Health and Metabolism Research Core

Center for Transformative Research in Metabolism

Report on current status, funding, and growth

March 2024

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Sustaining the Health and Metabolism Research Core is an investment in biomedicine and One Health that will return new research dollars to UAF

Summary

The UAF Molecular Imaging Facility (MIF), now within the Health and Metabolism Research (HaMR) Core, provides access to state-of-the-art magnetic resonance (MR) techniques for the UA system. It has been recognized by the Institute of Translational Health Sciences for its services and capacity in biomedicine. The ITHS promotes and supports translational research collaboration between clinicians, communities, and investigators across the five-state Washington, Wyoming, Alaska, Montana, and Idaho (WWAMI) region, and has recognized the MIF as an integral part of that network. Resources and expertise provided by this network are expected to increase opportunities for human subjects research and research proposals requiring use of the MIF (Fig. 1).



Fig. 1 The Northwest Participant and Clinical Interactions Network: Increasing opportunities for patients to participate in research across the Northwestern United States. From Baldwin et al., 2017 Journal of Clinical and Translational Science Apr;1(2):94-100.

Justification of Need

The long-term goal is to sustain the HaMR Core through a business model implemented as a recharge center providing access to a variety of services including imaging for human and animal subjects research and veterinary diagnostics. However, the business model requires continued subsidy. With this model, we will update and replace equipment from depreciation funds. A significant amount of current use is subsidized, but subsidy contributed to establishment of safety, legal and experimental protocols, and acquisition of preliminary data to establish feasibility of approach for proposals.

Brief History of Magnetic Resonance Imaging at UAF

UAF renewed their commitment to Life Sciences research through construction of the new Margaret Murie Life Sciences Building July 2013. The building was designed with a dedicated magnetic resonance (MR) imaging suite. Spearheaded by former UAF Chancellor, Brian Rogers, UAF and the Fairbanks Memorial Hospital (FMH) Foundation partnered to make a 1.5 Tesla MR scanner available to UAF. This instrument is housed within the Institute of Arctic Biology (IAB) Molecular Imaging Facility, managed by Dr. Carl Murphy.

The MIF imaging suite has the only research-dedicated MRI within the UA system and the state of Alaska.

The MIF supports unique Arctic animal subjects and Alaskan human subjects research unavailable elsewhere in the U.S.



Development of the Molecular Imaging Facility/Health and Metabolism Research Core

- **2011** Bruker 600 MHz Nuclear Magnetic Resonance (NMR) instrument arrived at UAF and along with the 300 MHz Varian NMR is managed by Dr. Carl Murphy
- **2014** The Molecular Imaging Facility is initiated to incorporate the MRI with the NMR instruments

MRI Installation and start-up (May 2014)

Risk and safety protocols developed and filed

Scheduled institution-wide safety trainings

2015 Animal subject research and veterinary diagnostic protocols approved

First veterinary diagnostic image acquired (May 2015)

Extended IACUC discussion to determine an appropriate process and acquisition of required anesthesia monitoring equipment.

First animal subjects research image acquired (September 2015)

2016 Human subjects' facility liability and insurance needs met - MRI facility was inspected and shown to meet the standards set by the American College of Radiology

First human volunteers scanned during applications training from Toshiba (July 2016)

2017 The Dual-energy X-ray Absorptiometry instrument is moved to the MIF Imaging Suite from CANHR

First human subjects research scanned (April 2017)

Intrahepatic lipid analyzed from spectra acquired with MRI magnetic resonance spectroscopy (MRS) (*Nov 2017*).

- **2019** The MIF became a recharge center as part of the Health and Metabolism Research (HaMR) Core within the new Center for Translational Research in Metabolism (TRiM). The HaMR Core also included the Animal Instrumentation Facility.
- **2022** The MIF recharge center was expanded to the HaMR Core recharge center. The HaMR core gained the Microscopy Facility and the Animal Support facility.
- 2024 The HaMR Core expands to include Cell Culture Consultation and other smaller services.

Overview of Instrumentation at the UAF-TRiM HaMR Core

https://trimalaska.com/health-metabolism/

Molecular Imaging Facility – NMR Suite - Reichardt 136

Varian Mercury 300 MHz NMR

Purchased in 1998 with NSF-ILI

Broadband probe, tunable to most nuclei including hydrogen, carbon, fluorine, phosphorus, nitrogen, and vanadium. It is capable of one and two-dimensional NMR experiments.

Bruker AV-600MHz NMR

Purchased in 2011 with DOD grant (PI-Barnes, \$850,000), installed March 2012 and supported Dr. Murphy FY11-FY14

This system includes both a broadband liquids probe that can tune to most nuclei, an HR-MAS probe designed for proton and carbon NMR on tissues and other semi-solids, and a CP-MAS solid state probe. It has a 60-position sample changer that allows for complete automation.



Molecular Imaging Facility – Imaging Suite - Murie 015

Toshiba Excelart/Vantage 1.5 T MRI

Relocated to UAF in FY14 with \$1.5M in capital funds; Operated with a one-time investment of \$300k FY14 - FY18 by Chancellor Rogers. Allocation was reapproved by Chancellors Powers and Thomas). Alaska INBRE contributed approximately \$90k / yr for FY16 and FY17 to support service contracts. The COBRE grant will took over the service contract in FY20.

The MRI is equipped with a short 1.4m magnet with a 65.5cm aperture, large enough to accommodate black bear, muskox and large dogs. Quiet pianissimo technology minimizes stress on the animals. It acquires images of high homogeneity (< 2ppm, 50cm FOV) and is capable of multiplanar imaging, direct visualization of arterial anatomy with quantification of blood flow and hydrogen MRS.



GE Lunar iDXA

Purchased with COBRE funds (PI-Boyer, \$80,000). Moved from CANHR to IAB in FY17

The Dual-energy X-ray Absorptiometry (DXA) instrument can measure lean body mass, adipose tissue, and bone mass as well as bone mineral density. The GE iDXA is compatible with the variable composition phantom that will be sent to all data collection sites by the Tufts University Body Composition analysis Center.



Animal Instrumentation

Small Animal Respirometry Systems

Three fully automated systems

Each system includes O₂, CO₂, and temperature monitoring.



Large Animal Respirometry Systems

Two fully automated system

These systems are similar to the small animal systems, but are adapted to be compatible with the metabolism of larger animals (bears).



Implantable Telemetry Systems

Two DSI Physiotel systems

These systems are capable of measuring pressure (arterial, left ventricular, ocular, bladder, and intra-cranial), biopotentials (ECG, EMG, EEG, EOG), or core body temperature from up to 16 individuals, when paired with the appropriate implanted transmitters



Microscopy

NX50 Cryostar Cryostat

Designed for the sectioning of frozen tissues Cools down to -25°C to keep samples frozen

Olympus Fluoview FV10i Confocal

Self-contained fully motorized laser scanning confocal microscope specially designed for livecell imaging

supports multi-area and multi-color imaging, enabling efficient and easy data acquisition

Nikon Eclipse Microscopes

80i (top) and TE2000-U (bottom)

Both scopes can be used for high sensitivity florescence imaging, differential interference contrast imaging, and phase contrast imaging and polarization

Both systems have a semi motorized system controlled by Nikon elements software for sample positioning

TE2000-U is an inverted style allowing for increased flexibility for tissue cultures or live cell imaging







Animal Support

Blood Gas Analyzer

Portable for easy switching between surgery rooms

Can measure pH, pCO_2 , pO_2 , glucose, lactate, electrolytes, and oximetry in blood samples as small as 65 uL

Pulse Oximeter

Measure heart rate and blood oxygen saturation of subject

Two meters available

Surgical Scope

microCapStar End-Tidal CO₂ Analyzer

Assists with surgery on small subjects.

an ideal tool for surgical training

Measures expired CO₂ and respiratory rate as an aide to anesthesia monitoring

The Observer view and built in camera make this

Designed for smaller animals such as mice, rats, and squirrels









Services Provided by the Health and Metabolism Research Core

300MHz NMR

- Structural analysis using H/C/P/F nuclei
- Reaction product verification
- Full range of standard NMR experiments adaptable to most applications

600MHz NMR

Quantitative NMR

- Metabolomics quantitative analysis of metabolites in plasma and tissues
- Drug stability quantitative analysis of novel formulations and mixtures at prescribed intervals.
- Structural analysis with more nuclei available
- Determination of diffusion coefficients
- Full range of quantitative NMR adaptable to most applications

iDXA

- Body composition analysis
- Bone Density
- Fat mass
- Lean tissue mass

MRI

General – Available for human and animal subject research

Full range of standard experiments available including

- T1,T2, and proton density weighted imaging
- 3D isometric imaging
- ECG, respiratory, and peripheral gating options available
- MR Spectroscopy available down to 1 cm3 voxel
- Semi-Quantitative intrahepatic lipid analysis

- ECG controlled Cardiac imaging
- Some functional *MRI capability*

MRI-veterinary diagnostics

 Licensed veterinarian and a veterinary technician oversee procedures. A contracted radiologist interprets scans.

Animal Instrumentation

- Small animal respirometry
- Large animal respirometry
- Implantable telemetry systems for internal monitoring during experiments

Animal Support

- Surgical Implantation of telemetry devices
- Cannulation of femoral artery or vein
- Student training as surgical assistants and surgeons

Microscopy

- Confocal imaging
- Nikon Eclipse 80i Fluorescence Microscope
- Nikon Eclipse TE200-U
- NX50 Cryostar Cryostat for tissue sectioning

Calibration Services

- Pipets
- Analytical Balances
- pH Meters

Cell Culture

- Consultation
- Support
- Training

Current and proposed major research faculty users of the UAF HaMR

- Kelly Drew PhD, Professor, Department of Chemistry and Biochemistry, IAB
- Lawrence Duffy PhD, Professor, Department of Chemistry and Biochemistry, CDR
- Kriya Dunlap PhD, Assistant Professor, Department of Chemistry and Biochemistry, CDR
- Vadim Fedorov PhD, Research Associate Professor, IAB
- Anya Goropashnaya PhD, Research Assistant Professor, IAB
- Thomas Green PhD, Professor Emeritus, Department of Chemistry and Biochemistry, IAB
- William Howard PhD, Associate Professor, Department of Chemistry and Biochemistry, CDR
- Sarah Ellen Johnston PhD, Assistant Professor, Department of Chemistry and Biochemistry, CDR
- John Keller, PhD, Professor Emeritus, Department of Chemistry and Biochemistry, CNSM
- Greg Pietsch, PhD, Assistant Professor, Department of Veterinary Medicine, CNSM
- Brian Rasley PhD, Associate Professor of Chemistry, CDR
- Oivind Tøien PhD, Research Assistant Professor, IAB
- Pat Tomco PhD, Assistant Professor, Department of Chemistry, UAA
- Maegan Weltzin PhD, Assistant Professor, Department of Chemistry and Biochemistry, CDR

Academic programs benefit from access to NMR/MRI/MRS

Course Development

Curriculum has been developed to improve the accessibility of the MR instruments to the students. Spring 2024 is the tenth offering of Practical NMR Spectroscopy (CHEM 419, prev. 494). This course is split as half lecture/half lab allowing students to both learn theory of NMR and gain hands on experience with instrument operation, and generating their own research plan for a student-driven project. In Fall 2016, a similar course was offered for the first time on the MRI, Practical MRI (DVM 793). Instead of individual research projects the students perform different lab experiments on a variety of non-living samples. This course has met with much positive feedback from the students involved.

Graduate Program Involvement

MS and PhD programs benefit from enhanced educational and research opportunities provided by the development of MR technology at UAF. Together, enrollment in these programs is about 150 students with 20-30 advanced degrees awarded annually:

- Biology and Wildlife
- Environmental Chemistry
- Biochemistry and Neuroscience

Veterinary Medicine

UAF and Colorado State University launched a collaborative Veterinary Medicine (VMED) training program, allowing UAF students to earn degrees from CSU's Professional VMED Program, and students and scientists from CSU to participate in internships and sabbaticals at UAF, where they will gain access to unique Arctic species and environments. This novel partnership provides new and compelling research opportunities for CSU as well as UAF faculty and graduate students. Several VMED courses offered during the 2-year UAF program will be enhanced by access to the MR instrument and 3-D images of Arctic species. MR studies are able to provide a variety of images to enhance anatomy, diagnostic, and radiological studies in the VMED program. Starting in the Spring of 2021, second year students in the UAF veterinary medicine program were given the option to assist with MRI for veterinary imaging as part of their course work in anesthesia.

Undergraduate Program Involvement

Several undergraduate courses use NMR (see list below). The student access to NMR as well as training in animal surgery, microscopy, and respirometry for undergraduates has resulted not only in independent projects, but also in student driven proposals submitted to programs including Undergraduate Research and Scholarly Activity (URSA), Biomedical Learning and Student Training (BLaST), and INBRE opportunities.

Courses using NMR and avg. enrollments

- CHEM 105 H Lab Honors Lab (20 students)
- CHEM 314 Instrumental Analysis (10 students)
- CHEM 321 Organic Chemistry I (80 students)
- CHEM 325 Organic Chemistry II (40 students)
- CHEM 419 Practical NMR (5-10 students)
- CHEM 434 Capstone Laboratory (10 students)
- CHEM 488 Chemical Research (5-10 students)

	FY20	FY21	FY22	FY23	FY24*
Hours of NMR research usage (300)	165.5	95	100	64	59
Hours of NMR research usage (600)	552.25	31.5	152.25	275	78.75
Projects using NMR	9	5	6	6	8
Hours of NMR teaching usage (300)	29.75	15.25	0	18.75	80
Hours of NMR teaching usage (600)	65	36	54.5	123.75	33
Courses Using NMR	7	4	2	4	6
Billable Liters LN2			253	181.5	196
Projects using Microscopy					4
Projects using MRI	2	3	2	1	2
Hours MRI research (human)	12	4	8	0	0
Hours MRI research (animal)	23	6	5	2	4
Hours MRI Research (Nonliving)	0	0	0	0	1
Courses Using MRI	2	0	0	1	0
Hours of MRI teaching usage	3	0	0	1	0
vet imaging sessions	44	56	38	37	17
Hours DXA Research	4.25	3.25	6.25	1	1.5
Projects using DXA	1	2	1	1	2
Courses Using DXA	0	0	0	0	0

Table 1, Hall	MR Core Instrumer	nt Use and Service	s (*FY24 up throu	ah Feb 28, 2024)
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Table 2. HaMR Core Budget, FY20-FY26

	FY20 GY1	FY21 GY2	FY22 GY3	FY23 GY4	FY24 GY5	FY25	FY26
Account Title	Actuals	Actuals	Actuals	Actuals	Projection	Gap Year	Gap Year?
Salaries & Benefits	\$179,288	\$194,584	171,741	\$225,238	\$248,992	\$192,890	\$196,748
Travel	\$2,054	\$0	0	\$2,315	\$2,000	\$0	\$0
Contractual Services	\$127,962	\$126,458	124,056	\$144,110	\$132,406	\$105,130	\$105,130
Commodities	\$31,000	\$60,408	18,505	\$44,912	\$35,388	\$27,968	\$27,968
Equipment	\$45,034	\$0	0	\$0	\$10,567	\$0	\$0
Expenditure Total	\$385,339	\$381,450	314,302	\$416,575	\$429,353	\$325,988	\$329,846
Institutional Support	\$170,000	\$100,000	100,000	\$100,000	\$100,000	\$100,000	\$100,000
PY Carry Forward (UFB)		\$60,749	57,345	\$61,905	\$33,379	\$133	\$2,517
COBRE-TRIM (support)	\$207,797	\$192,625	142,988	\$178,303	\$178,500	\$93,652	\$50,000
INBRE (Support)		\$7,800		\$8,862	\$5,000	\$5,000	\$5,000
FY25 Pending Request							
External Revenue (non-UA)	\$3,345		500	\$4,999			
External Revenue (Vet-MRI)	\$51,690	\$64,850	64,350	\$66,380	\$55,200	\$60,000	\$60,000
Internal Revenue (UA-Users/Non-CoBRE)	\$11,117	\$12,772	11,025	\$29,537	\$57 <i>,</i> 407	\$69,720	\$117,220
Revenue Total	\$443,950	\$438,796	376,208	\$449,986	\$429,486	\$328,505	\$334,737
Rollover/Shortfall	\$58,610	\$57,345	61,905	\$33,411	\$133	\$2,517	\$4,891

The FY24 projection includes all accounting through February 2024.

Plans for continuing as a recharge center

- Not hinder research
- Simplify accounting and tracking of usage
- Project registration forms for project tracking
- Service award applications to subsidize new research for generating proposals
- Improve accessibility/available of equipment for researchers.
- Expand and adapt the services being offered to meet researcher needs
- Improve communication of project outcomes
- Enhance product output: proposals, manuscripts, patents, etc.
- Keep up to date with user needs/expectations thought periodic user surveys

FY25 Proposed Rates:

MIF Rates:					
Internal (UA) users NMR R	ate per	Hour			
	ΦZΟ \$50				
	\$30 \$120/h	our			
Toshiba Excelart\Vantage	MRI res	earch rates			
Nonliving subject	\$130/h	our			
Living Subject	\$220/h	our			
Veterinarian	\$90/ho	ur			
Vet Tech Rate	\$50/ho	ur			
MIF Staff Assistance	\$90/ho	ur			
Anesthesia/supplies	\$40/ses	ssion			
LN2 Rate:	\$3.50 p	er liter (wher	n available)		
Microscopy/Histology Rate					
Microscopy Staff Rate	\$60/ho	ur			
Microscopy rate:	\$100 annual fee per user after training at staff rate				
Histology rate:	\$20/slic	de			
Standard Single Pipet Cali	bration:	\$25/pij	pet		
Multichannel Pipet:	\$35/pip	et			
Electronic Pipet:	\$45/pip	lenee			
Balance Calibration:	\$70/bai	lance			
Parts:	quoted	as needed			
	•				
Animal Support Rates:					
Vet Tech staff rate:		\$50/hour			
Surgery rate:	e e	\$40 + staff tin	ne		
Non-surgery procedure rate: \$30 + staff			ne		
Staff Consultation Rate:	ç	\$40/hour			
Animal Instrumentation Ra	tes:				
Vet Tech staff rate	163.		\$50/bour		
Respirometry staff rate			\$60/hour		
Respirometry rate (up to o	ne week	<):	\$100 + staff time (minimum 3 hours)		
Respirometry rate (up to o	ne mont	h):	\$300 + staff time (minimum 3 hours)		
Respirometry rate (up to si	x month	is):	\$500 + staff time (minimum 3 hours)		
Respirometry rate (After si	x month	s):	\$100/month + staff time (minimum 3		
nours)					

Cell Culture/Western Blot Rates: Manager Consultation Staff rate: \$75/hour Research tech: \$40/hour Project supplies: quoted as needed

Projects that are not funded through the University of Alaska system are subject to a 55% surcharge.

The rates listed below are for inherently external services, and already include the additional 55% within their rates.

Walk-in DXA Full-Body scan - \$200/scan

Veterinary Diagnostic MRI - \$2400/session now includes the radiologist fee Vet MRI Deposit - \$360 covers instrument and staff time for preparing and waiting for patient, contributes towards diagnostic fee if patient shows up for MRI. Additional \$300 for after-hours/weekend emergency Additional \$300 for additional regions Additional \$300 for scans requiring breath holds and/or cardiac gating

Appendix A: Publications resulting from HaMR instrument/service usage

Manuscripts, published (July 2022-February 2024):

Coker, Melynda S., Zeinab Barati, **Carl J. Murphy**, Terry Bateman, Bradley R. Newcomer, Robert R. Wolfe, and Robert H. Coker. 2022. Essential amino acid enriched meal replacement improves body composition and physical function in obese older adults: A randomized controlled trial. *Clinical Nutrition* ESPEN 51:104–111. https://doi.org/10.1016/j. clnesp.2022.07.004.

Coker, R. H., B. C. Ruby, M. S. Coker, L. Bartlett, B. Kowalski, A. V. Goropashnaya, T. Bateman, M. Shankaran, M. Hellerstein, and W. J. Evans. 2023. Alaska Backcountry Expeditionary Hunting Promotes Sustained Muscle Protein Synthesis. *Wilderness Environ Med* 34 (3):341–345. https://doi.org/10.1016/j.wem.2023.05.003.

Drew, K. L., S. Bhowmick, **B. W. Laughlin, A. V. Goropashnaya, Ø. Tøien, M. H. Sugiura,** A. Wong, K. Pourrezaei, Z. Barati, and C. Y. Chen. 2023. Opportunities and barriers to translating the hibernation phenotype for neurocritical care. *Front Neurol* 14:1009718. https://doi.org/10.3389/fneur.2023.1009718.

Krishnan, J.K.S, **S.A. Rice,** M. Mikes, **M.H. Sugiura, K.L. Drew**, Z. B. Barati, and S. Oliver. Prehibernation diet alters skeletal muscle relaxation kinetics, but not force development in torpid arctic ground squirrels. J Comp Physiol B 194 (1): 65-79 https://doi.org/10.1007/s00360-023-01527-z

Wong, A., M. I. H. Bhuiyan, J. Rothman, **K. Drew**, K. Pourrezaei, D. Sun, and Z. Barati. 2023. Near infrared spectroscopy detection of hemispheric cerebral ischemia following middle cerebral artery occlusion in rats. *Neurochem Int* 162:105460. https://doi.org/10.1016/j.neuint.2022.105460.

Zanetti, F., C. Y. Chen, H. A. Baker, **M. H. Sugiura**, **K. L. Drew**, and Z. Barati. 2023. Cardiac Rhythms and Variation in Hibernating Arctic Ground Squirrels. *Physiol Biochem Zool* 96 (3):167–176. <u>https://doi.org/10.1086/724688</u>.

Appendix B: Funding efforts for research and instrumentation using the HaMR Core at FY2023

Grants Awarded:

Drew, Kelly. *I*NBRE Exceptional Request Award for HaMR Core Supplies. INBRE. \$9,506. Awarded 5.2.2023. Drew, Kelly. INBRE Exceptional Request Award for HSW Local Travel Costs. INBRE. \$2,850. Awarded 6.23.23.

Duffy, Larry (PI), Carl Murphy (Co-PI), and Tom Green (Co-PI). Fucoidan extraction and characterization of Alaskan Saccharina latissimi (sugar kelp) and Costaria costata (5-ribbed kelp) and the identification of future market opportunities. IAB Internal Award: Alaska State Legislature Finance Committee. \$167,364. Awarded 9.15.2023.

Dunlap, Kriya. Vitamin D and healthy aging: Establishing the sled dog sentinel for the Circumpolar North. NIA R03. Requested \$155,000. Awarded \$77,500. 5.11.2023.

Raisley, Brian. Dynamic isocyanate-free self-healing military coating systems. Naval Research Laboratory. Requested \$47,000. Awarded \$47,000 5.15.23.

Tøien, Øivind and Sarah Rice. Modernizing a shared-use large animal facility supporting translational hibernation research at UAF. R24, NIH ORIP. Requested \$345,000. Awarded 6.26.2023.

Weltzin, Maegan. Visinin-like protein-1 modulation of nicotinic receptors. NIH NIGMS SuRE First R16. Requested \$793,792. Awarded \$793,792. 8.1.2023.

Weltzin, Maegan. Nicotinic receptor selective cell penetrating peptide for brain cargo delivery. NIH NIMH R03. Requested \$155,000. Awarded Submitted 2.1.2023.

Grants pending or denied:

Goropashnaya, Anya. Molecular changes in skeletal muscles during hibernation season as a pathway to ischemiareperfusion injury protection. NIAMS R21. Requested \$426,427. Submitted 2.26.2023. Denied.

Howard, William (PI), Maegan Weltzin (Co-PI), and Carl Murphy (Co-PI). Non-Reducible, glucosylated platinum(IV) complexes as improved chemotherapy drugs. NIH SuRE First R16. Requested \$193,750. Submitted 9.28.23. Pending.

Tøien, Øivind. Adaptations of sleep and cardiac rhythms in the hypometabolic state of a human-sized hibernator. NIH NHLBI R01. Requested \$1,162,500. Submitted 3.6.2023. Denied.

Tøien, Øivind. Modernizing large animal isolation facility. Federal funds capital request for Capital Improvement Plan Project. Requested \$500,000. Submitted 3.7.2023. Denied.

Appendix C: Support of Commercialization

- 1. Assisted in commercialization of BCP-191 for Drew laboratory/Be Cool Pharmaceutics
- 2. Assisted commercialization of NeurOx for Barati Medical
- 3. Provided data for fatty liver that contributed to disclosure of an invention to UAF by Essential Blends.
- 4. Weltzin Two provisional patents in progress

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- P20GM130443

NIH-INBRE

- P20GM103395







