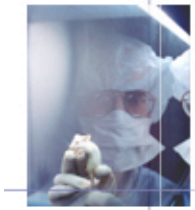
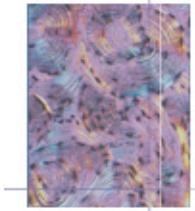
Non-Invasive and Minimally Invasive Techniques for Measuring Physiological Parameters in Laboratory Rodents





Kathleen A. Murray,DVM,MS,DACLAM
Sr. Director, Animal Program Management
Charles River Laboratories

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Physiological Parameters

- Body temperature
- Cardiovascular system
  - Blood pressure
  - Heart rate
  - Electrocardiogram
- Respiratory system
  - Saturated Oxygen level
  - Respiratory function
  - Oxygen consumption – metabolic rate
- Blood collection & Biomarkers

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Body Temperature

- Historic method – colonic or rectal temperature with probe
- More recent advances:
  - Infrared thermometer
  - Transponders – animal ID & temperature
  - Radiotelemetry

Temperature and Toxicology: An Integrative Comparative and Environmental Approach.

Christopher J. Gordon, Taylor and Francis CRC Press, 2005.

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Infrared Thermometer

- Murine Infectious disease models
  - (fungal, bacterial infections)
- Measured ear, back and/or abdomen
  - Calibrated using implantable microchip
- Identified temperature point at which animals rarely recovered
  - 33.3°C ; 30°C
- Advantage – cost and ease of use

Warn, P.A. et.al Infrared Body Temperature Measurement of Mice as an Early Predictor of Death in Experimental Fungal Infection. Laboratory Animals (37)2: 126-131, 2003.

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Implantable Microchips

- Electronic Animal Monitoring System
  - Both Animal ID and Temperature
    - RFID
- Subcutaneous implant
  - Intraperitoneal implant?
- Advantage:
  - Cost – more than IR, less than telemetry
  - Ease of use
  - Animal identification a bonus

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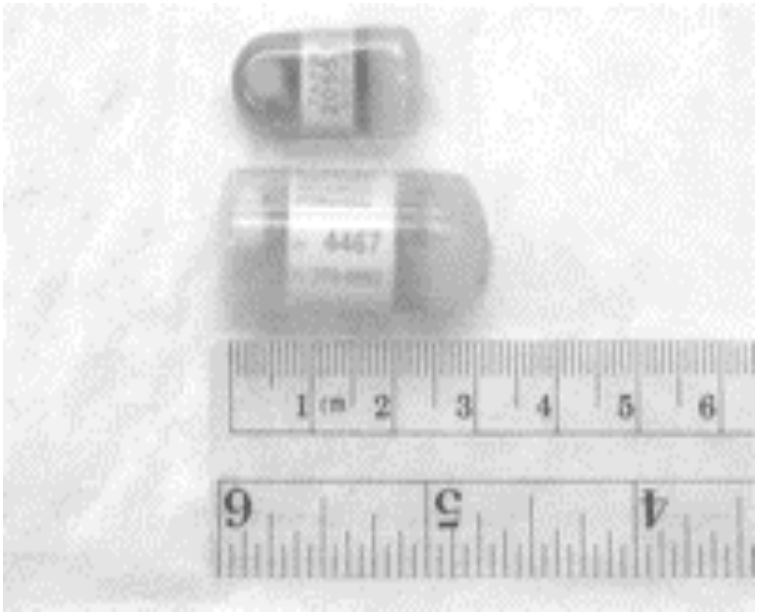
Radiotelemetry – Body Temperature

- Much published literature
- Advantage:
  - “gold standard”
  - Continuous monitoring
- Disadvantage:
  - Cost
  - Preparation – surgery and recovery time



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Cardiovascular System: Blood Pressure & Heart Rate

- Historical methods – anesthetized animals with surgical procedures for direct access
- More recent methods:
  - Tail cuff – indirect measurement
  - Radiotelemetry

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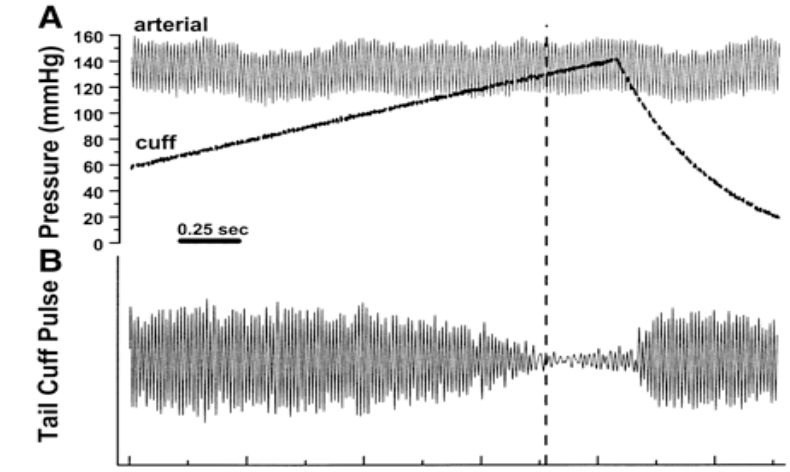
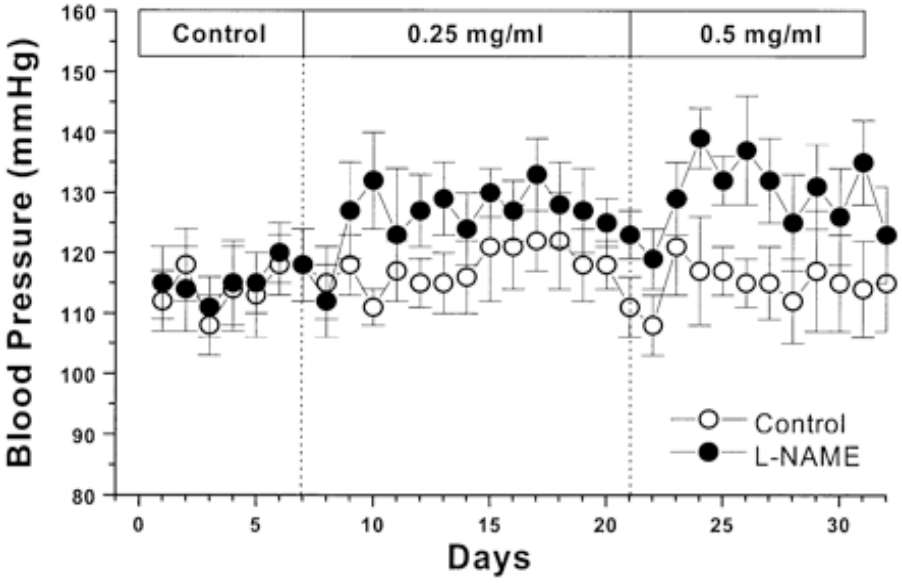
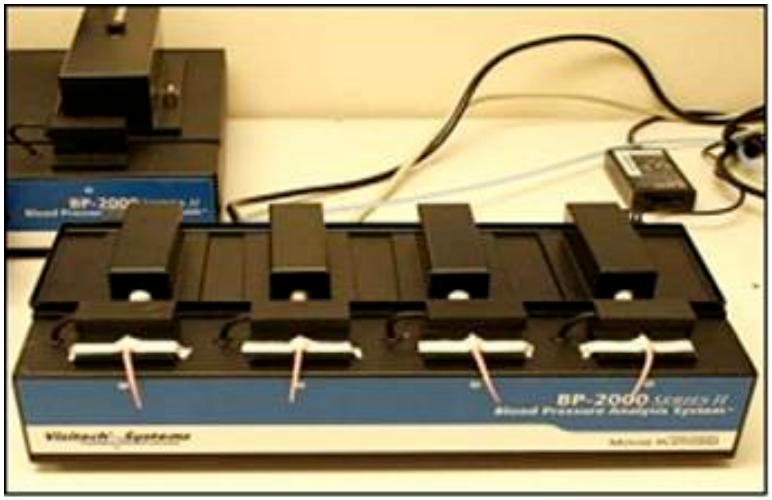
Blood Pressure – Tail Cuff







Lorenz, John N., A Practical Guide to Evaluating Cardiovascular, Renal and Pulmonary Function in Mice, Am J Physiol Regulatory Integrative Comp Physiol 282:R1565-R1582, 2002

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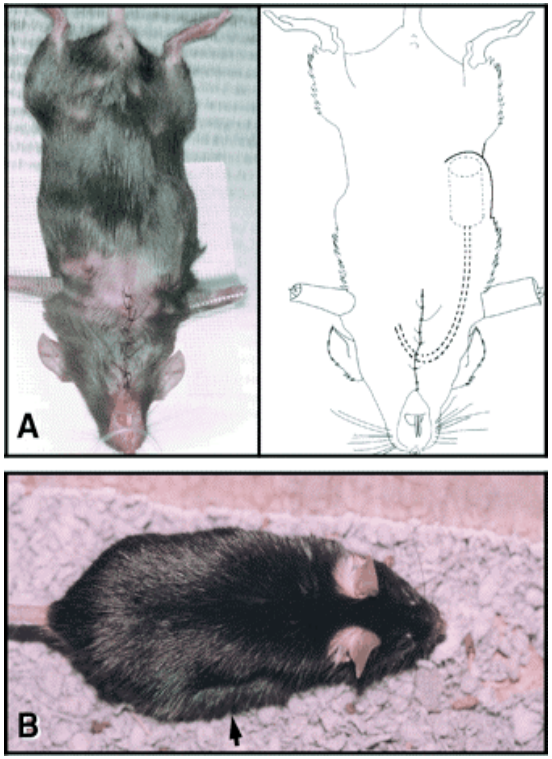
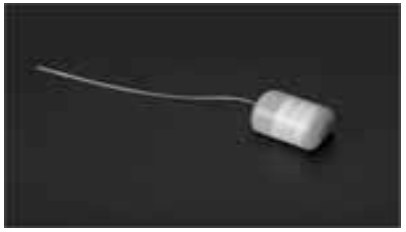
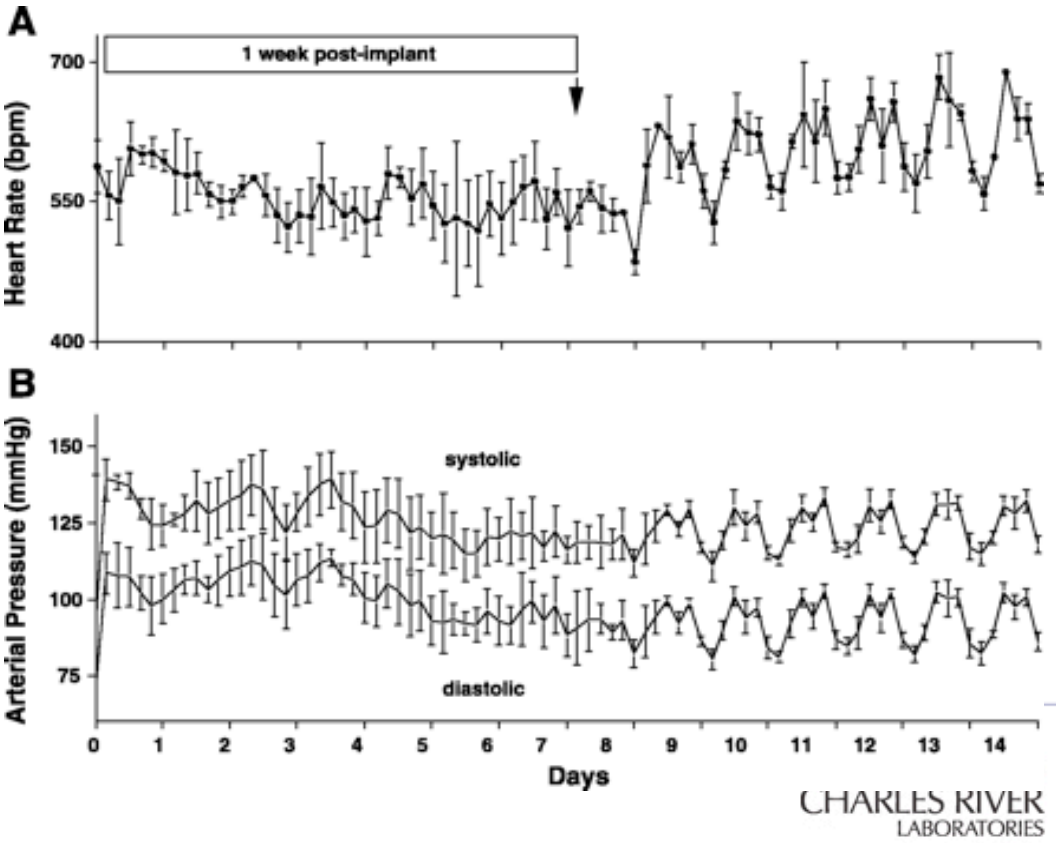
Blood Pressure – Radiotelemetry







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Whitesall, S.E. et al, Comparison of Simultaneous Measurement of Mouse Systolic Arterial Blood Pressure by Radiotelemetry and Tail-Cuff Methods. Am J Physiol Heart Circ Physiol 286: H2408-H2415, 2004

Blood Pressure Measurement

Tail Cuff

- Indirect measurement
- Cost effective
- Acclimation needed but not surgery
- High Throughput
- Restraint & heat required = stress
- Fixed time point
- Less reliable

Telemetry

- Direct measurement
- Expensive
- Requires surgery & recovery time
- Non-restrained
- Continuous reading, day & night
- Single housing
- More reliable

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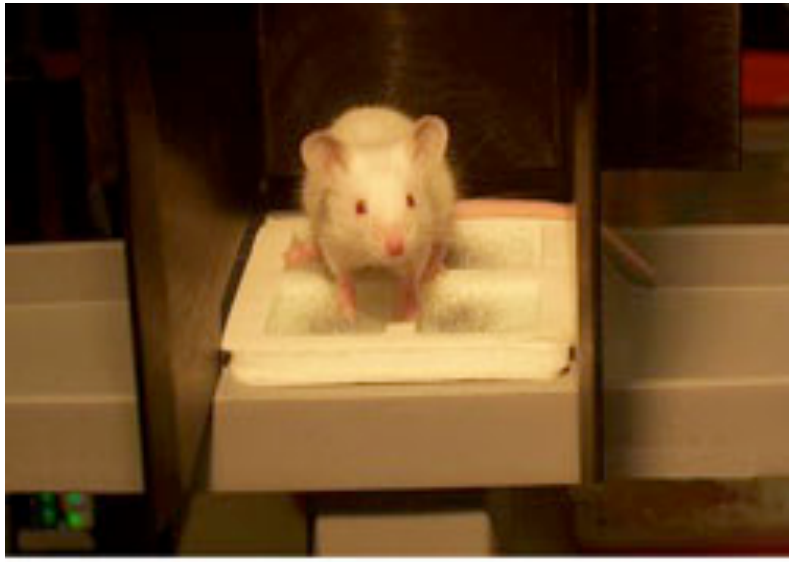
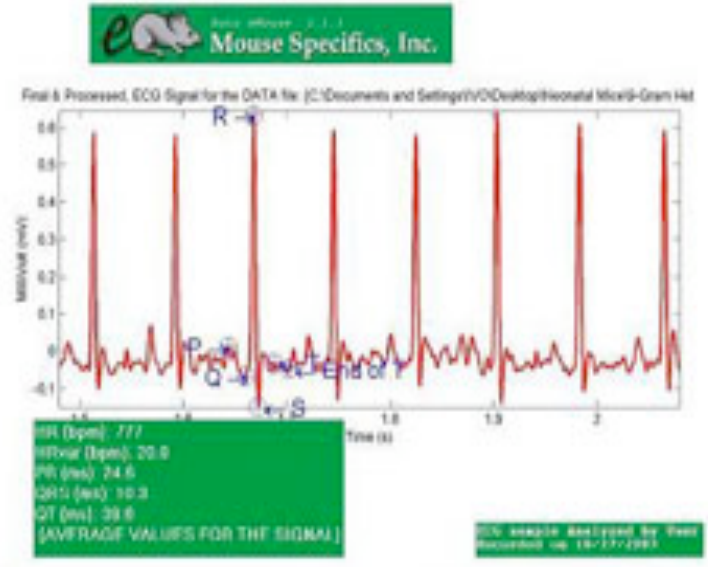
Cardiovascular System– Electrocardiogram & Heart Rate

- Historical methods – anesthetized animals with traditional ECG leads
- More recent methods:
  - Mouse Specifics
    - Concious mouse, foot contact with leads





Respiratory System: Oxygen Saturation (SaO_2)

- Historical methods – Arterial Blood Gas
- More recent methods:
  - Pulse oximetry
    - Base of tail, thigh, foot

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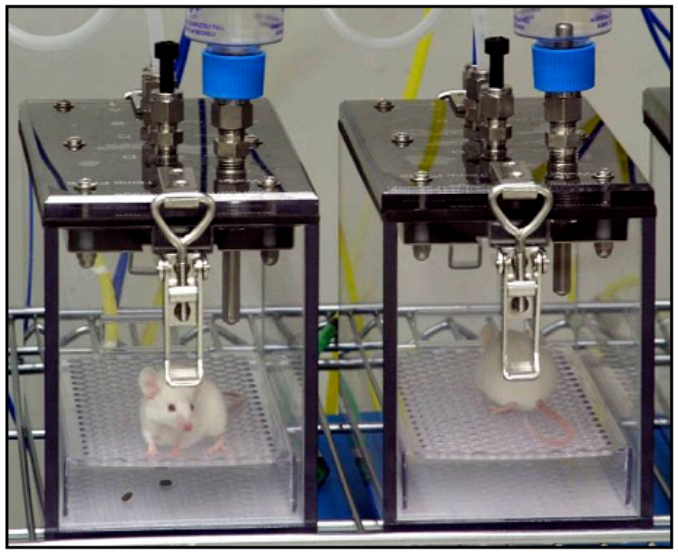
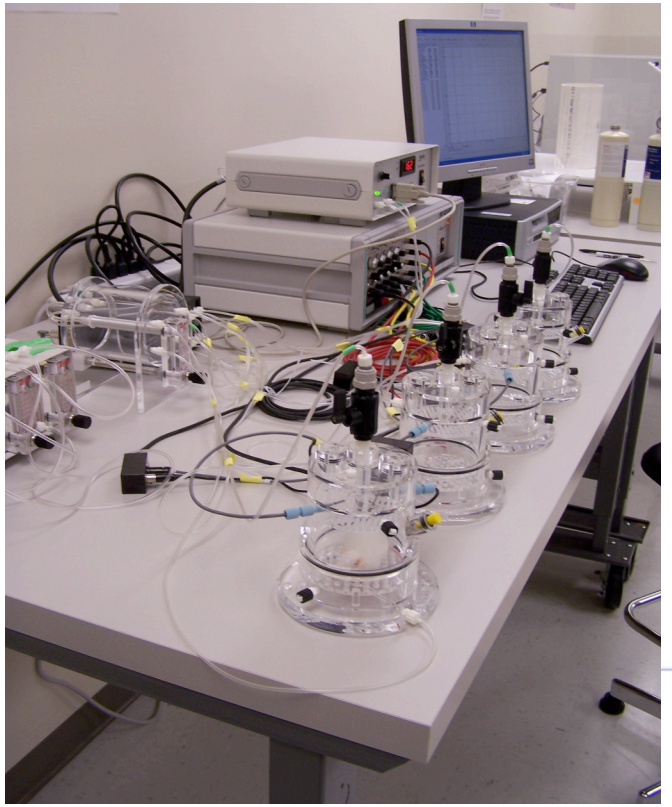
Respiratory System: Respiratory Function

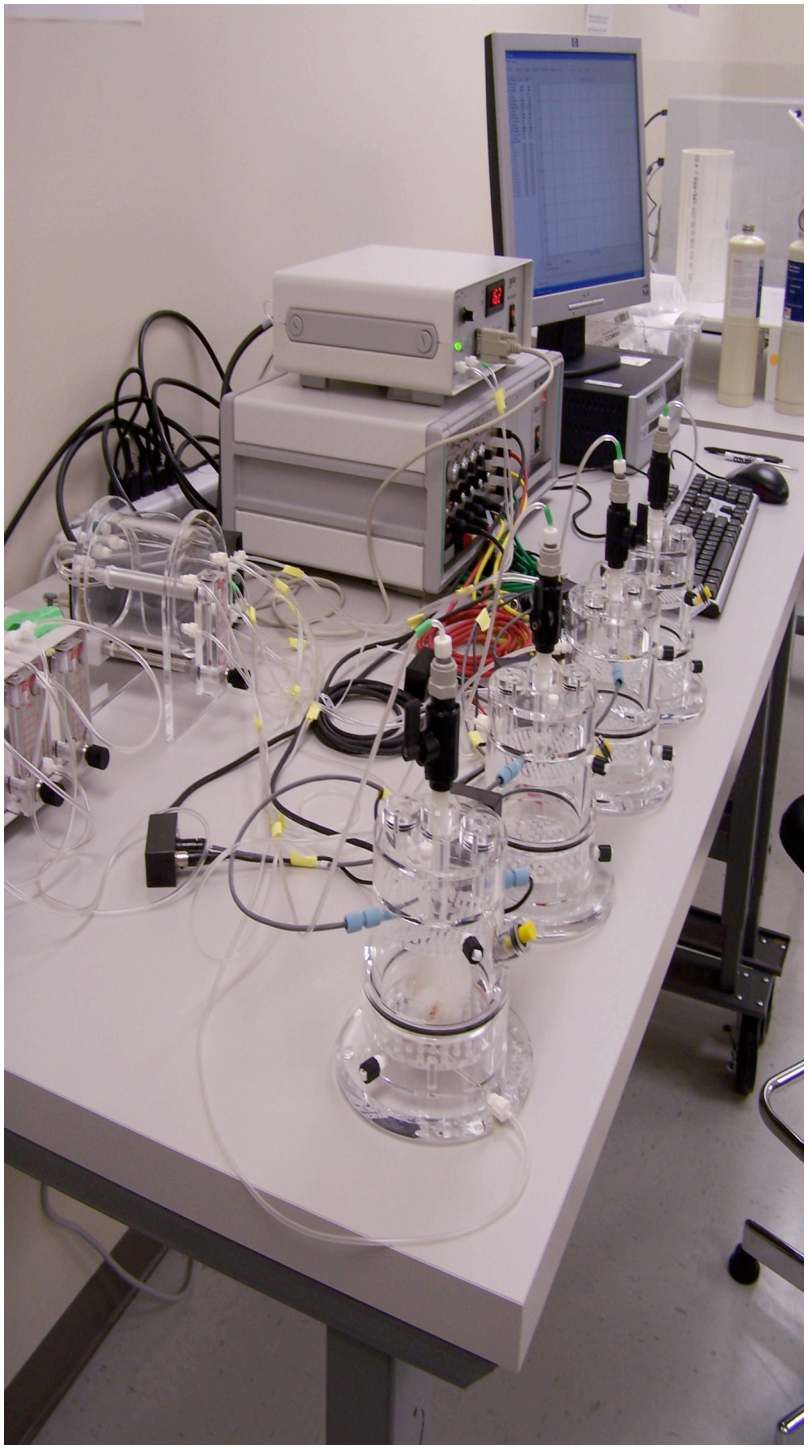
- Historical methods – intubated, anesthetized
- More recent methods:
  - Whole body Plethysmograph - conscious & unrestrained
  - Inspiratory & expiratory time, peak inspiratory and expiratory flow, tidal volume, relaxation time, minute volume, frequency of breathing rate, end-inspiratory and end-expiratory pause & enhanced pause





Oxygen Consumption & Metabolic Rate

- Respiratory Gas Analyzer
  - VO2
  - VCO2
  - Respiratory Quotient (RQ)
  - Metabolic Rate



CLAMS – Comprehensive Laboratory Animal Monitoring System (Columbus Instruments)

Blood Sample Collection

- Orbital Sinus
- Jugular
- Saphenous
- Submandibular

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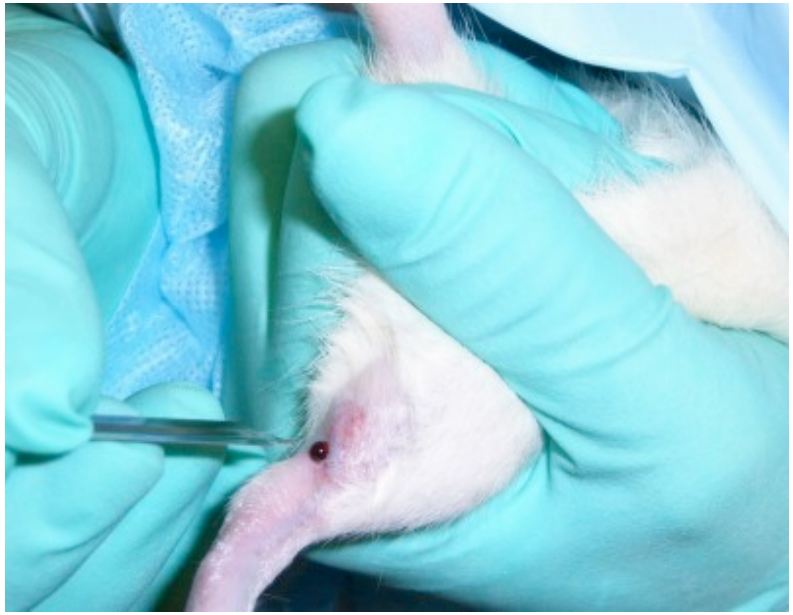
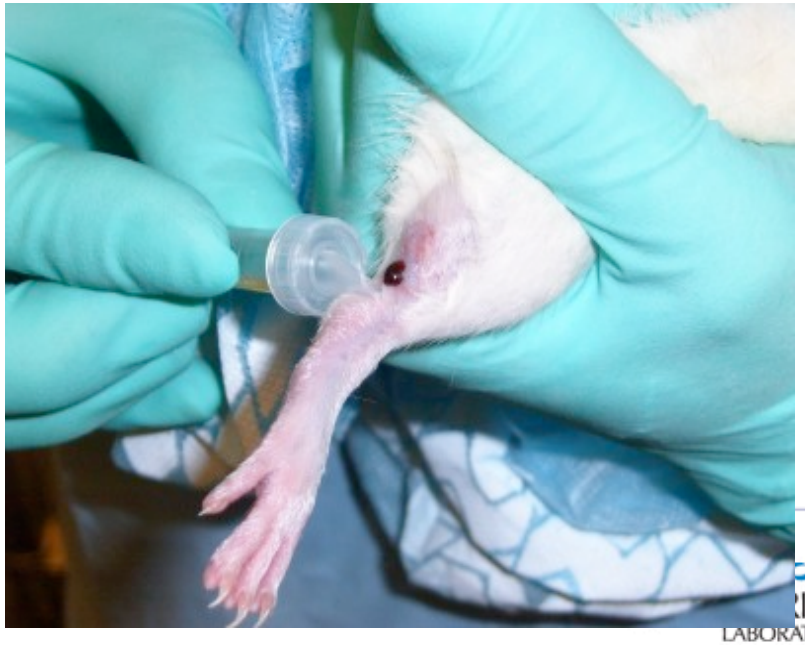
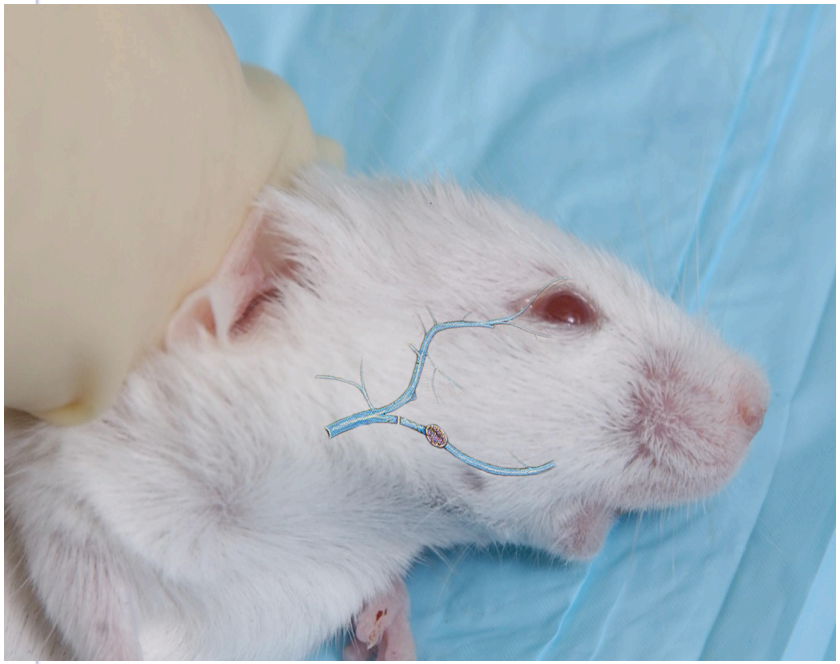
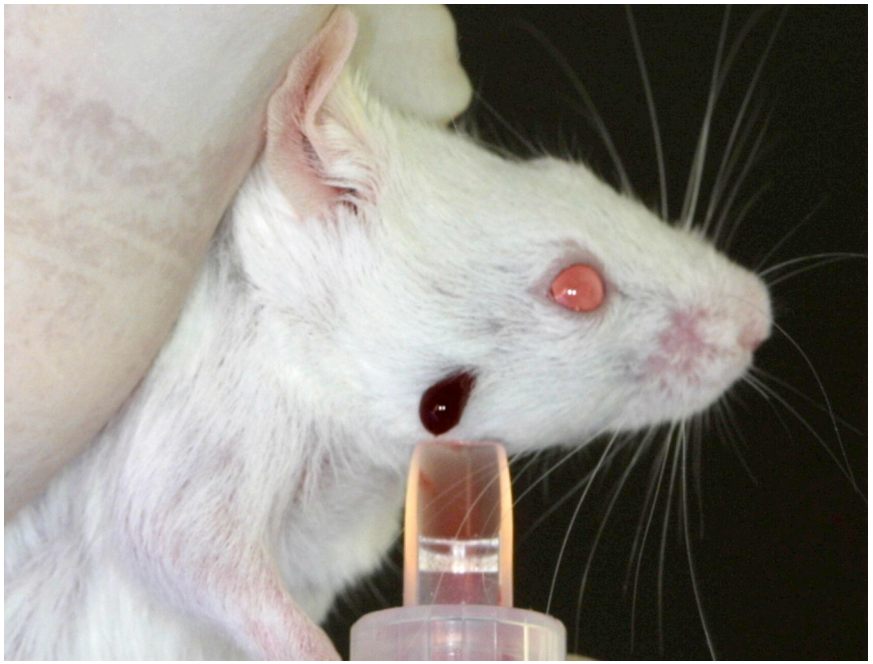
Saphenous





Submandibular





- www.medipoint.com

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Biomarkers

- Historical methods – Traditional Assays
- More recent methods:
  - Multi-Analyte Profile (Rules Based Medicine)
    - 60 plus analytes from 50 microliter plasma

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RodentMap™ | Antigen

Version 2.0

1. Apolipoprotein A1
2. C-Reactive Protein
3. CD40
4. CD40 Ligand
5. Endothelin-1
6. Eotaxin
7. EGF
8. Factor VII
9. Fibrinogen
10. FGF-basic
11. FGF-9
12. GCP-2
13. GM-CSF
14. GST-alpha
15. Haptoglobin
16. Immunoglobulin A
17. Inducible Protein-10
18. Interferon-gamma
19. Interleukin-1 alpha
20. Interleukin-1 beta
21. Interleukin-2
22. Interleukin-3
23. Interleukin-4
24. Interleukin-5
25. Interleukin-6
26. Interleukin-7
27. Interleukin-10
28. Interleukin-11
29. Interleukin-12p70
30. Interleukin-17
31. KC/GRO alpha
32. LIF
33. Lymphotactin
34. M-CSF
35. MDC
36. MIP-1 alpha
37. MIP-1 beta
38. MIP-1 gamma
39. MIP-2
40. MIP-3 beta
41. MMP-9
42. MCP-1
43. MCP-3
44. MCP-5
45. Myeloperoxidase
46. Myoglobin
47. Oncostatin M
48. RANTES
49. Serum Amyloid P
50. SGOT
51. Stem Cell Factor
52. Thrombopoietin
53. TIMP 1
54. Tissue Factor
55. TNF-alpha
56. VCAM-1
57. VEGF
58. von Willebrand Factor

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RodentMap™ | Autoimmune

Version 2.0

1. Beta-2 Glycoprotein Ab
2. Insulin Ab
3. Jo-1 Ab
4. Mitochondrial Ab
5. Myeloperoxidase Ab
6. PCNA Ab
7. Proteinase 3 Ab
8. RNP Ab
9. Ribosomal P Ab
10. Scleroderma-70 Ab
11. Smith Ab
12. SSA Ab
13. SSB Ab13

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Rat Kidney MAP

Version 1.0

1. Beta-2 Microglobulin
2. Calbindin
3. Clusterin
4. Cystatin C
5. Epidermal Growth Factor
6. Glutathione S-Transferase-alpha (GST-alpha)
7. Glutathione S-Transferase Yb1 (GST Yb1)
8. Kidney Injury Molecule-1 (KIM-1)
9. Neutrophil Gelatinase-Associated Lipocalin (NGAL)
10. Osteopontin
11. Tissue Inhibitor of Metalloproteinase-1 (TIMP-1)
12. Vascular Endothelial Growth Factor (VEGF)

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