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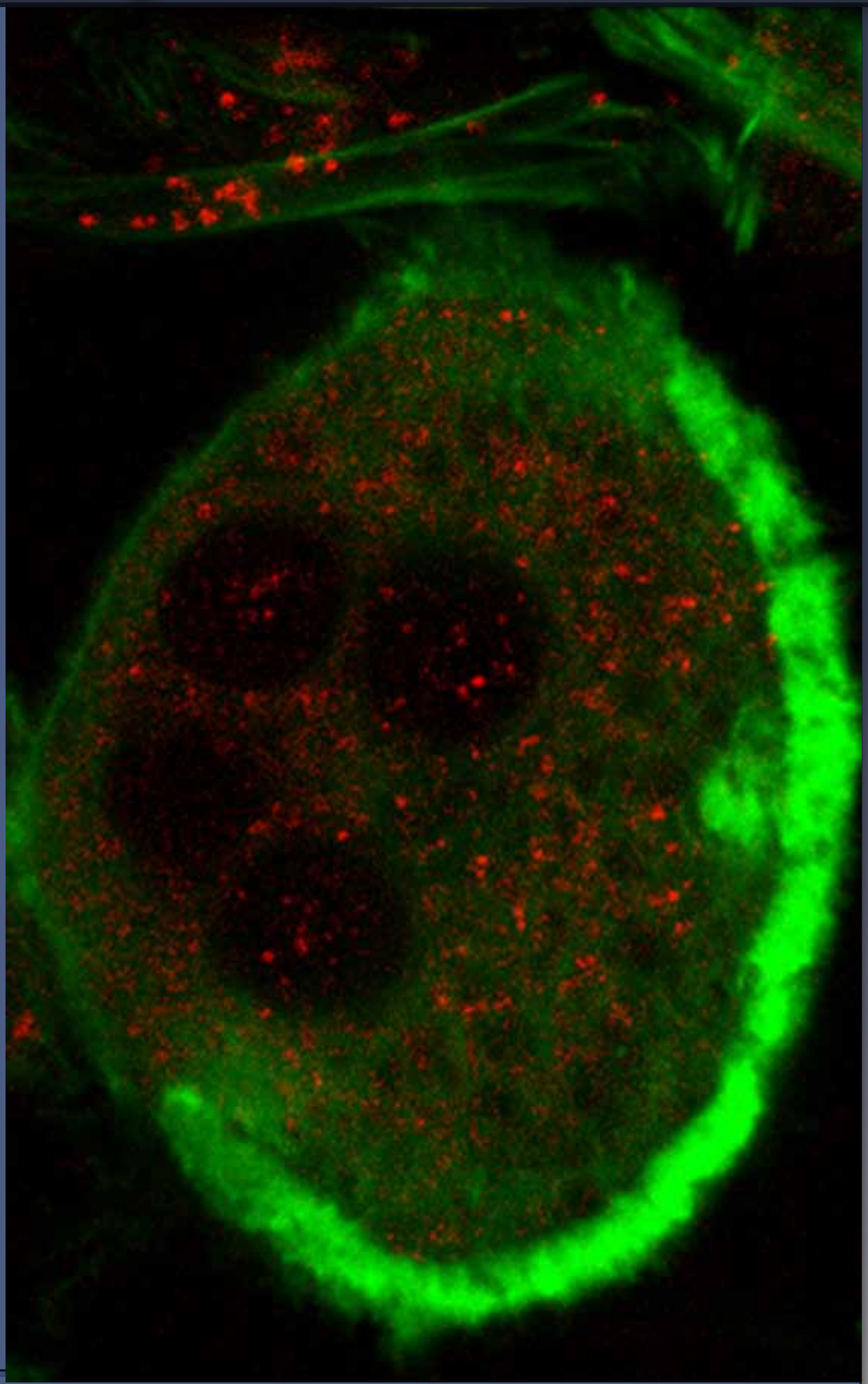

M.J. Hirovonen et al. J Histochem Cytochem. 60:537-549, 2012

In this Issue...

Rab 13 is unpregulated during osteoclast differentiation and associates with small vesicles revealing polarized distribution in resorbing cells.

On the Road to Open Access

Meg McGough

In the two weeks since I began to write an update on Open Access (OA), the landscape for publishers, societies, and researchers has completely shifted. In that time, the British national government announced the endorsement of the UK sponsored Finch Report, which recommended that all publically funded research be made freely available on an OA basis and that the subscription-based model of publishing be phased out. With what seemed a coordinated effort, the Research Council of the UK (RCUK) announced a mandate that all research supported by their funds either be made freely available within six months in an institutional repository or that the research must be published in an OA journal, allowing immediate access to the articles. The European Commission announced on July 17th that all research published by its research-funding program, Horizon 2020, will be made OA, with the same parameters required by the RCUK and the UK national government. Within two years, all nationally funded research within the European Union and the UK will be required to be published under some form of OA. That's astounding.

In the US, the Federal Research Public Access Act (FRPAA) languishes in Congress, waiting for the election to be over. If passed, it will mandate a maximum six-month embargo for publications derived from The National Institutes of Health (NIH) supported research. It seems inevitable that Congress will join the UK and EU, and the bill is likely to pass early in 2013. Australia's National Scholarly Communication Forum began in July requiring "deposit of publication outputs arising from NHMRC funded research into an institutional repository within 12 months of publication." Will it only be a matter of time before that also becomes six months? It is likely that other OA recommendations or mandates are being considered by other worldwide agencies that support research and all trends point in the same direction: research publications will be freely open to all within two years.

Within two years, all nationally funded research within the European Union and the UK will be required to be published under some form of OA.

You may recall that there are two forms of OA, Green and Gold. Green OA refers to a model in which a researcher continues to publish in a subscription-based journal but also self-archives a copy of their article on their institution's repository or in a central repository such as PubMed Central (PMC). Following an embargo period, the article becomes freely available. Green OA proponents argue that in "true Green" OA, there is no embargo period.

In Green OA, the submission process, peer-review, and publication ostensibly are the same as traditional subscription based publishing. There are not many upfront charges for authors and a paper is accepted based on reviewer judging. In Green OA, the subscription component is what comes into question. This is because online subscriptions include embargo periods during which only subscribers are able to access the content. In the original NIH Public Access Policy, the embargo period was a compromise of twelve months that publishers fought hard for, reasoning that a six-month embargo would jeopardize their subscriptions. In May of this year, the Association of Learned, Professional, and Society Publishers (ALPSP) released a study, "The Potential Effect of Making Journal Articles Freely Available in Repositories after a Six-Month Embargo," that backed that argument. As Green OA activists had hoped, subscriptions would plummet. According to the study, based on librarian responses, 44% of libraries would cancel some or all scientific, medical and technical journals.

Simply stated, Green OA proponents never proclaimed that anything in subscription based publishing needs to change except for the embargo period, but by limiting the embargo period to a very short time or even nothing, Green OA advocates understood that subscription based publishing could not survive (and that this was always the goal). Steve Harnad,

On the Road to Open Access *cont.*

professor at Université du Québec à Montréal and the main proponent of Green OA, has said that Green OA would cause the demise of many journals and those remaining would be forced to economize and be more accountable to libraries.

As a result commercial publishers came up with their own version of OA, called Gold OA. Gold OA is a model in which the author pays to publish in an OA journal with a result of free and immediate access to the published article. Originally, commercial publishers formed hybrid journals in which researchers could pay to have their article published along with other articles that were published under traditional subscription models. Other publishers such as Public Library of Science, (PLoS) began publishing 100% OA-only journals that were paid for by article processing charges (APC). True OA journals have no subscriptions and, with the push from national governments, it appears that OA will be the norm for publishing research in the future.

True OA journals have no subscriptions ...

The issue with Gold OA is, of course, that the APC charges can be steep, ranging from $1350 up to $3000. These are current actual costs, and the announcements coming out of the UK and EU acknowledge these costs and agree that funding bodies or academic institutions will need to underwrite them. Many academic institutions are wondering where that money will come from. It's not as if these institutions have surplus money, all of them have been hit hard by the world economic downturn and have been forced to cut back across the board. Some may reduce library budgets but as library budgets for journals cannot cover all of these costs, this is not a feasible long-term solution. Moreover, libraries will be impacted in other ways. Many see this as a disintermediation of librarians and libraries. Many of the resources that libraries and their staff provide can be accessed from anyone's personal computer.

Another question may be how institutions (outside of funding bodies like the NIH and the Wellcome Trust) will decide who gets funded for publishing. Will it be by seniority, by discipline, by how much grant money a researcher brings to a department? And will grant money be able to be used for more than one paper? Authors will need to consider how far their publishing funds will stretch and how many articles will they be able to get out of each grant. Publishing will become a line item for authors and if Gold OA becomes the de facto method of publishing, the cost of publishing a paper is unlikely to remain the same or go down. With government mandates guaranteeing that publishing will be funded, publishers may begin refiguring the cost of publishing articles, as they add in new technologies to online journals. Expect these costs to rise, with authors bearing the final responsibility for payment.

Green OA would cause the demise of many journals and those remaining would be forced to economize and be more accountable to libraries.

Even though Gold OA was developed by commercial publishers, society publishers responded in kind and added their own versions of Gold OA to their publications. Unfortunately, society publishers may not find much security with the move to 100% gold publishing. Societies have traditionally depended on income from their journal subscriptions to fund other society activities. The loss of that income on societies cannot be underestimated. Societies will need to make hard decisions about how they will fund society activities and will need to consider reinventing themselves in terms of what they alone can provide members and price it accordingly.

A final consideration is how scientific publishing will continue to foster quality control moving to a pay-to-publish system. In 2004 Elsevier wrote to the UK Science and Technology Select Committee their concern about author-pays models of publishing "undermining of public trust in the integrity and quality of scientific publications. The subscription model, in which the users pay (and institutions like libraries that serve them), ensures high quality, independent peer review and prevents commercial interests from influencing decisions to publish." The author-pay model removes these controls. Instead of the reader, and the institution as customer, the author becomes the ultimate customer. And because authors must publish and OA publishers must increase the output of articles, scientific impartiality of publishing cannot be maintained.

Whatever your opinion of OA and what this article has described, I think we all would agree that the goal of OA is still worthwhile, as it

On the Road to Open Access *cont.*

can provide free and open access to the literature. The purpose here is to make you aware of the possible consequences of OA and suggest that we all need to prepare for it with our eyes wide open, fully comprehending the consequences. The result will impact everyone engaged in research and publishing of science. All of us need to understand how OA will work, who will be affected by it, how it will be paid for and how it will change scientific research. We don't know the answers to these questions but they are worth considering.

The Society's journal JHC, Journal of Histochemistry & Cytochemistry has for many years had a version of Green OA. JHC's articles are made freely available to the public on the JHC website after twelve months: ***http://jhc.sagepub.com.*** JHC also deposits all published articles in PMC and again, the articles are freely available on the PMC site after twelve months. In addition, JHC in collaboration with our publisher SAGE, participates in Gold OA whereby the author may choose to pay to have their accepted paper published and made immediately available to all readers. The cost is $3000.

For more information, please visit here: ***http://www.sagepub.com/*** sagechoice.sp. JHC is working closely with Council and Sage to anticipate continued changes to publishing and ensure the sustainable success of JHC.

Meg McGough
Director Marketing, HCS and JHC

NEW! JHC Forum

You probably received an email in the last few weeks alerting you to the new JHC blog, "JHC Forum," ***http://jhcforum.org/***. The Forum came about as we pondered how to bring the research in JHC to a wider audience. JHC does have a Facebook page where we post short descriptions by authors of their articles but we thought we should try to do more.

There have been some recent studies showing that authors writing about their work increase the readership of their work and influence citations. We know from talking with authors that they don't have time to write about their work so we came upon the idea of a blog or forum for authors to talk about their work, but where JHC staff would do more of the "work."

We set up telephone interviews with JHC authors, sending them a list of questions in advance. Authors are free to answer any or all of the questions. We tape ten to fifteen minute interviews, and transcribe them, posting the text every week on the Forum. If a phone interview is not possible, the authors are free to send us their text answers to the questions. Authors are not required to participate but those that have seemed to enjoy answering the questions. It is very early in the process but we are hoping that interest will grow and we will post to JHC Facebook when a new post goes live.

The JHC Forum is open to all readers, but to post a comment or ask a question, you must register with your name and email address. To register, scroll to the bottom of the post you want to comment on and you will see a "Leave a Reply" box. If you are not registered and try to post a comment, it will prompt you for your email and name. Following registration, you will be able to comment in the "Leave a Reply box.

Please stop by and have a read at the Forum. If you are an author of a JHC article from the past twelve months, we would be happy to include your work. Please email us at ***mgm5@uw.edu***

2012 MARC Awardees

Jose A. Torres completed a B.S. in biology from Inter American University of Puerto Rico. He also holds a M.S. from Universidad Del Turabo in environmental sciences. Currently, he is pursuing a doctoral degree in environmental toxicology at Texas Southern University, Houston, TX.

Mr. Torres' research interest is in the field of environmental neurotoxicology - neurotoxic effects of simulated microgravity (adverse effect) on rat cortical astrocytes. He was awarded a competitive NASA Jenkins Fellowship to support his pre-doctoral research and career development. Mr. Torres' future goal is to pursue a postdoctoral research program that focus on in vivo orin silico neurotoxicant models.

Claretta J. Sullivan received her Bachelors of Science degree from Tougaloo College in Mississippi in 1987 and worked in a variety of industry and education jobs thereafter. As coordinator of summer internships at Oak Ridge National Laboratory, she was so inspired by the interns' research that she decided to pursue a career in science. She earned her doctorate degree in life sciences from the University of Tennessee in Knoxville, Tennessee in 2007 before joining the Department of Surgery at Eastern Virginia Medical School in Norfolk, Virginia as a research assistant professor in 2008. Her research interests are related to the application of atomic force microscopy and other nanotechnologies to investigate bacterial pathogenesis. Currently, she is focused on understanding the role of bacterial membrane vesicles in sepsis. In addition to science, she enjoys live music, well-told stories and interesting characters.

2012 MARC Awardees

Danilea M. Carmona-Matos is a graduate student from the University of Puerto Rico at Mayagüez. Her career goal is to obtain a PhD in Molecular Biology with an emphasis in Neurobiology. She participates in the Laboratory of Cell and Developmental Neurobiology under Dr. Franklin Carrero-Martinez's mentorship. The research conducted in this lab focuses on Drosophila melanogaster's neuromuscular system; her research particularly focused on the in vivo manipulation of Neuromuscular Junctions in D.melanogaster larval stages.

Being an avid researcher Ms. Carmona participated in the Histochemical Short Course and Annual Meeting during 2012 for her professional development. Also, she has participated as a volunteer since 2005 for Shriner's Children Hospital at the Puerto Rico Veteran's Hospital at San Juan.

Adriana Méndez Suárez is an undergraduate student at the University of Puerto Rico-Mayagüez Campus, pursuing a dual degree as an M.D/ Ph.D. Her career interests are in Neuroscience. She participates in research at the Laboratory of Cell and Developmental Neurobiology, under the mentorship of Dr. Franklin Carrero Martinez. The lab studies the Drosophila melanogaster neuromuscular system. She participates in activities that enrich development as a professional scientist, such as in the Histochemical Short Course and Annual Meeting. Currently, she is undergoing doctor shadowing at the University of Puerto Rico- Medical Sciences Campus in the Neurosurgery Department. Also, she is participating as an assistant in the program "Puerto Rico NASA Space Grant".

FASEB PRESS RELEASE: July 25, 2012

House Funding Bill Will Delay Research Progress and Place New Burdens on the National Institutes of Health

Bethesda, MD – The fiscal year (FY) 2013 appropriations bill adopted by the House Labor, Health and Human Services, Education and Related Agencies (LHHS) Subcommittee on July 18th fails short of the needed investment in biomedical research at the National Institutes of Health (NIH) and will delay efforts to improve the well-being of our nation's citizens, reduce human suffering, and protect the nation against new and emerging health threats. "We are deeply concerned that the LHHS Subcommittee provided flat funding for NIH when the opportunities for major advances are unprecedented," stated FASEB President Judith S. Bond, PhD.

FASEB has been advocating for an appropriation of at least $32 billion for NIH as the baseline funding to sustain the research that capitalizes on the increasing scientific opportunities and the demonstrated capacity of the research enterprise. "The proposed funding level is substantially below that necessary to sustain the current research effort. Without adequate funding, NIH will have to sacrifice valuable lines of research and lose talented young scientists to keep up with rising costs and a continued loss of purchasing power" said Bond. Failing to continue the federal investment in NIH could endanger the U.S.'s position as a world leader in biomedical research.

FASEB is also concerned that policy language included in the LHHS bill could jeopardize NIH's ability to manage its portfolio effectively. For example, the bill prohibits NIH from spending funds on any research project until the director certifies that the project is of significantly high scientific value and will have a measureable impact on public health. "The NIH already has a peer review process that ensures that the research it supports is scientifically valuable," said Bond. "Therefore, it is neither necessary nor feasible for the Department of Health and Human Services to review the tens of thousands of activities funded annually by the agency." Moreover, this stipulation could have a deleterious impact on NIH's ability to fund the basic science that lays the foundation for the biomedical research enterprise. Much of the research that NIH supports is aimed at discovering what causes disease and how organisms function, yet the impact these studies would have on human health is not always immediately obvious.

The legislation also unwisely prescribes the number of training awards that NIH should fund in FY 2013. NIH is currently in the process of reviewing and determining how to implement the recommendations of its Advisory Committee to the Director Working Group on the Biomedical Research Workforce. "Mandating a certain number of awards could constrain the agency's ability to support the optimal number of research trainees," commented Bond.

FASEB looks forward to working with Congress, NIH, and the research community to sustain the nation's commitment to biomedical research and ensure that any policy changes do not constrain agency efforts to facilitate long-term progress in science and technology.

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Visit: ***www.histochemicalsociety.org***
Use the "Membership" tab to renew..

40 Years Ago

Gordon Research Conference on Immuno-electron Microscopy in 1972: A Tipping Point for Immuno-enzyme Technology

The following is an excerpt from an article by Past-President Gwen Childs on the development of immuno-enzyme technology and the First and only Gordon Research Conference on the subject held in 1972. She relates the collegial exchange of information and intense examination of concepts and methods associated with immune-electron microscopy at a critical turning point in the history of this methodology.

Dr. Childs is Chair of the Dept. of Neurobiology and Developmental Sciences at the University of Arkansas for Medicinal Sciences. The article with the key to the group photo, as well as cited references is available at http://histochemicalsociety.org/Publications/Newsletters.aspx - Wm Stahl

The first and only Gordon Research conference on Immuno-electron microscopy (EM) was held at Wayland Academy, Beaver Dam, Wisconsin, 40 years ago, July 31—August 4, 1972. **Dr. Sydney Breese** chaired the conference. I was a brand new Ph.D. having just defended my dissertation May 2, 1972. I was privileged to attend as the guest of **Dr. Ludwig Sternberger.** My name at that time was **Gwen Childs Moriarty.**

To set the stage, I need to give you a view of what was going on during the previous decade. The earliest and most notable successes in immuno-EM were with conjugates of antibody and ferritin first reported by **Professor Seymour Jonathan Singer** in 1959 (Singer, 1959). The immunoferritin approach was still growing, and probably most useful for surface antigens, because it penetrated tissue poorly and added non-specifically to plastic ultrathin sections. In 1970, my advisor, **Dr. N.S. Halmi** had suggested I try the immunoferritin approach to detect adrenocorticotropin in the pituitary for my dissertation research, however, after I read some of the literature on the latest technology with immunoperoxidase, I convinced him to try this approach.

The immunoperoxidase approaches were promising because they allowed detection at both light and EM levels. The pioneering studies by Graham and Karnovsky in 1966 on the ultrastructural detection of peroxidase paved the way for this development (Graham and Karnovsky, 1966) and led to two reports of successful immunoenzyme labeling during 1966. One of the groups, led by Stratis Avrameas at the Pasteur Institute in Paris described the protocol for the conjugation of enzyme to antibody and its application at the EM level, in 1966 (Avrameas and Uriel, 1966; Bouteille and Avrameas, 1967). He developed conjugates of peroxidase and anti-IgG with the use of glutaraldehyde as the bifunctional reagent. At the same time, Dr. Paul Nakane, a young Assistant Professor working with GB Pierce (Ram and Pierce, 1966) at the University of Michigan, used conjugates of peroxidase and anti-IgG were made with a bifunctional reagent, p,p'-difluoro-m,m'-dinitrodiphenyl sulfone (FNPS) and the technique was published in a letter to the editor in 1966 (Nakane and Pierce, 1966), with a full description of the technology published the following year (Nakane and Pierce, 1967), including its application at the EM level.

There were challenges with the early conjugates of peroxidase and antibody in that it was difficult to get a high yield of conjugated antibody and separate the unlabeled antibody. This drove the development of different approaches in three different laboratories. These groups used anti-peroxidase antibodies to attach the peroxidase to the complex, in a bridge, taking advantage of the bivalent properties of IgG binding. **Dr. Ludwig Sternberger,** a Professor at Johns Hopkins University and also at Edgewood Arsenal, Maryland, referred to the approach as the "unlabeled antibody method" (Sternberger LA, 1969) whereas **Dr. Samuel Spicer,** from the Medical University of South Carolina, called the protocol the "immunoglobulin-enzyme bridge" method (Mason et al., 1969). **Dr. Avrameas** called his approach the "mixed antibody method" (Avrameas, 1969; Avrameas, 1970). The big challenge with this method involved the elution of high-affinity anti-peroxidase molecules. Often the highest affinity molecules remained on the column. So, **Dr. Sternberger** developed the technology one step further with the peroxidase-antiperoxidase (PAP) technique (Sternberger et al., 1970) and essentially solved the problem of elution of anti-peroxidase. In this sequence, the third antibody to peroxidase is added in a complex with peroxidase (PAP complex), which is soluble and brings 3 peroxidase molecules to the antigen-antibody sequence. The result was a publication that became a citation classic in 1983, with over 1280 citations. Today, the Web of Science lists over 5,799 citations for this landmark paper. After trials with the conjugate, I used PAP for my dissertation work and the strong labeling with relatively low background surprised everyone, including me (Moriarty and Halmi, 1972). It really showed that the immunoenzyme technology was extremely sensitive and feasible for both light and EM. Thus, the stage was set for a highly informative Gordon Research Conference in 1972.

The 1972 Schedule for Gordon Research Conferences carried the theme "Frontiers of Science" and the program broadly covered all aspects of the field, although the use of colloidal gold was notably absent. Faulk and Taylor had just published their landmark paper (Faulk and Taylor, 1971) and unfortunately they were not represented.

It began, July 31, 1972 with a lively discussion of "Protein Chemistry of Antibody Labeling" with **Drs. Nakane and Sternberger** as speakers. **Dr. Nakane** was discussion leader. The second session was "Immune-Ferritin Preparation" by **Drs. Konrad C Hsu**, Columbia University; **Arnold Vogt**, Hygiene-Institut der Universitat; and **Sidney S. Breese** (Plum Island Animal Disease Lab and the Chairman of the conference). Tuesday, August 1, was devoted to "Immuno-Ferritin (viral applications)" by **Drs. Councilman Morgan,** Columbia University and **Calderon Howe,** Louisiana State University and "Immuno-Ferritin (tissue applications)" with **Drs. Samuel Dales,** Public Health Research Institute of New York, and **Margaret J. Polley**, Cornell University Medical College. Wednesday morning, there was an "Immuno-Ferritin" workshop led by **Drs. Sidney Breese, KC Hsu**, and **Guiseppe Andres**, Medical School State University of New York.

On the afternoon of August 2, "Immuno-enzyme techniques (peroxidase)" were discussed, led by **Dr. Stratis Avrameas,** Institute Recherches sur le Cancer, as discussion leader, and speakers **Drs Ph.J Hoedemaeker,** Dept Pathology, Groningen, and **Robert L Vernier,** University of Minnesota. **Dr. JP Kraehenbuhl**, Rockefeller University then discussed the pioneering use of cytochrome as an enzyme marker. Thursday, August 3 involved **Dr. Nakane's** "Immuno-enzyme Technique Workshop" with **Dr. Guiseppe Andres**, and a "Hybrid Antibody Technique" presentation by **Drs. T Aoki,** National Cancer Institute and **Christopher Stackpole,** Sloan Kettering Institute for Cancer Research.

Finally, on Friday, August 5, half of the morning session was devoted to the "Unlabeled Antibody Enzyme tech-

40 Years Ago *cont.*

nique" with **Dr. Ludwig Sternberger.** The remaining half ended with a discussion of "Immunizing markers and tracers" led by **Dr. Stratis Avrameas**.

As you can tell, the time-honored immunoferritin approaches received top billing as they had been around for 13 years. The second approach that was emphasized was the immunoperoxidase conjugate techniques. **Dr. Sternberger** had been invited to present his newest "unlabeled antibody methods" and he invited me to present my dissertation research photos during that session, showing how well the PAP complex worked.

I can state that the opportunity to meet and listen to so many pioneers in this field was enriching and very empowering. I was probably not prepared for the level of discourse, challenges and debating. All throughout the conference, the immunoperoxidase technology was greeted with many questions. **Dr. Sternberger** was the sole representative of the newest "unlabeled antibody approach". He did not hesitate to challenge and question each of the speakers all week long. Some of the participants learned about our results with the PAP complex and asked for an early mini-workshop during the meeting. We accommodated whoever wanted to attend this informal session, on the side.

When it came time for **Dr. Sternberger's** formal session, the participants were more than ready to return the favor of debating and questioning. Of course, because I presented my dissertation work during that session, this was a true baptism by fire for a young Ph.D. These scientists were a tough crowd; the data were greeted with appropriate skeptism and many questions and challenges, some quite daunting.

I kept a stiff upper lip, as I recall, but felt that I must have failed miserably in convincing them about our work. At the airport later that day, I heard my name being called from the bar and a group of the toughest questioners invited me to join them for a beer. This was also a revelation! Immediately I recognized that I had just joined the club of fellow researchers who could challenge one another one minute and celebrate, collegially, with a beer the next. Sometime later, when corresponding with **Dr. James Jamieson**, (who was at Rockefeller University at that time and one of the more active questioners), he apologized saying "I realize my comments to you may have come out sounding harsh or hypercritical. They were not meant to be, but if so, I am sorry. I must say that your work was very impressive and in my opinion the best shown at the meeting. Your pictures were truly gorgeous and I want to congratulate you on your results."

Above is a photograph of the participants in this conference and we have appended names and a key.**(Available at: *http://histochemicalsociety.org/Publications/Newsletters.aspx)*** I believe that the Conference was clearly a tipping point for the field as it showed how well immunolabeling had progressed. I recently sent out the photo to some of the conferees and asked for their recollections. I received a wonderful response from *Stratis Avrameas*. I will share this from him.

"Thank you for your e-mail. Unfortunately I don't remember much things from that Gordon Conference meeting although I remember that I have read, following that meeting ,several published articles by G.Moriarty. I am also almost sure that Coons and Leduc were not present.

The only thing I certainly remember, because I met it during all my scientific life, was the interest, but at the same time, the high skepticism with which was received the new, at that time, field of immunoenzymatic technology. It came to my mind that the ideas of Bertrand Russell, who I was reading at that time, applied equally well to religion and science. That is, with my own words, "A new truth disturbs especially the authority. However all the long history of hardness and intolerance, it is the highest acquisition of our clever but stubborn human species". Stratis Avrameas, personal communication, July 8, 2012.

I invite members of the Society, who may have participated, or whose mentor may have participated to send me their recollections of this meeting (***Childsgwenv@uams.edu***). I am writing a chapter on the history of immunocytochemistry and it would be great to have additional input from other participants! If you follow publications from the participants, you can tell that this conference and the publications in 1972-73 eventually led

to some of the best early electron and light microscopic immunolabeling, stemming from advances in the EM protocols. During the subsequent decade, I found myself in many training sessions by phone or letters helping people with their protocols. I often wonder today how having email would have improved communication. It has been gratifying to watch the growth of the field in both cellular endocrinology and neuroscience thanks to these early immunolabeling advances.

Electron Micrograph Legend

One of the first set of EMs of anterior pituitary corticotropes immunolabeled for adrenocorticotropin (ACTH) with antiserum to the C terminal fragment of ACTH and the PAP complex in a post-embedding method. This was the first time the PAP technique had been used on ultrathin sections and it was done in March-April, 1971. (Sent to Dr. Sternberger in a letter dated April 26, 1971.) The cells were fixed in paraformaldehyde-picric acid (no Osmium tetroxide) and embedded in methacrylate. Ultrathin sections on formvar coated nickel grids. were floated on drops of 1:20 anti-17-39 ACTH for 3 min i Then, diaminobenzidine:3 min, wash and 3 min on a drop of Osmium tetroxide. Note label on the granules shows the particulate morphology typical of the PAP complex. At the edge, note the pentagonal (or sometimes U-shaped) PAP molecules (arrows), which is evident in post-embedding reactions with this molecule. The fixation does not preserve membranes, so cytoplasmic detail and mitochondria are not delineated. The value in the early labeling was in its ability to identify cell types, correlating the morphology of labeled granules with the known morphology of each pituitary cell type. Note the antigens outside the granules. This caused some concern and was clearly difficult to explain. Now we know that this can happen with weaker cross-linking fixatives.

By 1972, we had discovered improved antigen preservation in glutaraldehyde followed by Araldite embedding (Moriarty and Halmi, 1972a and b). Likely the photographs presented at the Gordon Research Conference were from those papers and showed improved morphology. By 1973, we also discovered that one could use highly dilute antisera following an overnight or 48 h incubation. Some antigens were even preserved after osmium tetroxide postfixation.

Obviously, we have much better methods for preserving antigens and morphology today, and the colloidal gold techniques also show significant refinement over the older methods. However, in 1971-1972, the immunoreaction in this photograph was so striking, it convinced many individuals in the early 1970's to try the PAP complex method. Bar=300 nm; C=corticotrope; U=unstained cell; N=nucleus.

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Update on ICHC2012 • Kyoto, Japan

On Sunday, August 26th
Moise Bendayan (Montréal, Canada) will present
David Glick Lecture 1 entitled
Gastric leptin: From immunocytochemistry to clinical application

On Monday, August 27the HCS has organized the session:
Correlative integrative microscopy

SPONSORS: Applied Precision, Inc., A GE Healthcare Company and FEI

Chair: C. Frevert (Seattle, USA)
1. ***On-line correlative light and electron cryo-microscopy: Development of an integrated fluorescence and electron microscope***
Hirofumi Iijima (Tokyo, Japan)

2. ***Merging ultrastructural and molecular data for connectomics***
Robert E. Marc (Salt Lake City, USA)

3. ***Live correlative light and electron microscopy of mammalian and yeast cells***
Yasushi Hiraoka (Osaka, Japan)

4. ***Building a synaptome: Tools for delineating true boundaries for segmenting and reconstructing synapses in their three-dimensional space***
Eduardo Rosa-Molinar (San Juan, USA)

On Wednesday, August 29th
JHC Lecture:
Protein phosphorylation remains a black box in signal transduction: developing a new method to search for substrates of protein kinases
Kozo Kaibuchi (Nagoya, Japan)

For detailed information on the scientific program go to:
http://www.acplan.jp/ichc2012/
and navigate to the "Program Lectures" to the left of the home page for the meeting.

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Kyoto, Japan, August 2012.

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JHC Plenary Lecturer

Kozo Kaibuchi MD, PhD, Professor in the Dept of Cell Pharmacology at Nagoya University Graduate School of Medicine

"Protein phosphorylation remains a black box in signal transduction: developing a new method to search for substrates of protein kinases"

Kozo Kaibuchi, M.D., Ph.D. is a Professor in the Department of Cell Pharmacology at Nagoya University Graduate School of Medicine. His work in the field of neurobiology has included studies of neuronal cytoskeleton, polarity and its regulation in migration. In particular he has made seminal discoveries on the functions of the small G proteins of the Rho superfamily, and their regulation of downstream kinases and other targets. These protein networks are powerful regulators of cytoskeletal architecture and cell movement.

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2012-2013

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