THE BIOMED SCIENTIST

Newsletter of The Association of African Biomedical Scientists, Inc.

Web Address: http://www.aabs-inc.org

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The Association of African Biomedical Scientists, Inc. (AABS) is a not-for-profit organization whose membership is open to those who share the following goals: 1) Foster the development of Science in Africa; 2) Promote career development opportunities for Biomedical Scientists in North America; 3) Provide opportunities for young developing scientists; and 3) Encourage research collaboration in pursuit of advancing scientific knowledge.

For comments or suggestions, please send email to webmaster@popmail.med.nyu.edu.

EDITOR'S CORNER

Welcome to The BioMed Scientist, our official newsletter, which will be published quarterly. I hope that you enjoy reading it. Please send your comments, suggestions or criticisms to me at yakubu_ma@tsu.edu. We invite articles that are in the spirit of our goals for the next issue. Brief discussions and articles of scientific nature are welcome.

Let us utilize this forum to network and to establish relationships that enable us help one another succeed in our professional endeavors.

Momoh Yakubu
yakubu_ma@tsu.edu

MESSAGE FROM THE PRESIDENT

Vincent K. Tsiagbe

Fellow members of AABS:
The struggle to succeed in getting grant support and to attain professional recognition is apt to dampen our ability to benefit from the successes and trials of one another. The inevitable truth remains paramount, that there is strength in unity. It, therefore gives me great joy that we continue to grow in strength from our humble beginning five years ago.

During the Experimental Biology 1998 meeting of the Federation of Associations of American Societies of Experimental Biology (FASEB), seven brave young men and women convened, informally, on one of the stairs of the Convention Center. This was accomplished by simple hand gestures of invitation. It was then decided that it would be in our great interest, and that of the marginalized minority group of scientists, if we should organize into an association that addresses our unique difficulties and aspirations. A small group of three was charged to plan the strategy for organizing us into an Association.
These humble beginning led to the birth of "The Association of African Biomedical Scientists, Inc." at the Experimental Biology 1999 meeting of the FASEB in Washington, DC. We unveiled and promulgated our Bye-laws and Statutes of Incorporation. Our numbers grew from the initial seven to 16 at this meeting. With the help of our dedicated Board of Directors, not to mention their generous spouses we have continued to make study progress. During Experimental Biology 2002 meeting we held a very successful banquet cum scientific presentations that set the tone for our future activities.
Some of our major achievements include the setting up of a list server to facilitate our communications. This was followed by the development of a web site, and a brochure that speaks for our mission.
Our listed membership has grown to ~100.

I hope you will enjoy this issue of our newsletter "The BioMed Scientist".
Although we have been slow in our efforts to organize, the study progress we are making gives me confidence that we will accomplish our goals in due time.

We have established a website for AABS. Visit your site at: http://www.aabs-inc.org. We also encourage you to use our list server at http://endeavor.med.nyu.edu/mailman/listinfo/aabs, to be a part of the communication. You can also browse archives of previous communications at this site. If you are not yet enlisted, please do so, in order to keep up with our communications.

We are grateful to NYU School of Medicine for hosting our web site.
We thank the American Association of Immunologists (AAI) for sponsoring our meetings at Experimental Biology.

Our special gratitude goes to Deborah Tsiagbe for providing pro-bono legal service in the incorporation of AABS, and for her continued legal counsel.
Long Live AABS!

KEEP UP THE SPIRIT!

BRIEF SCIENTIFIC DISCUSSIONS / REPORTS

HORMONAL REGULATION OF RENAL FUNCTION AND BLOOD PRESSURE

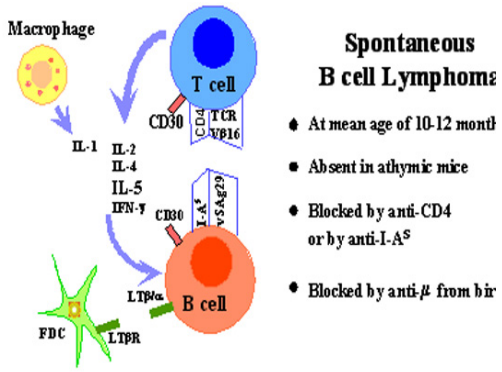
Nitric oxide (NO) or endothelium-derived relaxing factor (EDRF), endothelin-1 (ET-1) and metabolites of arachidonic acid via the cytochrome P450 monooxygenase (CYP) pathway, especially 20-hydroxyeicosatetraenoic acid (20-HETE) are important humoral factors involved in the regulation of vasomotor tone, and salt and water excretion. These mediators are produced and exert profound effects in the kidney and are implicated in the genesis of hypertension and renal failure. NO is crucial in the maintenance of a state of basal systemic and renal vasodilatation, inhibiting the production and actions of ET-1 and 20-HETE, and antagonizing the vasoconstrictor tone in the renal afferent arteriole, a major site for the production and action of the vasoconstrictor, 20-HETE. The physiological actions of NO are attributed to its affinity for heme-containing enzymes including CYP enzymes. Our studies showed that NO tonically regulates the activity and production of 20-HETE and this interaction is involved in the maintenance of normal renal function and blood pressure. Thus, when NO production is inhibited, there is a disinhibition of 20-HETE effect, leading to perturbations in renal function. Inhibition of 20-HETE production therefore diminished the changes in renal and systemic hemodynamic as well as tubular effects brought about by inhibition of NO production. Our studies also provide evidence for a role for ET in NO-20-HETE interactions as administration of endothelin in the isolated perfused kidney or in the whole animal increased 20-HETE production while ETA receptor antagonism blunted 20-HETE production and attenuated the renal hemodynamic and tubular effects consequent to inhibition of NO production. A pathologic correlate for NO-20-HETE interactions was established in mineralocorticoid (volume)-dependent hypertension, an ET-sensitive model of hypertension. Thus, the attendant organ hypertrophy and renal injury in hypertension was diminished in rats treated with inhibitors of 20-HETE production and ETA receptor antagonist. In conclusion, our studies suggest that NO interacts with 20-HETE and that 20-HETE subserves a second messenger role for ET-1 in the kidney in physiological and pathological settings.

BAYO O. OYEKAN D.V.M., PH.D
Professor, Director, Center for Cardiovascular Diseases
College of Pharmacy and Health Sciences
Texas Southern University
Houston, TX 77004

Endogenous Retroviral Superantigen Driven Germinal Center Derived Lymphomagenesis

Many human non-Hodgkin's B cell lymphomas (B-NHL) are thought to be derived from germinal-center (GC) cells, including follicular small and large center cell lymphoma (FCC), diffuse large cell lymphoma (DLCL), and Burkitt's lymphoma (BL). For the generation of normal GCs, antigen-specific T cells are needed as helpers. B-NHL frequently contain CD4 as well as CD8 T cells. Unlike most solid tumors,

they express HLA class II molecules and are capable of presenting antigens to CD4+ T lymphocytes. Whether these CD4 T cells interact with, and/or respond antigen to the malignant lymphoma B cells remains obscure. Such interactions are difficult to explore in humans and studies addressing such issues are rare.



Legend to Fig. The mouse model for human germinal center derived B cell lymphoma. The spontaneous lymphomas of SJL mice are dependent on growth factors (most notably IL-5 and IL-4) produced by host CD4 T cells bearing BV16 in their T cell receptor, in response to endogenous retrovirus (*Mtv29*) encoded superantigen, vSAg29. Over 90% of the mice die form lymphoma within one year of age. Cellular interactions pertinent to lymphomagenesis include those between CD30 (on lymphoma B cells) and CD30L on host CD4 T cells; as well as those between lymphotoxin(LT)-beta (on lymphoma cells) and LT-beta receptor on follicular dendritic cells (FDC).

Studies with inbred mouse strains are, therefore, crucial for the understanding of host- lymphoma cell relationships. Analysis of the SJL mouse model for human GC-derived lymphomas has provided the most insight into the significance of normal host CD4 T cells frequently found in GC-derived B cell lymphomas. Transplantable lymphoma growth and/or primary lymphoma incidence are greatly diminished in gamma-irradiated and anti-CD4-treated normal mice. This dependence of SJL lymphoma growth on host CD4 T cells, in responsive to the lymphoma cells, is the hallmark of the phenomenon that has been dubbed “revers immunological surveillance”. The stimulatory moiety on the lymphoma cells proved to be a viral superantigen, vSAg29 (Mtv29-LTR) that stimulates host $CD4^+BV16^+$ T cells. The responding T cells elaborate cytokines (notably IL-5 and IL-4) upon which the lymphoma cells depend for their growth. This phenomenon has now also been described for lymphomas from other mouse strains of mice harboring Mtv29, and for Mtv7-encoded vSAgs. Other cellular interactions are important for lymphomagenesis, including those between CD30 (present on the lymphoma B cells and its ligand, CD30L (present on activated host T cells); as well as interactions between lymphotoxin (LT) beta bearing lymphoma B cells and LT-beta receptor bearing follicular dendritic cells (FDC). Blocking such interactions with antibodies or with other blocking reagents drastically reduce lymphoma growth.

We are now extending our studies on the mouse model into human lymphomas- looking at the repertoire of lymphoma-infiltrating T cells as well as seeking potential retrovirus-encoded superantigens or nominal antigens. Such a venture is not far-fetched, since the human genome in known to be laden with retroviral sequences (~0.6% of the genome), some of which have the potential to code for superantigens. Knowledge gained from deciphering the characteristics of CD4 T cells found in human B lymphomas, as well as the stimulating moieties on the lymphoma cells could be of great value in understanding the lymphoma process, as

well as in formulation of therapeutic strategies.

VINCENT K. TSIAGBE, PH.D.
Associate Professor of Pathology
Department of Pathology
New York University School of medicine
New York, NY 10016

Voltage-dependent Ca2+ - Channel in Cerebral Microvascular Endothelial Cells

We have investigated the presence of voltage-dependent Ca2+-channel, effects of potential vasospastic agents on [Ca2+]I, and endothelin-1 production by cerebral microvascular endothelial cells. Primary cultures of endothelial cells isolated from piglet cerebral microvessels were established and used in these studies. To investigate the role extracellular Ca2+ in vasoactive agents induced ET-1 biosynthesis, confluent endothelial cells were washed with PBS and exposed to either the thromboxane receptor agonist U-46619 (1 υM), 5-HT (0.1 mM), or LPA (1 υM) alone or following pretreatment with the Ca2+-chelating agent EDTA (100 mM), the L-type Ca2+-channel blocker verapamil (10 υM), or the antagonist of receptor operated Ca2+-channel SKF 96365 HCl (10 υM) for 15 min. ET-1 levels were elevated from 1.2±0.2 fmol/υg protein in control to 8.2±2.7 (U-46619), 4.9±1 (5-HT), or 3.9±1.9 (LPA) fmol/υg protein, respectively. Such elevated ET-1 biosynthesis was attenuated following pretreatment of cells with verapamil, EDTA, or SKF 96365 HCL. To investigate the presence of L-type Ca2+-channel in endothelial cells, [Ca2+]i was determined by fluorimeteric measurement using the Ca2+ indicator Fura-2. Superfusion of confluent endothelial cells with U-46619, 5-HT, or LPA significantly increased [Ca2+]i. Pretreatment of endothelial cells with high K+ (60 mM) or the voltage-sensitive Ca2+ channel blocker nifedipine (4 υM) diminished increases in [Ca2+]i induced by the vasoactive agents.

The novelty of the present findings are that 1) primary culture of cerebral microvascular endothelial cells expresses receptor-operated and L-type voltage-dependent Ca2+-channels, 2) breakdown products of blood-induced elevation of cytosolic Ca2+ in endothelial cells via both receptor- and voltage-operated Ca2+-channels, and 3) increases in ET-1 production from cerebral microvascular endothelial cells caused by structurally dissimilar vasoactive agents found in blood hemolysates are attenuated by Ca2+-free media, L-type voltage-dependent, and receptor-operated Ca2+-channel blockade. Elevated intracellular Ca2+ plays an important role in the modulation of endothelial functions. Regulations of endothelial cell responses by various extracellular signals are mediated via specific second messenger systems that involve cytosolic Ca2+. The regulation of intracellular Ca2+ signals is the most important functional task of ion channels in endothelial cells. The functional roles of the voltage-dependent Ca2+-channels involves the production and release of many vasoactive endothelial factors that regulate vascular tone as well as control of macromolecular traffics such as endocytosis, exocytosis, biosynthetic-secretory pathway, and transcytosis. Synthesis and release of vascular factors such as ET-1, nitric oxide, and prostacyclin by endothelial cells are

regulated by Ca2+ signaling via sustained Ca2+ entry. The presence of voltage-gated Ca2+ channel in endothelial cell is very important for such functions and has wide implications as they could play a significant role in the physiology and pathology of vascular systems. However, the presences of voltage-gated Ca2+-channels in endothelial cells have been a source of controversy in recent time. Endothelial ion channels provide Ca2+-entry pathways or the driving force for the Ca2+-influx through these pathways. Voltage-gated Ca2+-channels are responsible for the long-lasting increase in free [Ca2+]i during different stimuli and provide the signal for maintaining endothelial functions.

In conclusion, elevated intracellular Ca2+ plays a significant role in the increased production of ET-1 caused by specific spasmogenic agents and thus could be involved in the mechanism of hemorrhage-induced alteration of cerebral microvascular reactivities and development of vasospasm. In addition, we have shown the presence of voltage dependent calcium channels in cerebral microvascular endothelial cells. The increases in [Ca2+]i induced by these vasoactive agents are due in part to the activation of these voltage dependent calcium channels. The presence of voltage-gated calcium channel in endothelial cell is very important and has wide implications. Pharmacological manipulation of voltage-gated calcium channel in many cases is readily accomplished, and is also of therapeutic significance. L-type channels are very accessible to pharmacological modification and could be manipulated to influence release of mediators of endothelium-dependent relaxing factors.

Momoh A. Yakubu, PhD
Senior Scientist and Head, Vascular Biology Unit
Center for Cardiovascular Diseases
TSU, Houston

MEMBERSHIP DRIVE

AABS members are encouraged to spread the news of AABS to fellow Biomedical Scientists who are not yet registered members and encourage them to visit our web site, www.aabs-inc.org, in order to apply for their membership.

For those who haven't done so, please send your annual dues for the Treasurer at the following address:

Dr. Mohamed A. Bayorh
Department of Pharmacology
Morehouse Sch. of Medicine
720 Westview Drive, S.W.
Atlanta, GA 30310-14595
United States of America

The membership dues for the current year are:

Faculty / Scientist:	US$50.00
Postdoctoral fellow:	US$30.00
Student	US$10.00

Donations to our course are always welcome. Remember that your dues and donations are tax-deductible.

ANNOUNCEMENTS:

AABS will hold a general meeting and scientific session at Experimental Biology 2004 meeting in Washington, DC.
Date: April 19th April 2004
Place: Grand Hyatt Washington Hotel
Time: 3 p.m.
Light dinner will be provided.

SUMMER 2004 INTERNSHIPS FOR UNDERGRADUATES:

Applications are open for undergraduate students in the life sciences to pursue a 10-week paid internship in the Center for Cardiovascular Diseases, College of Pharmacy and Health Sciences, Texas Southern University, Houston.
The Internship starts on June 1, 2004.

Application forms can be obtained from the Main Office of the Center for Cardiovascular Diseases (Room 260, Gray Hall). Applications close on May 20, 2004. For more information, call 713-313-4258.

SCIENTIFIC MEETINGS:

The International Congress of the African Association of Physiological Sciences (AAPS) will hold its 4th International meeting in Tangiers, Morocco, November 21- 26, 2004. Visit the AAPS web site for details - http://uae.ac.ma/AAPSmorocco04/index/

STAFF EXCHANGE PROGRAM:

The University of Science and Technology in Kumasi, Ghana is interested in making contacts with individuals, universities or research centers who can provide sponsorship for: a) Sabbatical Teaching and Research Programs for Faculty members; b) short term staff visits for teaching and research; c) Student internships; Short term training for laboratory technicians; and d) Equipment donations.
Interested individuals should contact Prof. Sampson Agodzo at skagodzo7@usa.net
Head, International Programs Office
KNUST, Kumasi, Ghana
Tel: 233-51-60242/62168/60137
Fax: 233-51-60137.