

NEWSLETTER

A new chair brings current insights
in the role of inflammation, fibrosis and reparative mechanisms.....



Dr. Ellen Puré joined the School of Veterinary Medicine in July as Professor of Biomedical Science and Chair of the Department of Animal Biology. Dr. Puré earned her A.B. from Washington University where she conducted research on vascular arachidonic

acid metabolism and the function of its eicosanoid products, including the role of the then novel product prostacyclin. Her dissertation focused on antigen-induced T cell-dependent B lymphocyte activation and with her collaborators, co-discovered

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PERFECT SCORES for TWO NIH TRAINING GRANTS

Michael Atchison, Department of Animal Biology and **Christopher Hunter**, Department of Pathobiology, renewed successfully their NIH T32 training programs. Dr. Atchison's grant, entitled VMD-PhD Training in **Infectious Disease-Related Research**, and Dr. Hunter's grant entitled: **Parasitology, Modern Approaches** both received **perfect scores of 10**. Dr. Atchison's award supports four positions for VMD-PhD predoctoral trainees for five years. Dr. Hunter's award supports six PhD students. Many trainees from these programs are now faculty members at academic institutions.

A New Vice Provost for Research

As Penn Vet's Steven Fluharty becomes dean of the School of Arts and Sciences July 1, Provost Vincent Price announces the *new* vice provost for research, **Dawn A. Bonnell**. Dr. Bonnell, a leader in nano-technology research, has been at Penn since 1988. Dr. Bonnell hails from the University of Michigan where she earned her Ph.D., M.S. and B.S.E. in materials science and engineering. As a Fulbright Scholar, she studied at the Max Planck Institute in Stuttgart, Germany. At Penn she is the founding director of the Nano/bio Interface Center that was created with NSF funding. An editor of seven books and an author of more than 200 papers, Dr. Bonnell was elected this year to the National Academy of Engineering, one of the highest honors in her field.



DR. Puré CONTINUED FROM PAGE 1
interleukin-4 and its role in B cell differentiation. After receiving her Ph.D. from the University of Texas-Southwestern Medical School she worked as a postdoctoral fellow at the Rockefeller University where she then joined the Faculty as Assistant Professor in 1984. Dr. Puré moved to Philadelphia in 1992 as Associate Professor at the Wistar Institute where she has been Professor since 1998. In addition to her scientific program, Dr. Puré is devoted to building institutional infra-structures designed to facilitate their scientific missions and the career development of junior investigators. She served as Assistant Dean at the Rockefeller University, as Director of Training and Vice President of Academic Affairs at the Wistar Institute, as Director of the Office of Academic Affairs for the Ludwig Institute for Cancer Research and is an Associate Director of the Cancer Research Institute. She has served on a number of Scientific Advisory Boards, review panels and Editorial Boards including the Journal of Experimental Medicine, the Journal of Clinical Investigation and is a Founding Senior Editor of Cancer Immunology Research.

Dr. Puré's research is focused on mechanisms of homeostasis, the role of inflammation and fibrosis in the reparative response to disruptions in homeostasis and the cellular, molecular, biochemical and biomechanical mechanisms by which chronic inflammation and fibrosis results in a wide variety of organ specific,

multi-organ and systemic pathologic states and diseases ranging from cardiovascular disease to cancer. The goal of her group's research is to reveal targets for the development of novel therapeutics and to exploit the unique features of pathologic states to improve the selectivity of drug delivery.

How reparative mechanisms go awry - giving rise to some of the most prevalent diseases associated with morbidity and mortality

Development is a highly dynamic phase but once fully developed most tissues achieve a state of relative quiescence devoting the vast majority of energy to carrying out tissue specific functions but also, invoke mechanisms to maintain their basal status. All tissues are complex with multiple compartments including parenchymal cells, mesenchymal stromal cells, extracellular matrix, resident hematopoietic cells, neural cells and vasculature and are dependent on precise orchestration of compartmental cross-talk. Tissue dysfunction can arise due to intrinsic and extrinsic insult or injury such as infection, wounding and oncogenic mutations, respectively. Resident leukocytes and stromal cells act as sentinels and activate reparative and regenerative responses that include inflammation and fibrosis in response to any stress that disrupts homeostasis. As is typical for biologic responses, there are endogenous mechanisms that limit these responses to avoid pathology due to the response itself. Defects in these regulatory pathways and/or

prolonged or repeated insult leads to pathologic chronic inflammation and/or irreversible fibrosis, resulting in tissue dysfunction, organ failure and that can promote malignant transformation. We have come to appreciate over the past decade that inflammation is a common underlying cause of the diseases that have the greatest impact on human morbidity and mortality including cardiovascular disease and many cancers. The Puré lab is studying the molecular mechanisms mediated by stromal cells and extracellular matrix that maintain homeostasis, those invoked in response to stress to restore homeostasis and the factors that drive and sustain chronic inflammation and fibrosis. Specifically, they are defining the stromal cell populations and the stromal cell-dependent mechanisms involved and the role of extracellular matrix remodeling. For example, they have demonstrated that an alternative molecular form of the most abundant extracellular matrix glycosaminoglycan hyaluronan, that accumulates at sites of inflammation and in tumors, differentially regulates cell growth, cell migration and inflammation relative to the predominant form of hyaluronan in normal tissues and that the function of hyaluronan reflects the balance between the two forms and the degree of inflammation. In recent studies, they have also defined fibroblast activation protein (FAP) as a marker of activated stromal cells associated with matrix remodeling and shown that

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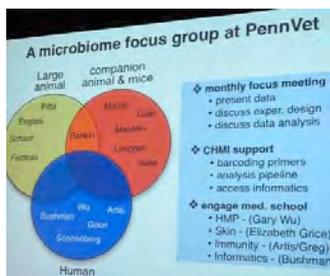
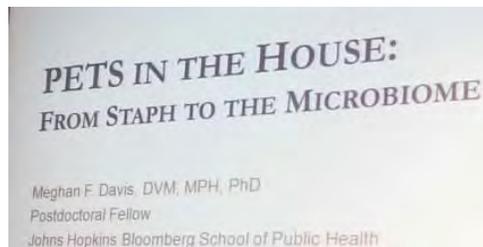
2013 ANNUAL FACULTY RESEARCH RETREAT



A full house



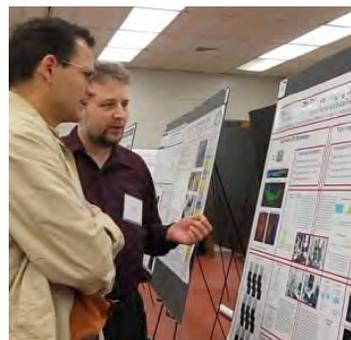
Chris Lengner and Manti Guha



Laurie Mack, Kristina Horback, Ines Rodriguez, & Seth Dunipace



Elizabeth Grice, Dan Morris, Christine Cain and Meghan Davis



William Beltran and Gordon Ruthel discuss poster

Five Penn Vet Swine Center Summer Interns were selected from over 70 veterinary students across the country to compete in the Student Research Symposium at the March 2013 American Association of Swine Veterinarian (AASV) meeting in San Diego. In the oral presentation contest, students **Alyssa Blaustein** tied for 3rd and won a \$1500 award and **Joseph Katz** tied for 5th and won a \$500 award. In the poster presentation contest, **Amy Martell** tied for second in the poster presentations and won a \$400 award while **Shawna Rossini** and **Katy Sullivan** tied for 5th and were awarded a \$200 prize. Swine Center postdoctoral fellows, **Laurie Mack**, **Kristina Horback**, and **Meghann Pierdon** were instrumental in directing the student research.

Highlighted Publications

Smoke carcinogens cause bone loss through the aryl hydrocarbon receptor and induction of CYP1 enzymes (2013) Iqbal J, Sun L, Cao J, Yuen T, Lu P, Bab I, Leu NA, Srinivasan, S, Wagage S, **Hunter CA**, Nebert DW, Zaidi M, **Avadhani NG**. *PNAS USA*, 110(27): 11115-20.



Jianhong Lu, Yonggang Qu, Yuliang Liu, Rakesh Jambusaria, Ziyang Han, Gordon Ruthel, **Bruce Freedman**, and **Ronald N. Harty** (2013) Host IQGAP1 and Ebola Virus VP40 Interactions Facilitate VLP Egress *J. Virol.* 87(13): 7777-80.



A 1.1-mb segmental deletion on the x chromosome causes meiotic failure in male mice (2013) Zhou J, McCarrey JR, **Wang PJ**. *Biol Reprod.* 2013 27;88(6): 159

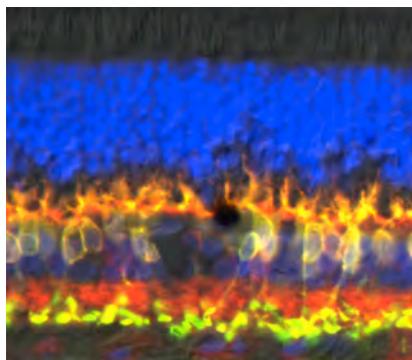
**PENN VET'S CENTER for
HOST-MICROBE
INTERACTIONS**



In launching the new Center for Host-Microbe Interactions, a Request for Applications (RFA) was announced for projects of up to \$50,000 each. Clinical and basic science laboratories throughout the School were invited to submit proposals for projects that leverage 'omic approaches to investigate host-microbe interactions. From a total of **19 applications** submitted, the projects awarded were to: **Drs. S Rankin, C Cain, E Mauldin and E Grice** for a project utilizing targeted and untargeted sequencing to interrogate the microbiome and metagenome of dogs with atopic dermatitis; **Dr. C Lengner** for a study on the regulation of intestinal microbiota by the host epithelial RNA binding protein Msi2; **Dr. D Pitta** for her project on meta-genomic analysis of the rumen microbiome in dairy cows with postpartum metabolic disorders during the transition period; **Dr. T Bale** for a study of prenatal stress effects on the vaginal and offspring microbiome; and **Dr. J Engiles** for a multi-disciplinary group investigation of the role of equine colonic microbiome in clinical disease.

Partial funding for arrays, RNA extractions and labeling kits, reagents, multiplexing, sequencing, and technical assistance was offered to **Drs. R. Harty, B. Freedman, O. Sunyer, R. Greenberg, G. Debes, and E. M. Fecteau.**

In September detailed information will be presented on the plans and activities of the newly established Center. ⌘ ⌘ ⌘ ⌘ ⌘



Legend: Rescue of bipolar cell dendrites following gene therapy for X-linked retinitis pigmentosa. (W^m Beltran)

William Beltran, DVM, PhD, assistant professor in the Department of Clinical Studies PHL, was honored at the 2013 ARVO Foundation for Eye Research Annual Meeting, held in Seattle. He was given the **First Place Prize** of the Merck Innovative Ophthalmology Research Awards. The Merck Innovative Ophthalmology awards encourage young researchers to undertake investigative work in critical areas of ophthalmology that may one day lead to meaningful improvements in patients' lives. "Gene therapy rescues photoreceptor blindness in dogs and paves the way for treating human X-linked retinitis pigmentosa". *PNAS USA* (2012) 109(6) : 2132-7.

**Morris Student Scholar
Award**

Anne M. Staudenmaier, V'15, was awarded Morris Student Scholar funding for her summer research project entitled "Immune Response in the Common Raccoon to Canine Distemper and Feline Panleukopenia Vaccines". Her mentor is Erica Miller, DVM.

Recent News

Gustavo Aguirre, VMD, PhD, professor in the Department of Clinical Studies Philadelphia, was featured along with colleague **Karina Guzewicz, Ph.D.** in the June 17th *Philadelphia Inquirer* for their ground-breaking studies using gene therapy on Best Disease with a canine model. 20 human eye diseases have a canine equivalent making their promising results truly translational in scope. Guzewicz, KE, Komaromy, AM, Iwabe, S, Cideciyan, AV, Dutrow, EV, Zangerl, B, Beltran, WA, Jacobson, SJ, Hauswirth, WW, Aguirre, G.D. (2013) *Sustained Therapeutic Reversal of Canine*



Bestro-phinopathy with Gene Therapy using Recombinant AAV2. ARVO Annual Meeting, May 5-9, 2013, Seattle, WA,



Commensal bacteria at the interface of host metabolism and the immune system. (2013) Brestoff, JR, and **David Artis**, *Nat. Immunol.* 14(7): 676-84.

2013 ANNUAL FACULTY RESEARCH RETREAT at NEW BOLTON CENTER

On June 7th Dean Joan Hendricks presented a Dean's Award to **Steven J. Fluharty, Ph.D.**, the Senior Vice Provost for Research (VPR) at the University of Pennsylvania and professor of pharmacology, psychology and neuroscience in the Schools of Veterinary Medicine, Arts and Sciences, and



Steven Fluharty accepts award

Medicine. In his capacity as the VPR, Dr. Fluharty shaped policy and advanced administrative initiatives for the University's research enterprise as well as having played a leadership role in strategic planning for research and the development of new research facilities campus-wide. Recently, Dr. Fluharty was named dean of the School of Arts and



Dean Hendricks and Marshak Lecture presenter, Dr. David Roos

Sciences at Penn. He will assume the deanship on July 1, 2013.



Dr. Mary Robinson introduces Dr. Soma

A Dean's Award was also presented by Dean Hendricks to **Lawrence R Soma, V.M.D.**, the Marilyn M. Simpson Professor of Anesthesia & Clinical Pharmacology in the Department of Clinical Studies, New Bolton Center. Dr. Soma has spent much of his career developing standards to effectively test for illegal substances in racehorses. He directs the New Bolton Center Equine Pharmacology Laboratory and works closely with the Pennsylvania Equine Toxicology and Research Laboratory (PETRL) at West Chester University to develop and implement methods for detecting drugs illegally used during competition in racehorses. In addition, **Carolina López, Ph.D.**, assistant professor in the Department of Patho-biology, received the **2013 Zoetis Award for Veterinary Research Excellence**, presented by Dr. Harvey Crumm of Zoetis. Pfizer

Animal Health recently became Zoetis™ with a renewed focus: *For animals. For health. For you.* Dr. López joined the Department of Pathobiology at Penn Vet in September of 2010. Her research centers on understanding the processes that lead to the generation of the immune response against viruses.



Carolina López

The theme of the 2013 Research Retreat was "**Genomics at the Intersection of Animal and Human Disease**". Dr. David Roos, Department of Biology, University of Pennsylvania delivered the Marshak Lecture and **Drs. Christopher Hunter, Dan Beiting, Gary Wu, Dipti Pitta, Tracy Bale, Meghan Davis, Elizabeth Grice, and Christopher Lengner** gave presentations. More than 150 participants attended the day long event at Penn Vet's large animal campus, New Bolton Center. 50 posters were presented by Penn Vet Faculty and their colleagues. A drenching downpour of rain fell throughout the day, but a good time was had by all. ☘ ☘ ☘

DR. Puré CONTINUED FROM PAGE 2

the protease activity of FAP plays a role in the collagenolysis characteristic of wound healing, reparative as well as chronic inflammatory and fibrotic responses and the matrix remodeling that occurs in the microenvironment of tumors and thereby regulates tumor growth, invasion and metastasis. These pathways are being studied using genomics, proteomics and state-of-the art imaging approaches using animal models of cardiovascular disease (atherosclerosis and restenosis) and lung, breast and pancreatic cancer. In addition to developing approaches to target stromal cell and matrix-dependent pathways therapeutically by disrupting key pathways at a molecular or cellular level using small molecular inhibitors as well as immune-based therapies, these hallmarks of chronic inflammation/fibrosis are being exploited to better target drug delivery to sites of inflammation and tumors.

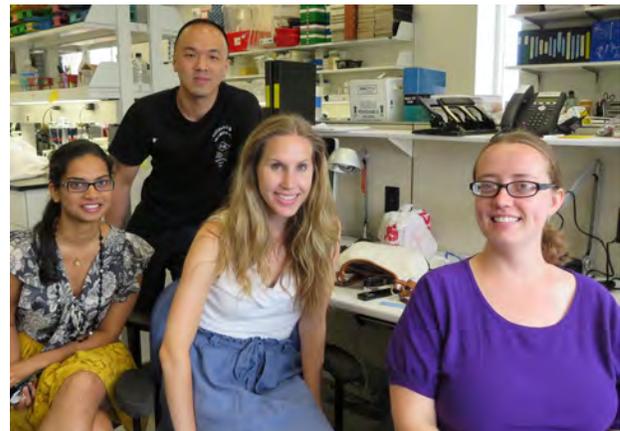
Putting disease in context: Shared risk factors - obesity and aging add insult to injury

High fat diet and obesity have been established for some time as major risks factors for both cardiovascular disease and some cancers and both are recognized as diseases of aging. The increasing incidence of obesity and the aging demographics of the population make it imperative that we delineate the mechanisms linking these risk factors to disease processes. Importantly, in addition to identifying inflammation as a critical component of both cardiovascular disease and cancer, recent studies have established a link between high fat/obesity and inflammation. In ongoing and future studies, the Puré lab will be focusing on studying mouse models of cardiovascular disease and cancer in contexts relevant to animal and human disease including the impact of high fat diet and advanced age. Specifically, they are testing the hypotheses that high fat diet and aging promote the development and progression of atherosclerosis and cancer at least in part by supporting inflammation, stromal cell activation and changes in matrix composition and architecture associated with matrix remodeling.

Dr. Puré’s research is funded by grants received from the following institutes at NIH: NHLBI and NCI. She has an office in 311 Hill Pavilion and her laboratory is also located on the third floor.

Selected References

1. Cuff, C., D. Kothapalli, I. Azonobi, S. Chun, Y. Zhang, R. Belkin, C. Yeh, A. Secreto, R.K. Assoian, D.J. Rader and E. Puré. 2001. The adhesion receptor CD44 promotes atherosclerosis by mediating inflammatory cell recruitment and vascular cell activation. *J. Clin. Invest.* 108:1031-1040. PMID: PMC200948
2. Santos, A.M., J. Jung, N. Aziz, J.L. Kissil and E. Puré. 2009. Targeting fibroblast activation protein inhibits tumor stromagenesis and growth. *J Clin Invest.* 119:3613-3625. PMID 19920354 PMC 2786791
3. Tchou, J., A.V. Kossenkov, L. Chang, C. Satija, M. Herlyn, L.C. Showe and E. Puré. 2012 Human breast cancer associated fibroblasts exhibit subtype specific gene expression profiles. *BMC Med. Genom.* 5:39. PMID: 22954256 PMC3505468



Priya Govindaraju, Albert Lo, Diana Avery & Rachel Blomberg



Dr. James Monslow, Research Investigator Senior, Puré laboratory

AWARDS/GRANTS

Chris Hunter

NIH R21
Host-parasite interactions during toxoplasmosis
\$275,000 5/1/13-4/30/15

Amy Durham

Pilot: "Evaluation of the role of an Epstein-Barr-like virus in Feline lymphoma" from Mari Lowe Comparative Oncology Center
\$50,000 7/1/13-6/30/14

Hannah Galantino-Homer

Grayson Jockey Club
Serum Biomarkers for Equine Laminitis
\$142,147 4/1/13-3/31/15

Hannah Galantino-Homer

Commonwealth of PA
COMP as a Laminitis and Sole Ulceration Serum Biomarker in Horses and Dairy Cows
\$20,579 1/1/13-6/30/13

Thomas Parsons

Commonwealth of PA
Improved Diagnostic Testing for Group Housed Sows
\$15,000 1/1/13-6/30/13

Christopher Hunter

NIH/NIAID
T32 in Parasitology: Modern Approaches
9/1/13-8/31/18 \$ 1,080,800

Cynthia Otto

Monell Chemical Senses Center
A Novel Approach to Ovarian Cancer Screening Using an Interdisciplinary Investigator of its Volatile Signature
\$19,500 4/1/13-3/31/14

Daniel Morris

Zoetis/Pfizer Animal Health
Epidemiologic evaluation of Pseudomonas otitis in dogs.
\$32,344 6/1/13-11/30/14

Margret Casal

AKC-CHF
Lethal Acrodermatitis in the Bull Terrier
\$12,960 6/1/13-5/31/14

Christine Cain

ACVD--Tracking antimicrobial resistance and genotypic relatedness in Staphylococcus schleiferi isolates: a comparison of geographic regions & temporal periods
\$7,420 5/1/13-5/31/14

Dorothy Brown

Integrated Chinese Medicine Holdings
Randomized Controlled Trials of the Effects of I'm-Yunity vs Standard of Care Chemotherapy in dogs with Splenic Hemangiosarcoma
\$214,934 5/1/13-4/30/15

Maryam Yousefi (Lengner Lab)

Howard Hughes Medical Institute
International Student Fellowship
\$129,000 9/1/13-9/1/2016

Dieter M Schifferli

USDA
Allelic variation of *Salmonella* colonization factors
\$350,000 9/30/13-9/29/16

REMINDER -

NIH grant proposal due dates:

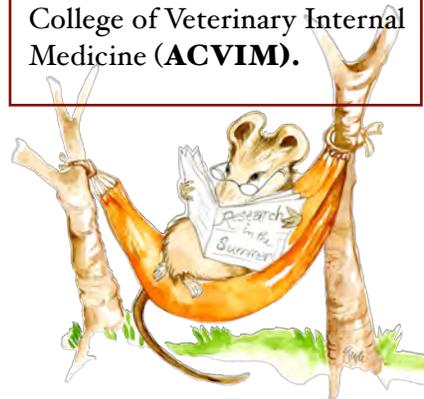
New R01 - October 5
New R21 - October 16

R01 renewal, resubmission, revision - November 5
R21 renewal, resubmission, revision - November 16

For other codes: <http://grants.nih.gov/grants/funding/submissionschedule.htm>

President elect.....

Charles Vite, Department of Clinical Studies Philadelphia is the **President Elect** of the **neurology specialty** in the American College of Veterinary Internal Medicine (**ACVIM**).



Five Career Pitfalls and How to Avoid them

Presented by Charles Haughton, August 20th, 2013; 9 am - 12:30 pm. Location: BRB 252. Discussion on the critical factors that make the difference between maintaining an upward trajectory and stalling (or falling) in your faculty career. Attention is paid to developing skills in scholarship, clinical practice, and teaching in faculty career development. Fee: \$15 due by Aug 9

Biomedical Postdoctoral Programs

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Highlights



Transient Photoreceptor Deconstruction by CNTF Enhances rAAV-Mediated Cone Functional Rescue in Late Stage CNGB3-Achroma-topsia (2013)
AM Komáromy, JS Rowlan, AT Parton, Corr, SL Reinstein, SL Boye, A E Cooper, A Gonzalez, B Levy, R Wen, W W Hauswirth, WA Beltran, and GD Aguirre. *Mol Ther* 21(6):1131-41.

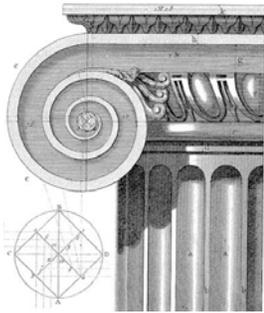


Cytotoxic T Cells Mediate Pathology and Metastasis in Cutaneous Leishmaniasis. (2013) *FO. Novais, LP Carvalho, JW Graff, DP Beiting, G Ruthel, DS Roos, MR Betts, MH Goldschmidt, ME Wilson, Cl de Oliveira, and P Scott.* *PLoS Pathog* 9(7): e1003504. doi:10.1371/journal.ppat.1003504



Features of brain MRI in dogs with treated and untreated mucopolysaccharidosis type I. (2013) **Charles Vite, Nestrasil I, Mlikotic A, Jens JK, Snella EM, Gross W, Shapiro EG, Kovac V, Provenzale JM, Chen S, Le SQ, Kan SH, Banakar S, Wang RY, Haskins ME,** *Ellinwood NM, Dickson PI. Comp Med.* 63(2): 163-73.

Complying with NIH public access policy



The [NIH Public Access Policy](#) ensures that the public has access to the published results of NIH funded research. The

policy changes to public access applies to all awards with start dates on or after July 1 2013. For non-competing continuation grant awards with a start date of July 1, 2013 or beyond:

1) NIH will delay processing of an award if publications arising from it are not in compliance with the [NIH public access policy](#).

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- 3) Check if your publications are compliant--go to My Bibliography and click: *Manage my Bibliography*.

Head Librarian, Margy Lindem will offer help with MyNCBI. (215) 898-8874

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The **Penn Vet Research Newsletter** is distributed quarterly. Suggestions, requests, comments, and story ideas should be directed to:

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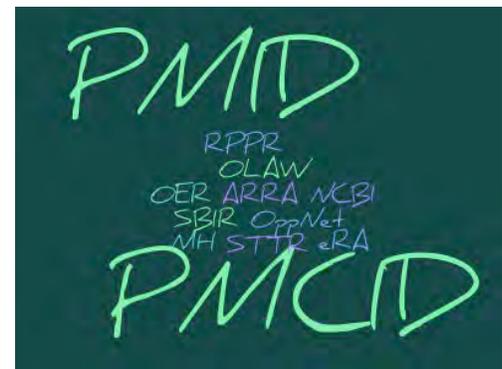


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PMID vs PMCID: what's the difference?

NIH grant proposals, applications and reports are required to include the

PubMed Central reference number (**PMCID**) for cited articles that have been archived in [PubMed Central](#) in compliance with the [NIH Public Access Policy](#). All articles added to PubMed Central are assigned a unique identifier – a PMCID – that will need to be submitted to the NIH. When looking at citations in [PubMed](#), when displaying results in the “Summary” format, you see a PMID number, a unique identifier assigned to each article as it is added to PubMed. This is **NOT** the same number !



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