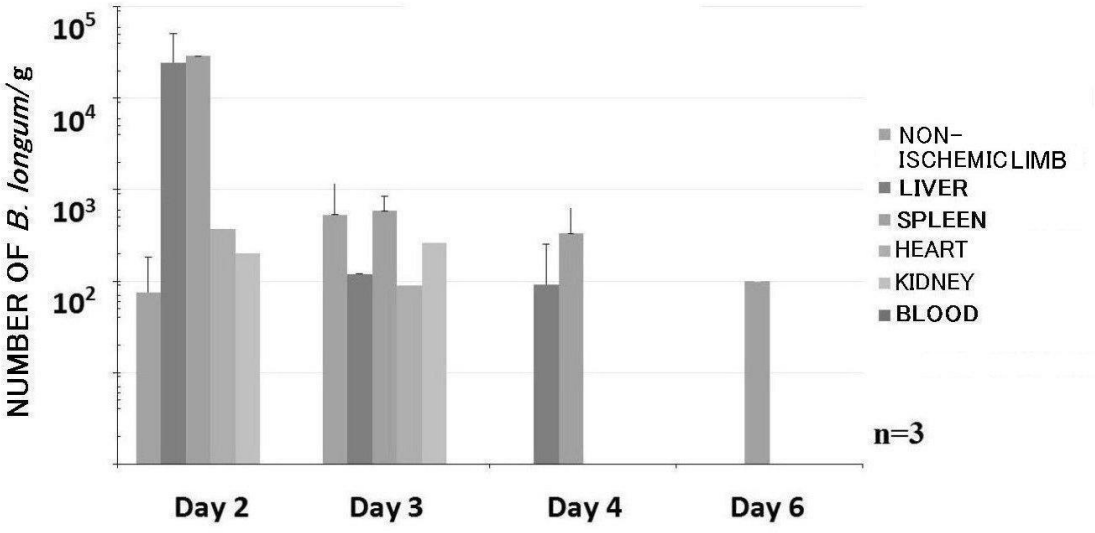
[Fig. 11]

ISCHEMIC MODEL 168 H AFTER SYSTEMIC ADMINISTRATION



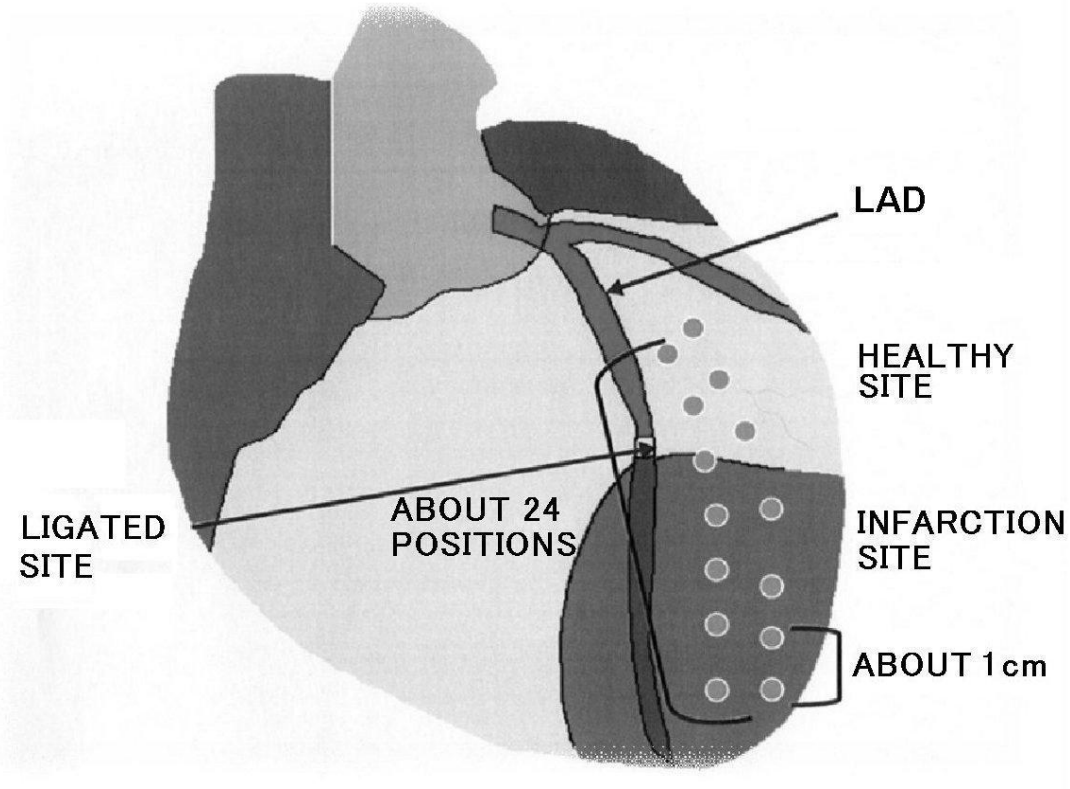
[Fig. 12]

NUMBER OF BACTERIA IN EACH ORGAN IN NECROTIC MODEL

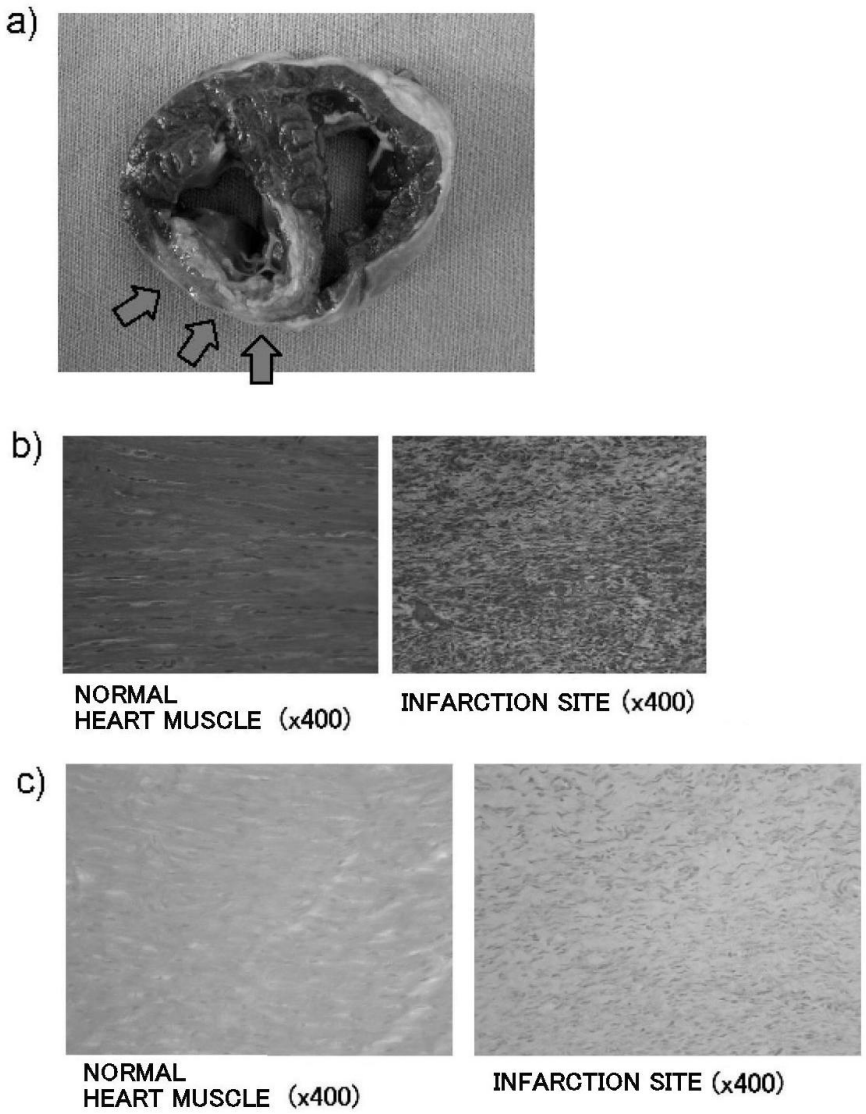


IN MANY CASES ACCOMPANYING LOWER LIMB NECROSIS, LUNG COULD NOT BE EXAMINED DUE TO CONTAMINATION.

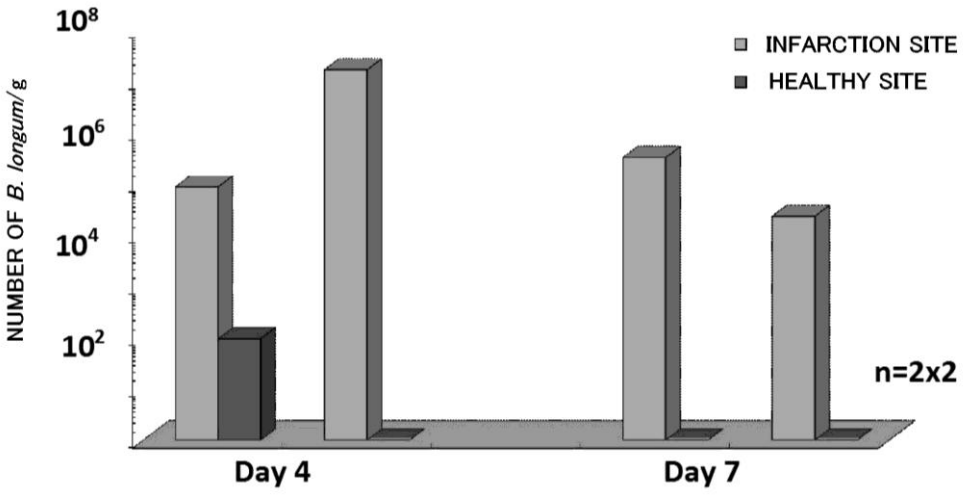
[Fig. 13]


LAD
HEALTHY SITE
LIGATED SITE
ABOUT 24 POSITIONS
INFARCTION SITE
ABOUT 1cm

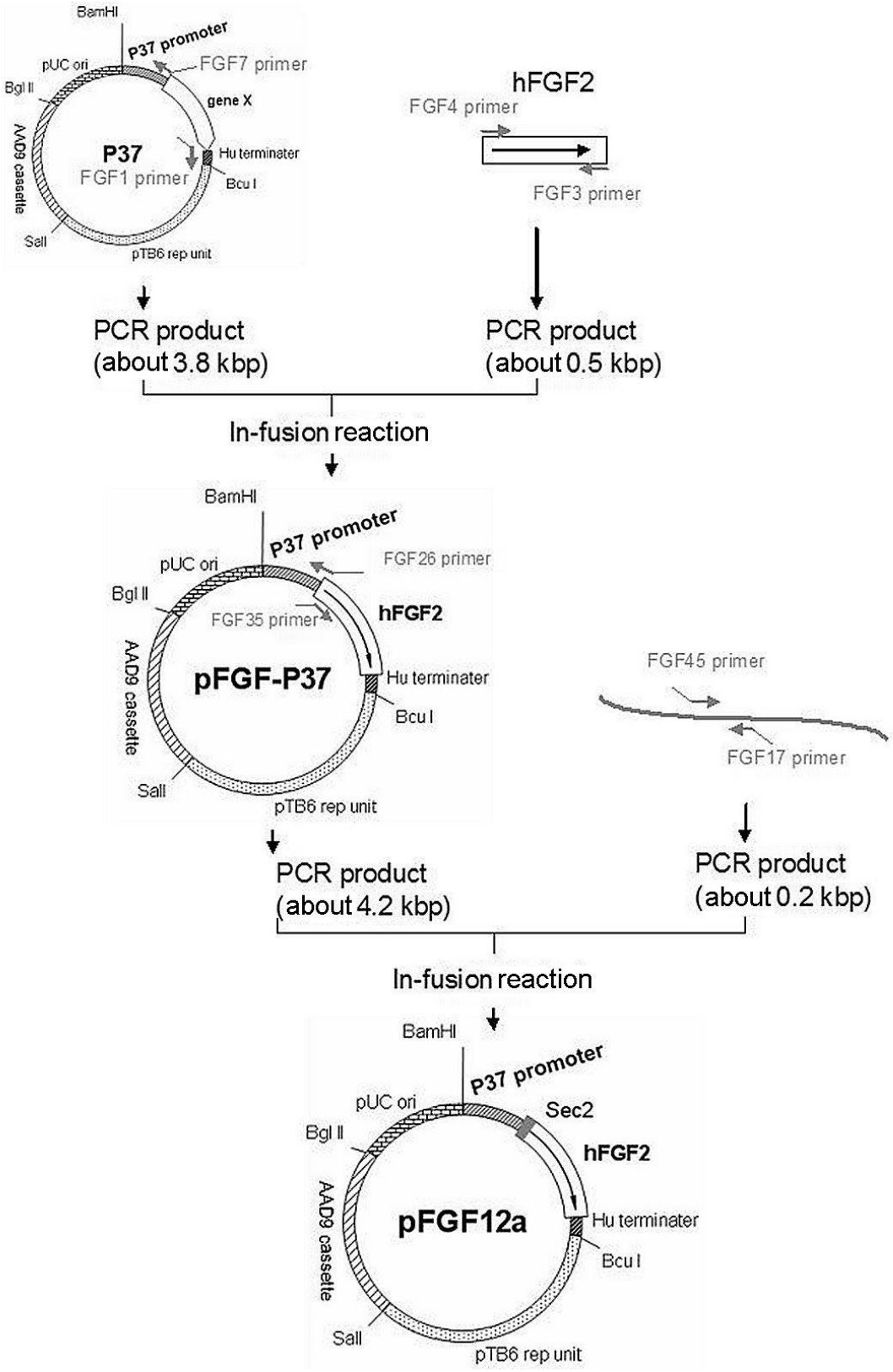
[Fig. 14]


a)
b)
NORMAL
HEART MUSCLE (x400)
INFARCTION SITE (x400)
c)
NORMAL
HEART MUSCLE (x400)
INFARCTION SITE (x400)

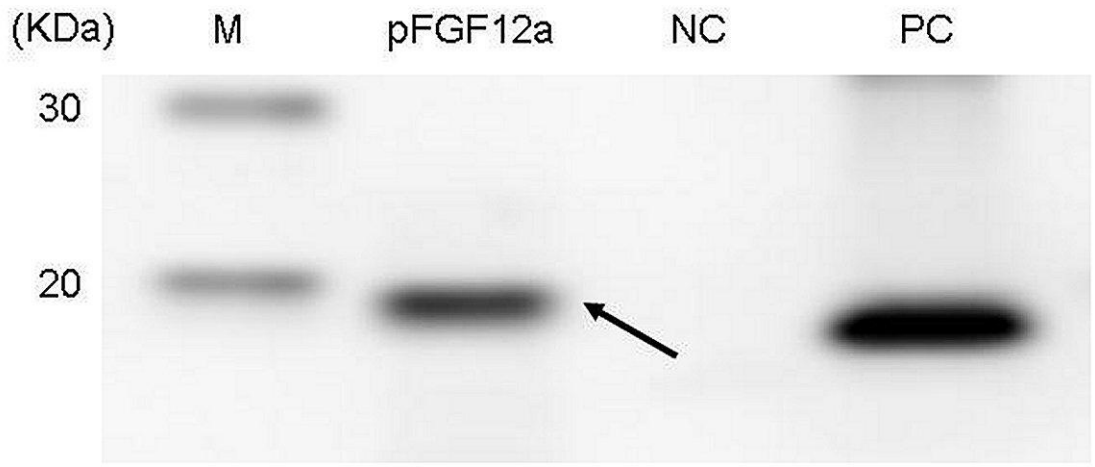
[Fig. 15]


NUMBER OF B. longum/g
10^8
10^6
10^4
10^2
INFARCTION SITE
HEALTHY SITE
n=2x2
Day 4
Day 7

[Fig. 16]

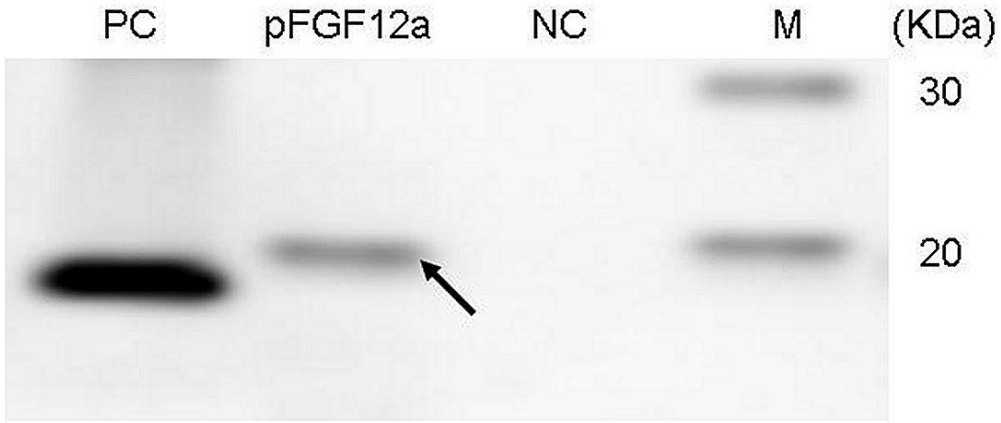

BamHI
P37 promoter
pUC ori
FGF7 primer
Bgl II
gene X
AAD9 cassette
P37
FGF1 primer
Hu terminater
Bcu I
SalI
pTB6 rep unit
hFGF2
FGF4 primer
FGF3 primer
PCR product
(about 3.8 kbp)
PCR product
(about 0.5 kbp)
In-fusion reaction
BamHI
P37 promoter
pUC ori
FGF26 primer
Bgl II
FGF35 primer
hFGF2
AAD9 cassette
pFGF-P37
Hu terminater
Bcu I
SalI
pTB6 rep unit
FGF45 primer
FGF17 primer
PCR product
(about 4.2 kbp)
PCR product
(about 0.2 kbp)
In-fusion reaction
BamHI
P37 promoter
pUC ori
Sec2
Bgl II
hFGF2
AAD9 cassette
pFGF12a
Hu terminater
Bcu I
SalI
pTB6 rep unit

[Fig. 17]



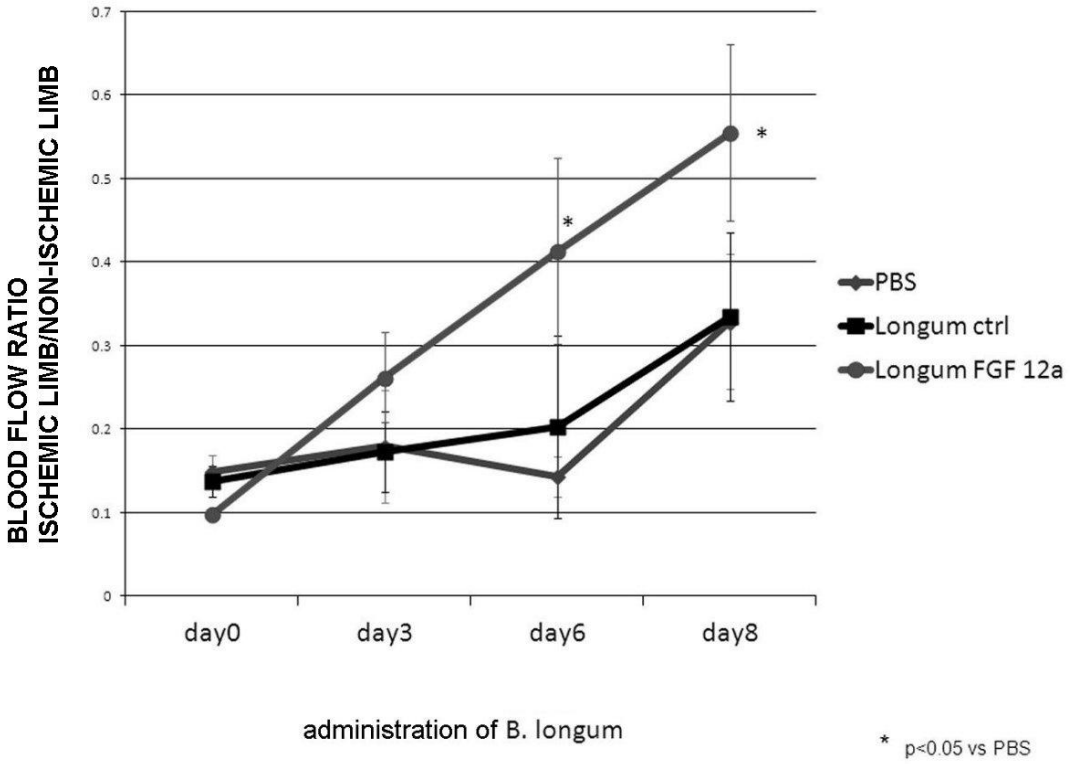
pFGF12a: *B. longum* 105A/pFGF12a
NC: *B. longum* 105A/pBEshuttle
PC: recombinant hFGF2 standard

[Fig. 18]

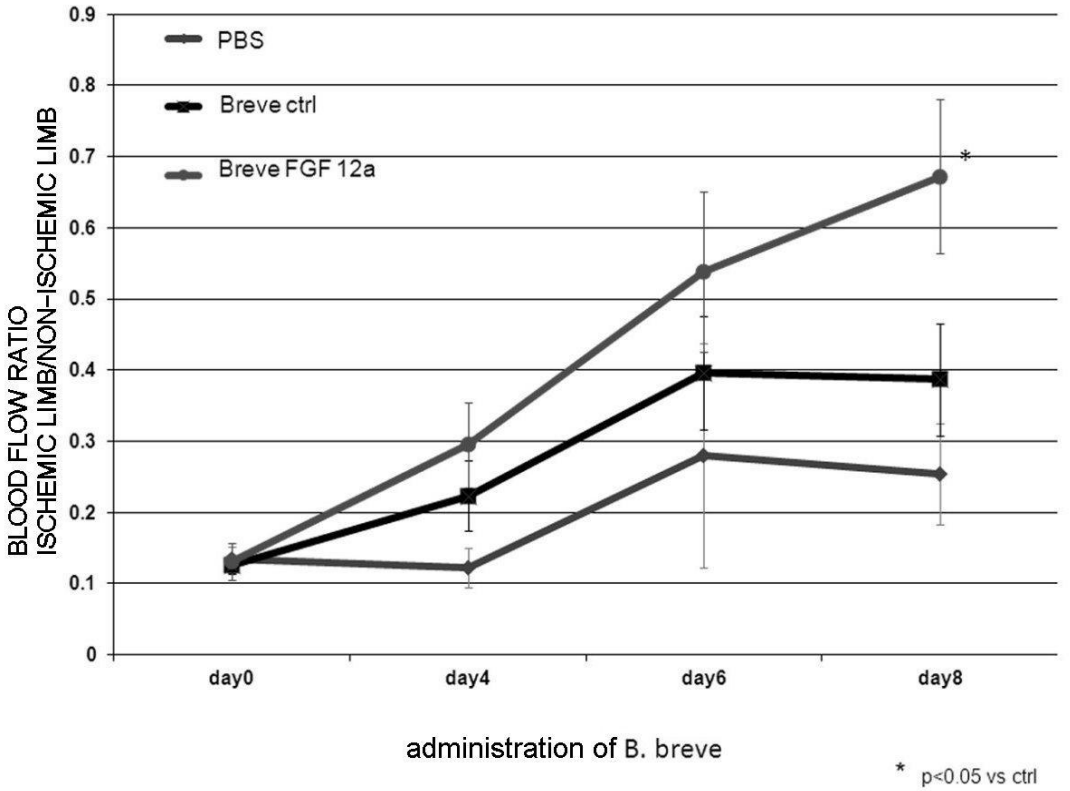


pFGF12a: *B. breve* JCM1192/pFGF12a
NC: *B. breve* JCM1192/pBEshuttle
PC: recombinant hFGF2 standard

[Fig. 19]


BLOOD FLOW RATIO
ISCHEMIC LIMB/NON-ISCHEMIC LIMB
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
*
*
PBS
Longum ctrl
Longum FGF 12a
day0
day3
day6
day8
administration of B. longum
* p<0.05 vs PBS

[Fig. 20]


BLOOD FLOW RATIO
ISCHEMIC LIMB/NON-ISCHEMIC LIMB
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
PBS
Breve ctrl
Breve FGF 12a
*
day0
day4
day6
day8
administration of B. breve
* p<0.05 vs ctrl