

PASPCR



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Newsletter

Introduction... by Bill Oetting

10th Anniversary of The PASPCR Newsletter!

This is the 10th volume of the *PASPCR Newsletter*. The *PASPCR Newsletter* has actually been in existence for more than 10 years. The first PASPCR Newsletter (Volume 1, Number 1) was produced by Dick King, DeWayne Townsend and Nels Granholm in May of 1990. This was a 6 page newsletter that contained information about the PASPCR meeting in Edmonton Alberta, a message from our first PASPCR President, James J. Nordlund and an update from the first Editor-in-Chief of Pigment Cell Research, Joseph T. Bagnara. A second Volume 1 Number 1 was created by Vince Hearing in 1993, and continued to be the editor of the newsletter until 1998 when I became the editor. With the exception of the 1990 newsletter, all issues are available at the PASPCR Web site. The PASPCR Newsletter has now undergone a "face-lift". This new format will hopefully make the newsletter easier and more enjoyable to read.

The *PASPCR Newsletter* is published quarterly and is intended to serve as a means of communication for the members of our Society. You are invited to contribute articles, or other information you feel will be of interest to members of the PASPCR. If you attend a scientific meeting and have heard results which you think will be of interest to the membership of the PASPCR, please write a few paragraphs summarizing what was presented and share it with us. Any information on upcoming meetings of interest will be added to the "Calendar of Events". We also want to note any change of affiliation or address that you may have had to help us keep our membership list up-to-date. This is your Newsletter, and we depend upon you to help us make sure it best serves the Society's needs.

Contributions and comments can be sent to me, preferably by E-mail, to bill@lenti.med.umn.edu.

There are now new web addresses that will take you to the home pages of the International Federation of Pigment Cell Societies (IFPCS) and the International Pigment Cell Conference (IPCC). The IFPCS web site can be found at www.ifpcs.info and the IPCC web site is at www.ipcc.info.

The PASPCR Web Site is the major, up-to-date source of current information for the PASPCR membership. Please check you address information to make sure that it is up-to-date. The PASPCR Web site is not only a source of new information, but also a repository on the history of the Society. If there is additional information that you would like to see on the Web site, or information of past PASPCR activities, please let me know and I will

The PASPCR Web Site can be found at:

<http://www.paspcr.org>

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Calendar of Events:

July 1-5, 2002 20th World Congress of Dermatology will be held in Paris.

Contact: Philippe Fournier, 12, rue de la Croix
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Phone: 33.(0).1.44.64.15.15
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July 14-19, 2002 XIXth IUPAC Conference on Photochemistry will be held in Budapest.

Contact: The Hungarian Chemical Society, (MKE),
Fu u. 68. Hungary, H-1027 Budapest,
Phone: 36-1-201-6886
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Sept 9 - 13, 2002 The XVIIIth International Pigment Cell Conference, to be held in The Hague, Holland.

Contact: Dr. Stan Pavel, President ESPCR,
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Sept 3-7, 2003 XIth Annual Meeting of the PanAmerican Society for Pigment Cell Research, to be held in Wood's Hole, MA.

Contact: Dr. Jean Bologna.
E-mail: jean_bologna@qm.yale.edu.

2003 XIth Annual Meeting of the European Society for Pigment Cell Research, to be held in Gent.

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The *PASPCR Newsletter* is published quarterly by the PanAmerican Society for Pigment Cell Research. All views are those of the authors. For further information or to submit articles, please contact members of the Publications Committee.

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Congratulations!!!

Congratulations to new members of the PASPCR council.

**Ruth Halaban
Bryan Fuller
Brian Potterf**

We wish to thank outgoing council members, **Meenhard Herlyn, Helene Z. Hill** and **Giselle Thibaudeau**, for their contributions to our society during the last 3 years.

Corporate Sponsors by **Raymond E. Boissy**

The PASPCR would like to acknowledge and thank our Corporate Sponsors; the list below reflects contributions over the past 2 years. Financial gifts from these sponsors have allowed our Society to increase benefits to the membership far out of proportion to the actual dues collected from members. Monies contributed by these sponsors have been used over the years to support various PASPCR functions including our Young Investigator Award program, meeting travel stipends, annual meeting expenses and this Newsletter.

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A Message from the President

Fellow PASPCR Members,

I am privileged and honored to be your new president. As I address this letter to you, I reflect on the remarkable achievements of our society since its inception in 1986. Over the years, a main goal of our society has been to encourage and nurture young scientists, and foster collaborations among pigment cell research laboratories. The Pan American Society for Pigment Cell Research gave us a voice, and helped put our specialty at the forefront of science. These achievements were the making of the entire membership, under the leadership of dedicated and insightful Officers and Council members. I was once the young scientist whose career was tremendously enriched and advanced by PASPCR.

As I begin my term as President, I pledge to use my experience as a member, previous council member and President-Elect, and the lessons I learned from previous officers, to serve our society. I count on your individual support and participation in PASPCR functions and activities. We have challenges to face and goals to meet. I seek your help in increasing the membership and visibility of PASPCR, and in participating in the various committees that will strengthen the structure of our organization. I encourage to voice your suggestions and concerns, and to communicate directly with the Officers and Council members. PASPCR is YOU, and its progress is entirely dependent on your contributions and participation.

On behalf of the entire membership, I extend our sincere gratitude to Richard King, the Past-President, and James Nordlund, the past Secretary-Treasurer, for their leadership and many years of service of our society. I also welcome the new Officers, John Pawelek, President-Elect, and Raymond Boissy, Secretary-Treasurer, and Bryan Fuller, and Brian Potterf.

Sincerely,

Zalfa

Mouse News

by Lynn Lamoreux

The Wellcome Trust Congenic Mouse Repository web site is:

<http://www.sghms.ac.uk/depts/anatomy/pages/WTFGMPMR.htm>

You will see on this web site several stocks that will soon be discontinued. They are described below.

1. Melanogenesis

It is obvious that the albino, slaty and brown loci control interacting functions within the pigment cell. With this in mind, we created a panel of congenic mutant mice that can be used to study the interacting functions of the albino, slaty and brown loci in all combinations without interference from unrelated background genes. If you are interested in receiving this panel of mice or any of its subunits please let us know. We also have slaty-light on C57BL/6J and would consider replacing slaty with slaty light in this panel if there is enough interest. If you can use a panel of congenic melanocytes derived from these mice, please be sure to let us know before the mice have left us in about 3 months (June). All stocks are congenic with C57BL/6J.

The key to these old-fashioned gene symbols, for those who think molecules, is below.

Wild type <u>albino locus</u>	<u>Chinchilla</u>	<u>Slaty</u>
C/C B/B Slt/Slt <i>wild type</i>	c^{ch}/c^{ch} B/B Slt/Slt <i>chinchilla</i>	C/C B/B slt/slt <i>slaty</i>
C/C <i>b/b</i> Slt/Slt <i>brown</i>	c^{ch}/c^{ch} <i>b/b</i> Slt/Slt <i>chinchilla brown</i>	-----
C/C/ <i>b/b</i> slt/slt <i>brown slaty</i>	c^{ch}/c^{ch} B/B slt/slt <i>chinchilla slaty</i>	c^{ch}/c^{ch} <i>b/b</i> slt/slt <i>chinchilla brown slaty</i>

Albino is	Tyr ^{c-2J}
Chinchilla is	Tyr ^{c-ch}
Black is	Tyrp1 ^B
Brown is	Tyrp1 ^b
+ Slaty is	Tyrp2 ^{Slt}
Slaty is	Tyrp2 ^{slt}

We also have the following mice control stocks. We will keep albino black because it is needed for

backcrossing. Albino brown and albino slaty will go. Regarding albino cordovan, which is used in another panel of stocks to evaluate silver, see below.

Albino with Black
Albino with slaty
Albino with brown
Albino with cordovan (see below): Cordovan is Tyrp2^{b*c-J}

2. Melanocyte survival (or not)

a. White Spotting

Our belted (*bt*) stocks are also well controlled, with all genotype combinations against a uniform C57BL/6J background.

	<u>Not yellow</u>	<u>Recessive yellow</u>
Not Belted	Bt/Bt E/E	Bt/Bt e/e
Belted	bt/bt E/E	bt/bt e/e

Yellow belted mice have smaller white spots than do nonyellow belted mice (Lamoreux & Russell, *J. Heredity*, 70:31-36, 1979). The spotting phenotype of the yellow belted mice, which often includes little islands and escaper pigmented cells within the white area, suggests that the melanocytes populate the entire mouse during development and are later unable to survive in some areas of the body. This may also be true of other spotted mice, but not of all types of spotting. Interestingly, the location of the belted spot, uniquely among white-spotted mice studied, does not vary as a result of differences in background genome (Lamoreux, *Pigment Cell Research*, 12:383-390, 1998).

You will probably be more interested in our observation that the recessive yellow belted mice have a much higher incidence of hydrocephaly than is the case with congenic normal C57BL/6J mice that are neither yellow nor spotted, and also higher than that observed in the congenic black belted mice. We plan to discontinue these stocks unless interest is expressed.

b. Silver

Another panel of congenic mutant mice that we are considering discontinuing illustrates a functional interaction between silver and brown. The phenotypes of these mice do not correspond to the literature descriptions. Our unpublished observations suggest this may be for two reasons: 1. These mice are not agouti;

2. There may be one or two interacting loci in the background genome that are segregating, that are not **Mouse news (continued)**

otherwise apparent in the phenotype, certain combinations of which may be necessary for the full expression of silver that has been described in the literature. Whatever the case, black silver (*B/B si/si*) on a C57BL/6J background is barely distinguishable from wild type. However silver brown (*b/b si/si*) and to a greater extent silver cordovan (*b^c/b^c si/si*) are definitely silver in phenotype compared with the non-silver littermates. Furthermore, on this background, silver is recessive with no intermediate phenotype.

So, all in all, it is probable that another one or two "pigment" genes remain to be found that interact in the melanosome. In any case, our silver stocks are well designed to study silver in absence of confusing phenotypic effects mediated at other loci. So please let us know if you have an interest either in these mice or in melanocytes of the same genotypes.

Silver	Black B/B si/si	Brown b/b si/si
Not Silver	B/B +/+	b/b +/+
Silver	Cordovan b ^c /b ^c si/si	albino/cordovan b ^c /b ^c si/si c ^{2J} /c ^{2J}
Not silver	b ^c /b ^c +/+	b ^c /b ^c +/+ c ^{2J} /c ^{2J}

The albino stock is included in this group as a control and because of the interesting observation by Budd & Jackson (*Genomics*, 29:35-43, 1995) slaty-light mice that are also albino do not lose melanocytes as do slaty-light mice that are not albino. This is a question that has not been asked of silver – or of the silver/brown combination.

Lynn Lamoreux (MLLamoreux@hotmail.com)

Speaking of Pigs --

We are delighted that the Sinclair Swine have been saved, and even better they have been saved without us doing any of the work!!

Nevertheless, Dr. Amoss has expressed his great appreciation to our vitiligo/melanoma group for their generous offer of help in case the worst had come about and the pigs completely lost.

LL

Keep the membership informed.

If you have news about a member of the PASPCR, please let us know. Contact a member of the publications committee and we will make sure that it is in the next issue.

Positions Wanted and Available

The **PASPCR Web Site** and the **PASPCR Newsletter** contains positions wanted and available related to pigment cell research. This information is presented as a service to the members of the The Pan-American Society for Pigment Cell Research (PASPCR).

Postings for **Positions Available** will be open to all individuals and institutions so long as the position is related to pigment cell research. Postings for **Positions Wanted** will be open only to members of the PanAmerican Society for Pigment Cell Research or its sister societies (JSPCR and ESPCR). Send postings to Bill Oetting at bill@lenti.med.umn.edu. Please provide an expiration date for any submitted postings. Final decisions will be made by the Publications Committee of the PASPCR.

Positions Wanted and Available can be seen on page 13 of this Newsletter.



Image from Bill Pavan, N.I.H.

And now for the rest of the story.

Jim Nordlund has been traveling to Africa for many years, working at medical clinics in many different settings. I ask Jim to write down some observations and thoughts about his experiences during his visits.

A Visit to Eden

James J. Nordlund, M.D.

The earliest humans were thought to have lived in Tanzania, probably in the Olduvai gorge. How fortunate for humanity to have arrived in a place that can be described most easily as a garden of Eden. The snow capped summit of Mount Kilimanjaro provides the backdrop for a countryside covered with flowers and exotic foliage. And the Serengeti plains are filled with spectacular animals, zebras, wildebeests, elephants, lions and rhinoceros. Even today, these sights must be similar to those viewed in wonderment by our first parents, Adam and Eve.

Tanzania the Nation

Tanzania is a union of two nations, Tanganyika and Zanzibar which merged after they achieved independence from Great Britain. From the two names was formed the contraction "Tan + zania". Zanzibar is an island lying just 20 miles from the mainland in the Indian ocean. It had been settled by Arabs for over a millennium. Marco Polo in the 12th century visited Zanzibar. Until the beginning of the 19th century, it was actively involved in the slave trade. Zanzibar still is the world's foremost grower of cloves. Its largest city is called "Old Town" built centuries ago. Its streets are just wide enough for two people or one bicycle to pass. The buildings are quaint and hundreds of years old but charming. The lives of the people there have not changed much. Most of the work is still done with ancient techniques without the assistance of machines. The beaches of Zanzibar are spectacular. The ocean is green, warm and the beaches lined with coconut trees. Local natives use a short hemp rope wrapped around their feet to climb the coconut palm trees that reach 60 or 70 feet in height.

Tanzania was a colony of Germany from the late 19th century until after World War I when it was handed over to England in reparation for that war. The British kept it as a colony until December 9, 1961 when it gained its independence under Julius Nyerere. Nyerere

was the first president and was highly respected by Tanzanians, most Africans and by the leaders of the western nations. He was affectionately called "Mwalimu" meaning "Teacher", a title of highest respect. He died in October, 1999 from leukemia. Under Nyerere, Tanzania was allied with China and espoused socialism. Many western expatriates departed for their homes and the country fell onto hard times for complex reasons. In the 1990's Tanzania joined the western political and economic systems but it is economically far behind. It is one of the 3 or 4 poorest nations in the world. The annual family income is about \$200. Tanzania has a subsistence economy and virtually all people farm and raise chickens, goats or occasionally a cow for meat. Maize and beans are the main sources of daily food. If the weather is bad and the crops poor, famine is a certainty unless the Western nations provide assistance.

The government of Tanzania collects a mere billion dollars a year in tax income. That amount is less than what most medium sized western cities have for an annual budget. A third of this tax money is used to pay interest to western nations for loans from the World Bank. There is little money to spend on improving the infrastructure of the country. Roads, railroads, electrical systems, telecommunications, water and schools are in disrepair and require extensive rebuilding. The government can spend just \$5 per person annually for medical care, less than the cost of a few anti fungal pills!

Remarkably the people living in Tanzania are happy and most have smiles on their faces but they are not satisfied with their poverty and hard lives. They live in huts often made of mud with a thatched roof. But the walkway from the road to their home is swept clean daily. Along the walk are flowers. Craft work, carvings, flowers and other attractive items proudly decorate the front of most homes. The interior of their homes are also adorned with hand made crafts. At night these homes are warm, dry and safe. Families are together. There usually is enough food even if not always the best food. We learned from observing them that happiness is a state of mind, not a function of wealth, a fancy house or modern goods.

Water is a problem. Very few families have running water. It must be obtained daily, usually from pumps or streams that might be a mile away. Each morning one member of the family goes off to get water carried in large buckets balanced on their heads as they walk home. And virtually all water available to these people is contaminated with amoebae or other pathogens.

Kilimanjaro Christian Medical Center (KCMC)

The hospital at the Kilimanjaro Christian Medical Center was built by the Good Samaritan Foundation in 1972. Presently there are over 40 physicians and specialists from Germany, the U.S., England and other countries who work at the KCMC. There are an equal number of well trained Tanzanian doctors practicing there. All specialties are represented except for a few surgical disciplines (neurosurgery, plastic and cardiac surgery) that are available only in Dar es Salaam. Surgery, anesthesiology, orthopedics, pediatrics, urology, radiology for routine X rays and CT scans are located in this three story facility. Dermatology has a female and a male ward located on the medical service.

The Tanzania doctors are employed by the government and receive about \$100-150 monthly. Often they have a private practice to supplement their incomes. The western doctors are volunteers, missionaries or supported by foundations. They all live in modern houses supplied with running water and electricity that are located just a few blocks from the hospital. Their children go to the International School of Moshi where they study with other children whose families are from anywhere and everywhere in the world.

The hospital has over 450 beds. Often occupancy is over 100% because there are more than one person per bed. It doesn't sound attractive but there are no other hospitals as capable as KCMC. After the aisles and hallways are filled with beds, there is no more room unless two patients share a bed. It works.

The KCMC serves the hundreds of thousands of people that live around Moshi. In addition it is a referral hospital for all of northern Tanzania and southern Kenya. People often travel days to get medical help. They arrive in the outpatient clinics desperately ill and without resources to return home. Admissions are necessary to work up the problem and get them started on the way to health. A day in the hospital there is inexpensive, about 75 cents. A cesarean section costs about \$15. But for the patients, the cost is high since most have just a few dollars. Often they must buy medications after leaving. The hospital does discount costs for those who cannot afford to pay.

KCMC is dedicated to teaching Tanzania students. There is a school of nursing, medical records, for assistant medical officers, for ophthalmology technicians, for nurse anesthetists, prosthetic technicians and of course the RDTC for dermatology. There is a library but its holdings are so inadequate that it has little value. Students cannot afford textbooks. Purchasing a mod-

ern textbook for \$200 is beyond any expectations. Students take notes in class from which they study.

There was only one medical school in Tanzania located at the University of Dar es Salaam. In 1998 KCMC started a second medical school called the Tumaini (Kiswahili for Hope) College of Medicine. The first class of 16 medical students matriculated in 1998 and the second class the following year. Students are given modern textbooks of physiology, anatomy and biochemistry to use. Two students share one book. Class notes are key to learning. Even paper and pencils are limited. The students are eager, interested and want to learn. They work very hard to be the best doctors they can. A year at medical school costs about \$3000 for board, room and tuition.

KCMC does receive some support from the Tanzanian government but the amount is meager. KCMC and the medical school get most of their support from non governmental sources, especially foundations and other international relief and charitable organizations. The medical school is trying to develop an endowment to subsidize the medical school since few of the students can afford the tuition and other fees. Medical school is 6 year program similar to the programs in England. After graduating, students spend another 4 years doing a family medicine type residency. Tanzania and other 3^d world countries mostly need family doctors with general skills. Specialists are needed only in the medical centers like KCMC and in Dar es Salaam.

Regional Dermatology Training Center (RDTC) at KCMC

In the 1970's, two very prescient dermatologists, Orlando Canizares and Morris Samitz, recognized the need for advanced training in dermatology in underdeveloped nations. (Samitz 1980; Samitz and Canizares 1981) The International Foundation for Dermatology was organized and plans for the RDTC implemented. In the last 10 years, Dr. Al Kopf in the United States (Ryan 1990; Kopf 1993; Kopf, Ryan et al. 1996; Ryan 1996) and Dr. Terence Ryan in London (Ryan 1990) have done a remarkable job generating international support of all types for the RDTC.

There were three full time members of the faculty. Dr. Henning Grossman is the principal (i.e., chairman of the department) of the dermatology program. Henning and his family are from Germany. He is a dermatologist and has extensive training in tropical diseases. He is an expert in leprosy. He came to KCMC in 1990 to start the RDTC. He was responsible for

getting the program started, overseeing the construction of the RDTC school and student hostel and endless other administrative tasks.

Dr. Barbara Leppard is from the U.K. She and her husband, Jim, came to Moshi about 8 years ago. Barbara is a certified dermatologist who gave up a faculty position in England to pursue her desire to teach and assist the underprivileged and to bring them the Christian religion. She works all week at the RDTC in the clinic seeing patients and teaching students. She developed the educational program for the students. On weekends she joins with local clergy to care for the souls of those less fortunate. She recently returned to England because of illness. Her contributions to the success of this facility are immeasurable.

Dr. John Masenga is a Tanzania physician who completed a residency in dermatology in Germany. He is an expert on sexually transmitted diseases and atopic dermatitis and has taken on the additional responsibility of being Dean of the school for assistant medical officers. He will assume the duties of principal in the coming year.

The RDTC matriculates 12 or so students each year. The students come from all over Tanzania and from many other surrounding countries such as Kenya, Malawi and Mozambique. Most are the equivalent of physician assistants, called in Tanzania "assistant medical officers" or AMO's for short. They all are experienced clinicians and knowledgeable in western and traditional medicine. They care for people with all sorts of diseases such as malaria, intestinal parasites, tuberculosis, onchocerciasis, many forms of sexually transmitted diseases. They come to the RDTC to learn dermatology. They depart from their spouses and children for two years and remain mostly at the RDTC. Travel from their homes to school by bus takes 3 to 4 days one way, occasionally longer. After completing their studies and passing the examinations they return to their villages where they use their skills to teach others and care for those with skin diseases. The students are a joy to teach. They care, are interested and work hard. Over 60 students have graduated and returned to their homes in Tanzania, Kenya, Malawi and other countries.

During 1998 a 4 year residency in dermatology for medical doctors was started at the RDTC. One student has completed his training and now has returned to his home in Ghana. Another resident from Kenya is continuing her studies. Other graduate doctors have applied to the dermatology residency for future years. The RDTC building is new and very modern and was

built with international support, especially from the International Foundation for Dermatology (IFD). The building provides a new, pleasant place with modern amenities to teach the students. And it houses a clinic where people from the surrounding and even distant communities can get dermatological care while the students learn. The students and residents function in clinic much like residents in the training programs in the U.S. They care for patients under the supervision of the faculty. The RDTC has a library with a large number of excellent books, only a few of which are outdated and old. New textbooks are purchased yearly and the library is the best in northern Tanzania. It has its own copy of *The Pigmentary System: Physiology and Pathophysiology*. Journals are often incomplete. There are many volumes of the *Journal of the American Academy of Dermatology* (JAAD), the *Archives of Dermatology*, the *British Journal of Dermatology* (BJD) and some journals dedicated to tropical diseases or sexually transmitted diseases. There are classrooms and offices on the second floor.

The educational program at the RDTC is remarkable for many reasons. Two qualities stand out. First the students are taught the most modern medicine and dermatology. In addition to learning the newest information about skin diseases, these students must learn how to treat disorders with inexpensive, local resources. Impetigo is easily treated with oral antibiotics or applications of mupirocin ointment. But these medications are not available in Tanzania and are too expensive for general care. So the students learn an extensive pharmacopoeia of older treatments such as the use of gentian violet, benzyl benzoate emulsion (for scabies) or tar for psoriasis. And they learn how to prepare these medications, even tar which is obtained from local construction sites. Often they combine modern medicine with the traditional medicines of herbs and potions prepared by local traditional doctors. Respect for traditional medicine and traditional practitioners is important for insuring that patients who are not responding to traditional medicine are referred for modern care. Often herbs are inexpensive ways to treat minor conditions that are self healing.

A second feature of the program is even more important. The students are trained to teach. They are expected to practice modern medicine but they also are trained to teach friends and colleagues to practice modern medicine. This program of training teachers produces an amplification system. Each of the 60 graduates can teach 5 or 10 more colleagues to practice medicine. The result could be a huge improvement in quality of medicine practiced. Teaching teachers is equivalent to showing people how to lift themselves up

with their own bootstraps.

Dermatology and Medicine in Tanzania

Three mornings a week there are clinics at the RDTC for patient care. Two are for general care and Friday morning is restricted for a pediatric clinic. The number of patients in any clinic can vary from as few as 30 or to as many as 130. Students and faculty together see patients in 6 exam rooms. Several excellent nurses, Sisters Urrio and Sandi, and their assistants keep order in the clinic and get the patients into the proper place. After being seen by the doctor, patients stop at the pharmacy where Mr. Kasanga, the pharmacy technician, dispenses topical medications and occasionally oral medications prescribed by the physicians. Many of the topical medications are prepared by him in a formulation room made out of a shipping container that is located behind the RDTC. From powders such as hydrocortisone or lindane purchased in the U.S or Germany, he prepares topical medications that are not available from other sources, at least not at a reasonable cost.

Many of the cutaneous disorders are similar to those we see in western countries. Various forms of eczema are one of the most common dermatological problems. Acne, scabies, tinea capitis (called shillingi because the round spots of hair loss resemble the shilling coins) are routine. Some problems are not found in the U.S. Myiasis or maggots is caused by flies laying eggs on clothes that are hanging out to dry after being laundered. The eggs hatch and the larvae burrow into the skin. Myiasis can be prevented by ironing all clothes but most people do not have electricity. I had myiasis once and the treatment is application of petrolatum. The larva crawls out of the skin and the lesion is healed.

Few people wear shoes. Most wear flip-flop sandals. Sand fleas (*tunga penetrans*) that live in the dust burrow into the toes and interdigital web spaces. If not treated, the space becomes a haven for *Clostridia tetani* and the patient can get tetanus. The lesions look like warts to the unknowledgeable clinician. Of course some patients have a tropical disease such as leprosy, onchocerciasis, filariasis or elephantiasis. We saw several people who survived attacks by wild animals such as leopards.

Knowing about most of the tropical diseases is not so difficult. A few months of study brings one up to par. But the challenge is to find treatments when there are few resources. Lindane is not easy to get and a 2 ounce bottle costing \$2-3 is prohibitively expensive for many families. Scabies often is treated with benzyl ben-

zoate emulsion (BBE). The entire family must be treated several times with BBE, a large number. Households are composed of husband, several wives, many children, grandparents and relatives. Treating 20-25 people for scabies is a challenge especially since often the people walk to the clinic, a distance that can be many miles and take many hours. Gentian violet, not Bactroban, is the treatment for impetigo. Topical steroids are scarce and limited in potency and available vehicles. It is finding how to solve problems that is the challenge.

Herpes zoster or shingles is very common and is almost always a manifestation of AIDS. It is thought that about 10% of the population of Tanzania has HIV. About 60% of those in the hospital are HIV positive. A great deal of effort is being expended by the government, religious groups, volunteers and Tanzanians to stop the spread of this disease. Kaposi's sarcoma (KS) was common and generally a manifestation of HIV although we did see patients with classical and endemic KS on occasion. In Tanzania there are no systemic treatment for KS, AIDS or its complications but the RDTC does have a radiation therapy unit to palliate KS. After living and working at the RDTC it is easier to understand the slowness of Tanzanians to do the difficult things that will halt the spread of HIV. Many of the solutions for halting the progression of HIV conflict with ancient customs that have permitted these people to flourish over the last 100,000 years. Their slowness to change reminded me that American people are equally intransigent about their health. Just a few examples of western intransigence to change are the use of cigarettes and illicit drugs, obesity, and lack of exercise.

It is puzzling to learn that albinism is 10 times more common (about 1:1800 births) on the entire African continent than in the western countries (about 1:18,000). Oculocutaneous albinism (OCA) has three known genetic forms. OCA1 is caused by abnormalities of the tyrosinase enzyme, the so called western albinism. It is uncommon in Africa. OCA2 is caused by defects in the p gene. (King 1998) The function of the p protein is not known. Mysteriously almost all the albinism in Africa, Central and South America is OCA2. (Spritz 1994; Spritz, Fukai et al. 1995; Stevens, van Beukering et al. 1995) The OCA2 phenotype is distinctive. The people have a slight orange color to their hair. The skin has a similar slight orange hue and is not like the white color of OCA1. (King 1998) Some have lentiginos on the sun exposed skin. (Lookingbill 1994; Lookingbill, Lookingbill et al. 1995; Lookingbill, Lookingbill et al. 1995) Studies are on going currently to determine how pigmented lentiginos can form in an albino. All patients

with OCA2 have sun damage visible as early as 6 months of age. Actinic keratoses, solar elastosis, atrophy and actinic cheilitis are ubiquitous among the albinos. Skin cancers are common in albinos. It is mysterious that most cancers are squamous cell carcinomas. Only a few are basal cell carcinomas and melanomas are inexplicably rare. Drs. Leppard and Lookingbill started an albino project about 4 years ago. (Lookingbill 1994; Lookingbill, Lookingbill et al. 1995; Lookingbill, Lookingbill et al. 1995) Its goal was to prevent the development of cancers in albino patients and to change the prevailing customs of ostracizing albinos from local societies. I had the privilege of accompanying the team to surrounding villages hidden in the mountains to assist in this project. Patients are followed carefully with standardized data collection forms. Each is given gratis a broad brim hat, sun screens and children are given stockings and long sleeved clothes to protect them from the sun. Dr. Leppard and others have prepared a booklet translated into Kiswahili that explains albinism to the patients and their families. The program is a social success and will be a biological success.

Probably the most exciting times were flying off with "The Flying Doctors" into the hinterlands. There are dozens of hospitals staffed and supported by missionaries from western countries. These are located in isolated places not readily accessible by car or bus. Roads often are impassable except by walking. Small planes that can take off and land on the plains of Africa make these hospitals accessible to the outside world. Each month the hospitals inform by radio a central station in Nairobi of their needs for consultants. Dermatologists are desired often. I went to Nzega and to Musoma. The small plane capable of carrying 4-5 doctors and the pilot leave on a Tuesday morning. One doctor is dropped off at a different hospital. Landing on the plains is interesting. There are no runways. The pilot uses a global positioning system to navigate. After several hours the plane reaches the first hospital. The plane buzzes the field and the hospital. That warns the animals and people to get off the landing strip and the informs the hospital staff to send a car to come to the "airport". The hospitals are rather modern and nicely appointed. The medical care is first rate considering the limited resources and remoteness of the mission. Most of the doctors are AMO's with a few doctors with the M.D. degree. Appendectomies, C sections and other routine surgery is done by the AMO.

The visiting consultant stays until Friday. Patients line up outside the door until they are examined. People walk to the clinic, trips that take hours or even a day to two. No one has an assigned appointment. Staffing these clinics is hard work. On some days we saw over

100 patients. We stopped only for tea. There is just one room, poorly lit with just a desk and a small window for light and air. The window is open and those waiting to see the doctor gaze in to watch. There are so few medications. One day we decided to take a biopsy from 4 of 100 patients we had treated. After the clinic was done we spent an hour searching for 4 bottles that had caps in which to put the tissue and formalin. We had just one punch, forceps and scissors. After a biopsy, the instruments are washed and sterilized, a process that takes 30-40 minutes. The next biopsy is obtained and the process repeated. The tissue is taken back to the KCMC where it is processed and evaluated. Three or four weeks later the result is mailed to the hospital. Obviously biopsies are not done to assist the doctor in making a clinical decision. Despite the limitations, the appreciation that the doctors and people have for the consultant, the honor they bestow on him for coming makes worth the minor inconveniences.

Working on the wards at the KCMC hospital is equally exciting. We all took turns every 2 months for 2 weeks at a time. The dermatology service can have 20 to 40 patients, adults and children. They all have a dermatological disorder. In addition they might have malaria, tuberculosis, AIDS, parasites or even cancers. The dermatologist takes care of all the problems. The students are an enormous help. They get the bloods drawn, biopsies taken and other routine work done. Blood tests are available but unnecessary repetition is not appreciated. Most of the lab work is done by hand. One of my greater challenges was managing a patient with malaria, parasites, generalized psoriasis and severe pancytopenia probably from chloramphenicol ingestion. After 4 weeks of trying to keep him alive, he did survive but I would not have predicted that outcome. One of the more sad outcomes was the death of an 8 year old girl badly burned when her dress caught on fire. The entire staff worked to help her live. Her parents arranged to have her air evacuated to Germany for the best care only to learn that she died upon arrival. Severe, extensive burns in children are common since open fires are the usual way that people cook in their homes.

Living and working in Tanzania was just the greatest experience. The satisfaction from treating a patient who is miserable is great. Teaching a student who will bring relief to thousands of the world's poor is indescribable. What has been accomplished required financial help from the government of Tanzania and from international foundations. But without resourcefulness of the faculty and the ability to get things done, the effects of the money would be a minimal. We will never forget this year, the kindness of the people, the fun, excitement, the thrills just the spectacular beauty of Tan-

zania. We hope to return again, next time for a longer visit if we are so fortunate.

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This section of the PASPCR Newsletter, 'and now for the rest of the story' is an opportunity for members of the PASPCR research community to find out some of the background information and details on certain research activities that usually do not make it into the publications.

If you wish to know how a particular line of investigation got started, or know of a story that would be interesting to readers of the PASPCR Newsletter, please email me at bill@lenti.med.umn.edu, and I will try to get **the rest of the story**.

Cutaneous melanoma at the beginning of the new millennium

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The past two decades have witnessed an unprecedented progress in our understanding of melanoma biology — both at the cellular and molecular level. For several areas of cancer research, the melanoma research community has been the frontrunner when establishing new biological paradigms. We now know that all major pathways of tumorigenesis and regulatory circuits, programs and networks ("gatekeepers", "caretakers" and "landscapers") suffer deregulation in melanoma, albeit through different mechano-molecular (intra- versus epigenetic, structural versus functional) strategies, at various frequency and variable order. Some of them may be redundant, some complementary, and some mutually exclusive. What's more, the pace of molecular cancer research is even likely to accelerate, with new scientific avenues lying ahead. Complex, compelling revelations that push the intellectual borders of current biological paradigms to its limits are anticipated.

Recently, powerful models have been emerging, such as artificial skin reconstructs and orthotopic skin grafts as well as adeno- or retrovirus-based transfection of cells to overexpress or downregulate specific genes, all of which will allow us to dissect more accurately these molecular pathways and cellular events leading to melanoma. High throughput technology such as cDNA-microarray chips and the rapidly emerging field of proteomics will allow us to faster and more efficiently analyse large quantities of samples for biochemical alterations and thus be a "quantum leap" towards a molecular pathology and epidemiology. Biological paradigm shifts regarding the role of the tumor microenvironment and tissue homeostasis as well as emerging new fields such as stem cell biology are likely to fundamentally alter our thinking about melanoma. Biological events are now beginning to be understood in terms of specific molecules affecting the surrounding microenvironment, cell-cell contact, melanoma cell-stroma crosstalk, cell adhesion and migration.

For instance, it is now becoming increasingly clear that fibroblast or endothelial cell recruitment and sub-

version for the benefit of the melanoma cell is a dynamic and intricate process. It is also apparent that bone marrow stroma-derived “mesenchymal” stem cells exhibit an hitherto under-appreciated plasticity and play important roles in various physiological and pathological scenarios; especially their contributions to neoplasia are coming into focus. These observations may have profound repercussions on the future treatment of invasive and metastasizing melanoma. Consequently, it is even conceivable that the stroma may be targeted for melanoma therapy (“stromal therapy”). Another case in point: since apoptotic programs can experimentally be manipulated to produce massive changes in cell death, the genes and proteins controlling apoptosis are attractive, yet still speculative drug targets. However, voluminous evidence suggests that such strategies are feasible. Genetically, biochemically, histopathologically and clinically, cutaneous melanoma is a highly heterogeneous neoplasia. Melanoma can be seen as a spectrum of different etiopathological entities and we believe that it will be classified according to the underlying causative molecular event(s), as it is already possible for hematologic malignancies. We now understand that the melanocortin receptor 1 (MC1R) is a genetic link to melanoma and non-melanoma skin cancer; and it is genetic assessment, not skin color, that is the best indicator of skin cancer risk. The exact biological role of UV-light during melanomagenesis is coming into focus and can be experimentally reproduced. Additionally, “master” genes or switches, such as HOX genes, AP-2, MITF have been identified that sit on top of regulatory pyramids and regulate whole batteries of crucial downstream targets.

And yet, these exciting and promising achievements notwithstanding, there is still an enormous deficit in translating these findings into more effective therapeutic strategies; after all, metastatic melanoma unfortunately still remains a fatal disease. This notion becomes especially painful when measured in “lost years”, as melanoma affects more and more younger individuals. The benefits of current adjuvant therapy, such as interferon-alpha, and standard chemotherapy for metastatic disease (e.g. dacarbazine), have to be viewed sceptically when balancing efficacy (disease-free and overall survival) and therapy-related morbidity. What is to be done?

Despite the aforementioned outstanding progress,

major weaknesses remain, especially when melanoma is compared to other types of cancer. The melanoma research community has fallen behind, chiefly because it has remained comparatively small. Of the approximately \$ 50 million support from the National Cancer Institute (NCI) per year for melanoma research in the US, a major proportion is directed towards a few clinical studies. The melanoma research community does not have major advocacy groups that could raise public awareness and support.

Only a small number of collaborative groups exist in basic melanoma research worldwide, and they often lack people, tools and infrastructure to take advantage of new biomedical discoveries in the extremely dynamic environment of molecular cancer research. The large European melanoma research community, for example, has a very strong clinical infrastructure, but few centers conduct interdisciplinary or translational research. In the US, clinical care of patients with pigmented lesions is often scattered among different departments, such as dermatology, surgery, pathology and medical oncology. The number of laboratories in dermatology departments conducting pigment cell research has remained stable at best. There is an increasing shortage of dermatologists interested in pigmented lesions and trained to bridge clinical and experimental research. Thus, more investigators have to be attracted to the field and sufficiently supported intellectually and financially, especially in the beginning of their academic career — the Achilles heel for most young investigators. All of the above should help us to better dissect and understand intracellular molecular signalling circuits and heterotypic cell-cell interactions in melanoma — and ultimately to identify new molecular targets for more rational therapeutic strategies.

For many, the relatively slow progress in melanoma research and therapy has been most disappointing. Progress has been held back not only by the fact that the biological and clinical terrain we have negotiated is far more intricate than one could have imagined. Yet, although there is much more to invest and learn, we anticipate that, in the near future, this information will produce new, rational strategies to exploit melanoma pathobiology for prophylactic, diagnostic and therapeutic benefit. It is up to all of us to determine the when and where!

Positions - Wanted and Available

Postings for **Positions Available** will be open to all individuals and institutions so long as the position is related to pigment cell research. Postings for **Positions Wanted** will be open only to members of the PanAmerican Society for Pigment Cell Research or its sister societies (JSPCR and ESPCR). Send postings to Bill Oetting at bill@lenti.med.umn.edu. Please provide an expiration date for any submitted postings. Final decisions will be made by the Publications Committee of the PASPCR.

Postdoctoral Position

Polarized Kit-ligand expression in the epidermis: Its role in human melanocyte homeostasis

A postdoctoral position (fully funded for the first year with the possibility of a 2 year extension) is immediately available in the Department of Pathology, Centre Medical Universitaire at the University of Geneva, Switzerland. The project is supervised by Dr. Bernhard Wehrle-Haller and Prof. Beat Imhof and is within the frame of a collaboration between the University of Geneva and Industry.

The aim of this project is to understand the role of kit-ligand in melanocyte homeostasis in the adult epidermis and how manipulation of kit-ligand expression or localization in keratinocytes affect melanocyte behavior. The project will employ cell-biological, pharmaceutical, biochemical as well transgenic approaches (mouse) to develop methods to modify Kit-ligand localization (polarity and cell surface expression) *in vivo* and to study melanocyte behavior in response to such altered Kit-ligand presentation. For references and rationale see Wehrle-Haller and Imhof (2001, J. Biol. Chem. 276, 12667-74) and Grichnik et al., (1998, J. Invest. Dermatol. 111, 233-38).

The Centre Medical Universitaire provides a stimulatory research environment located within the City of Geneva. Research in the department is centered around problems of autoimmunity, wound healing, inflammation, cell-cell junctions and cell migration. Geneva, located at the lake of Geneva in close proximity to the French Alps, provides a rich multicultural environment facilitating social integration.

Interested candidates preferably having experience in one or more of the aforementioned domains should send their CV (e.g. e-mail) including names and contacting information of two references to:

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Postdoctoral Research Position

A postdoctoral position is available immediately to study the transcriptional co-repressor and co-activator activities of the oncogenic protein Ski in human melanomas (PNAS (USA) 97:5924-5929, 2000). Seeking individuals with experience in EMSA, *in vitro* transcription-translation, site-directed mutagenesis and yeast two-hybrid screening. Interested individuals should send inquiries and applications (including CV, a brief description of past experience and future research interests, and the name of three references) to:

Estela E. Medrano, Ph.D.
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Baylor College of Medicine
One Baylor Plaza N-803.01
Houston, TX 77030

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Research Associate/Post Doctoral Fellow Position Available

Position available for either an entry level postdoctoral fellow or a more senior research associate to study the molecular and cellular biology of the melanocyte in general and the pathophysiology of vitiligo in specific. The research project will focus globally on the role of survival factors and apoptotic regulators on the viability of melanocytes in the skin and in culture. In addition, the project will focus on the genetic and cellular susceptibility of melanocytes from patients with vitiligo to under apoptosis in response to various stimuli. Postdoctoral fellow candidate should have experience with routine molecular and cellular techniques including cell

culturing, site directed mutagenesis, and protein biochemistry. Research Associate candidate should have similar experiences utilizing the melanocyte system. Candidate will become part of an interactive research group focusing of various aspects of pigmentation in the Department of Dermatology and on skin physiology in the Skin Sciences Institute within the University of Cincinnati College of Medicine. Send curriculum vitae and list of three references to:

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Principal Scientist- Clinical Research - Skin Science Research

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Research US, 45 River Road, Edgewater, NJ 07020 or E-Mail: job.mca@unilever.com . Please place only the letters "CR-SID" as the subject of your e-mail. Unilever is an Equal Opportunity Employer m/f/d/v.

Postdoctoral Fellows - Cancer and Developmental Biology

Two NIH-funded positions are available for fellows interested in studying the Hedgehog signaling pathway in development and disease using skin as a model system. One project centers on defining the function of the Hedgehog pathway during skin appendage morphogenesis (*Dev. Biol.* 205: 1-9, 1999); a second project focuses on understanding how deregulated activation of this pathway gives rise to basal cell carcinomas (*Nature Genet.* 24: 216-7, 2000). Applicants should have a solid background in molecular and cell biology, with experience in transgenic animal models desirable but not required. Interested individuals should send a CV, letter of interest, and names of three references to: Dr. Andrzej Dlugosz, University of Michigan, Department of Dermatology and Comprehensive Cancer Center, 3310 CCGC, Box 0932, 1500 East Medical Center Drive, Ann Arbor, MI 48109-0932 Email: dlugosza@umich.edu. The University of Michigan is an Equal Opportunity Employer.

Postdoctoral Research Associate - Position available to study the biology of human inherited disorders of pigmentation using gene transfer technology. The successful applicant will have a Ph.D. and/or M.D. with experience in cell biology and molecular biology. Experience in gene transfer/genome manipulation is preferred. Please send curriculum vitae along with the names of three references to Dr. Richard King, Division of Genetics, Department of Medicine, Box 485 Mayo, 420 Delaware St. S.E., University of Minnesota, Minneapolis, MN 55455. Equal Opportunity Employer.

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