

# O F A S

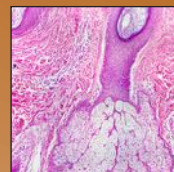
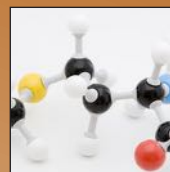
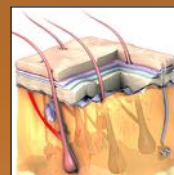
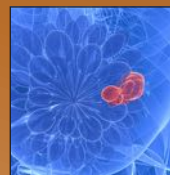
Report of the Directors

December 2011

# 50

CELEBRATING

1961 - 2011



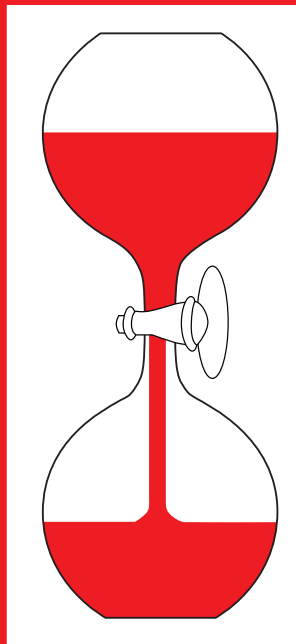
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*Life's blood flows through the hourglass; the stopcock represents the alteration of aging and disease as biomedical research progresses.*

## **1960s**

- 1961 OFAS incorporated on March 9
- 1965 -76 Plasmapheresis in dogs and rats
- 1967 First OFAS publication: aging as a significant factor in nail growth rate

## **1970s**

- 1972 -1984 Research on *Nothobranchius guentheri* first as an aging model, then as an aid in malaria control
- 1974 Reported on estrogen administration and breast cancer in MTF transsexuals
- 1975-76 Analysis of George Washington's hair
- 1997 Review: aging of skin and its appendages

## **1980s**

- 1980 Kaiser Permanente sera collection transferred to OFAS; verification of integrity of stored samples
- 1983 Improvement of animal model used for acne research
- 1985-89 Developed mouse model for androgenetic alopecia
- 1986 Developed long-hair Syrian hamster model for hirsutism research
- 1987 Moved to Biomedical Research Station in Cold Spring-on-Hudson, NY
- 1988-93 Testosterone & dihydrotestosterone metabolic studies
- 1989-93 Contact inhibitory factor (oncogene modulating factor) studies

## **1990s**

- 1990-93 Development of Plasmagel™
- 1991-2008 Serum Treasury research linking *H. pylori* infection & various cancers
- 1992-94 Extraction of 5 $\alpha$ -reductase inhibitor from saw palmetto berries
- 1992-94 Use of liposomes as drug delivery aid
- 1993 Publication of first peer-reviewed article on methionine restriction
- 1993 Collaborative study with Stanford University on effects of age on dehydroepiandrosterone sulfate concentrations in wild baboons
- 1993-2005 OFAS becomes the Editorial Office of Steroids, an international biomedical research journal
- 1995-2005 Studies on percutaneous absorption of organic chemicals, vitamins, & hormones through mouse & rat skin
- 1997 Development of skin penetration enhancers
- 1997 Lovastatin studies on hair follicles
- 1997-2000 Metformin in vitro & in vivo studies
- 1998 Studies of hypergastrinemia & risk of colorectal cancer
- 1999 Development of novel injectable materials for soft tissue augmentation

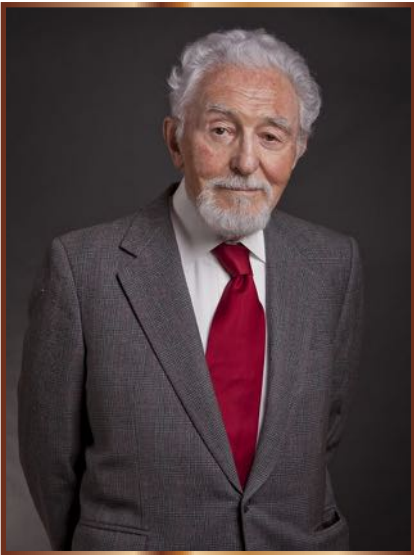
## **2000s**

- 2000 OSONE production
- 2000-03 Identification of prostate cancer serum markers
- 2001-03 Correlation between BMI, IGF-1, & binding proteins as risk factors for breast cancer
- 2001-02 Association between TNF $\alpha$  & its receptors as risk factors for breast cancer
- 2000-03 Human hair glycation as diabetes risk factor, compared with H $a_{1c}$
- 2002 Use of IGF-1 as a biomarker in epidemiologic studies
- 2003 Pet Animal Serum Treasury established
- 2004 Nanobacteria as cardiovascular risk factor
- 2004 Alzheimer's study—serum markers
- 2004 Publication of the first issue of VitaLongevity™, a newsletter on health strategies and lifespan
- 2005-06 Studies on prostate cancer risk factors in blacks & whites
- 2006 Study of effects of methionine restriction on adiposity & insulin sensitivity
- 2006 Dr. David Orentreich joins Dr. Norman Orentreich as Co-Director of the Foundation
- 2007 Studies on effect of blueberry consumption on hearing & cognition
- 2007 Therapeutic Silicone Technologies, Inc., founded
- 2008 Collaboration with Oxford University on methionine restriction effects on adiposity: implications of cysteine supplementation
- 2009 Dr. Perrone appointed Assistant Director of Scientific Affairs

## **2010s**

- 2010 Studies on methionine restriction & mitochondrial function
- 2010 Collaboration with Penn State University to develop methionine-restricted diet studies for humans
- 2011 Angiotensin-converting enzyme 2 as a biomarker of incident acute myocardial infarction independent of traditional risk factors
- 2011 Dietary methionine restriction increases fat oxidation in obese adults with metabolic syndrome X

# Co-Directors



**Norman Orentreich, MD, FACP**  
**Co-Director**

Norman Orentreich, MD, FACP, in six decades of dedicated service to medicine, has always been on the cutting edge of new discoveries and innovations in the fields of dermatology and cosmetic surgery. He pioneered hair transplant surgery; was the first President of the American Society for Dermatologic Surgery; was Clinical Professor in the Department of Dermatology at the New York University School of Medicine; advised numerous medical facilities; provided dermatologic services to international heads of state; and held membership in over 50 medical societies. Over the years, he created and developed numerous procedures and treatments for skin, hair, and nails. He has also invented and patented therapies and medical devices for rejuvenating scarred and aging skin, including the Buf-Puf™ (1975).

In 1961 Dr. O (as he is called by staff and patients) founded OFAS. His early work built upon the wound healing and aging studies of Dr. Alexis Carrel, which he had discovered during his undergraduate career. Under Dr. O's guidance, research at OFAS has expanded to encompass studies on aging, cancer, dermatology, and serum

biomarkers, resulting in over 200 papers in peer-reviewed periodicals and books.

Recognizing the potential benefit of serum biomarkers of disease and wanting to ensure its availability for future researchers, Dr. O coordinated the transfer of a collection of archived serum samples from the Kaiser Permanente Medical Care Program. This would become the OFAS-Kaiser Permanente Serum Treasury that was early on recognized by the World Health Organization as "among the most valuable resources currently available in biological banking."

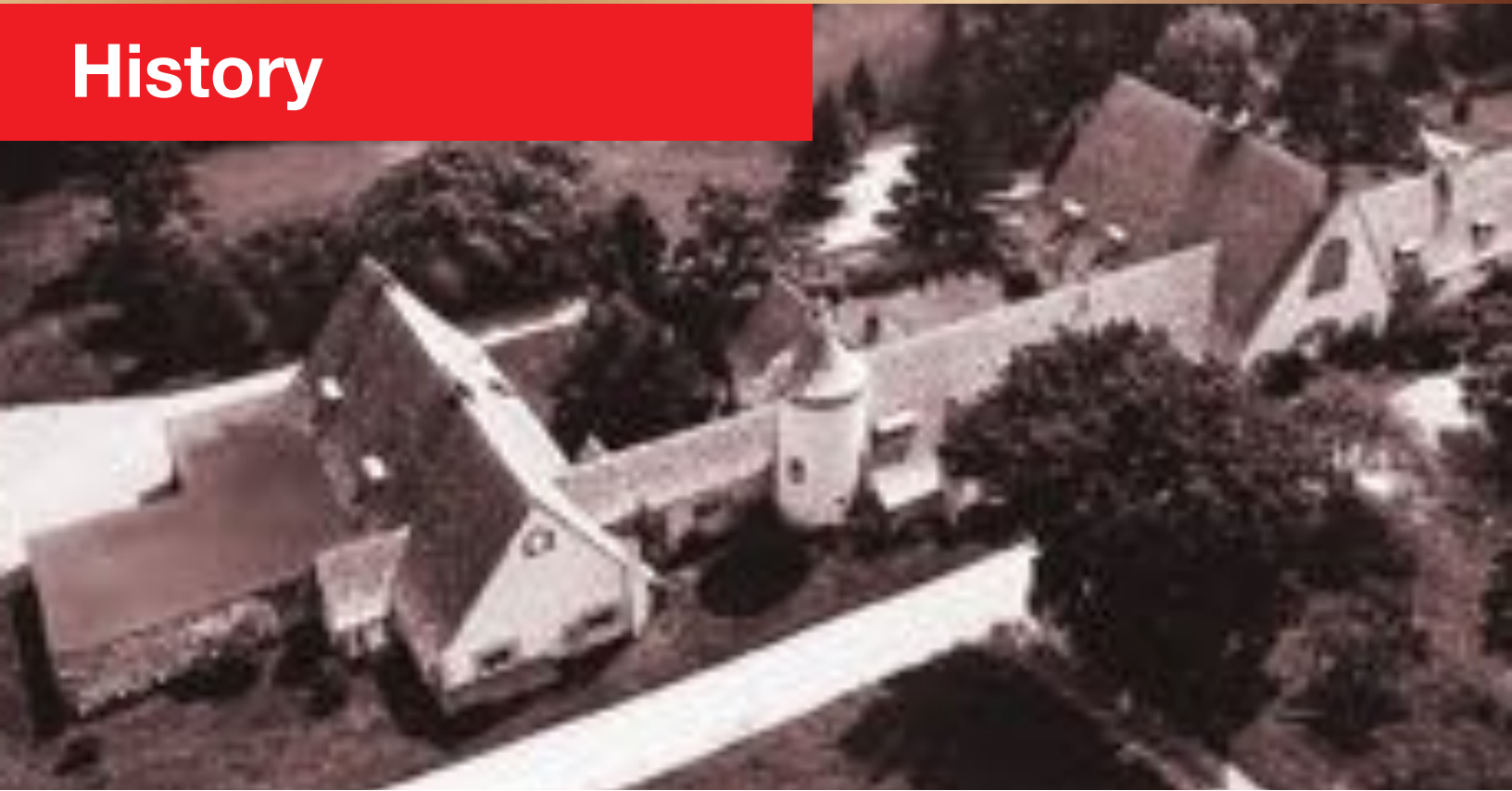
Dr. O, working with his son, fellow dermatologist, and Co-Director Dr. David Orentreich, has lectured internationally on procedures developed at the Orentreich Medical Group, LLC, and on research at OFAS; together they have written hundreds of articles for international publication in medical journals and textbooks.



**David Orentreich, MD**  
**Co-Director**

David Orentreich, MD, in practice since 1984, is one of the nation's leading dermatologists. He received his MD from Columbia University College of Physicians and Surgeons in 1980. At the Orentreich Medical Group, LLC, he has helped to create numerous therapeutic procedures and treatments for skin, hair, and nails and has developed medicines and medical devices for the rejuvenation of scarred and aging skin. He has been affiliated with OFAS since 1984 and in 2006 became its Co-Director. In addition to his clinical work and scientific research, he holds the appointment of Assistant Clinical Professor in the Mt. Sinai School of Medicine's Department of Dermatology and has served as a research consultant to Clinique Laboratories, LLC, since 1987. He lectures nationally and internationally on current medical and surgical procedures developed at the Orentreich Medical Group, LLC. He has authored and co-authored over 35 publications, including peer-reviewed articles and book chapters.

# History



Norman Orentreich founded the Orentreich Foundation for the Advancement of Science, Inc., in 1961. OFAS is a 501(c)(3) tax-exempt entity classified by the IRS as a private operating foundation, meaning that it performs its own research. Our earliest investigations evolved from our founder's clinical work as a dermatologist as well as from his interest in aging and wound healing.

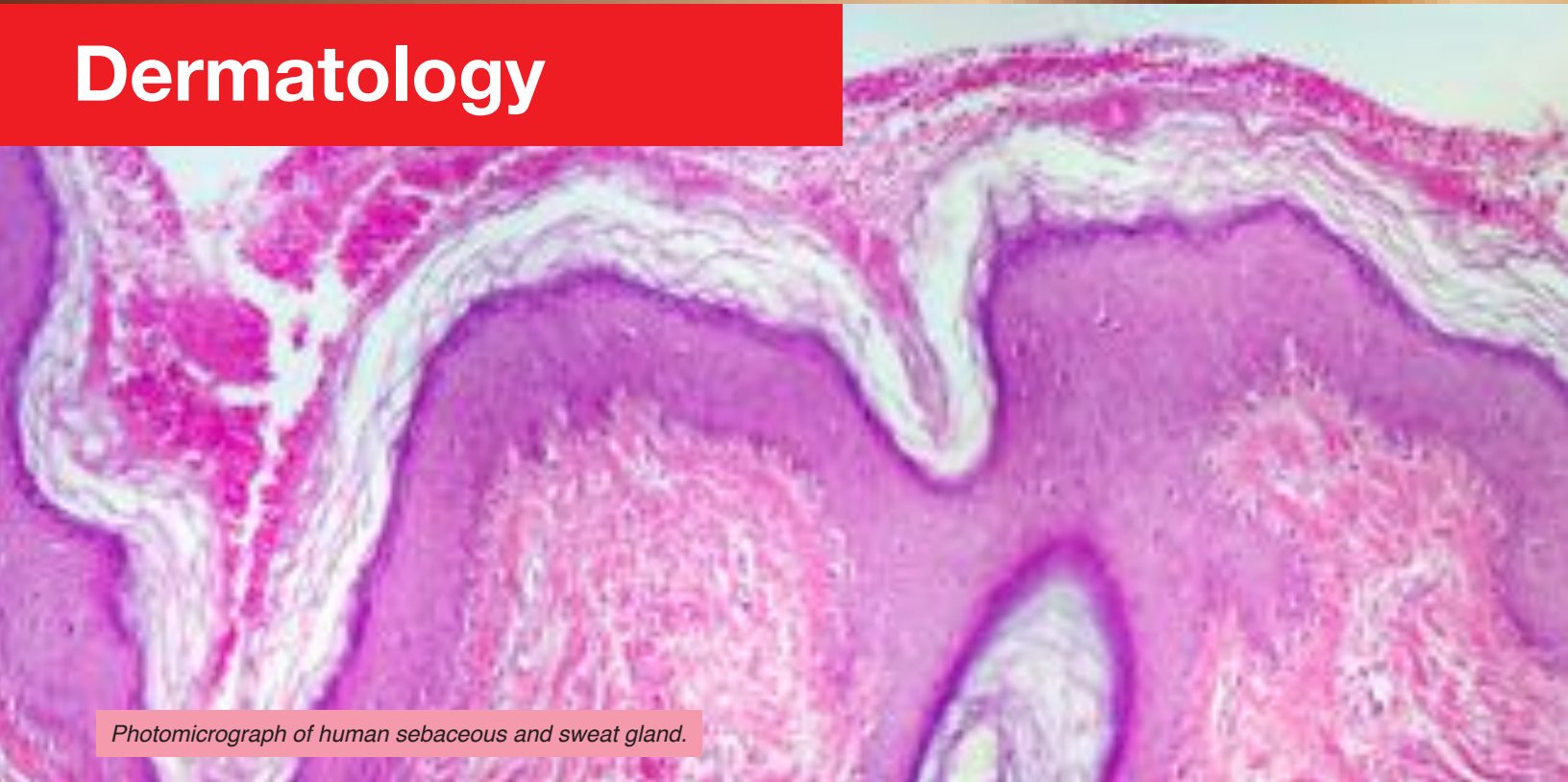
In time, OFAS became more broadly dedicated to biomedical research that prevents, halts, or reverses those disorders that decrease the quality or length of life. While studying the annual fish *N. guentheri* as a model for aging, we discovered its potential as an aid in malaria prevention, leading to our collaboration (one of our first) with the World Health Organization. During investigations into methionine as a hair-growth treatment, we discovered its potential significance for the development of aging and disease prevention strategies.

Creation of the OFAS-Kaiser Permanente Serum Treasury has been crucial to furthering our research goals. In 1984, OFAS published a paper confirming the integrity of the samples; despite their long time in deep freeze at Kaiser Permanente, they could be used as effectively as freshly drawn samples. Since that time, we have published, typically in conjunction with the Kaiser Permanente Division of Research, over 40 papers, amply demonstrating the utility of this unique resource; for example, the Serum Treasury was used to definitively establish the causal connection between *H. pylori* and stomach ulcers.

In the mid-1980s, the need for consolidated facilities became evident. Our laboratories at that time were spread throughout New York City. As our research program expanded and the need to coordinate the work of our laboratories grew, we sought a new location where we could fully integrate our labs. We found the perfect location in Cold Spring-on-Hudson, NY. Our new quarters, housed in a renovated English-style barn, satisfied both scientific and aesthetic considerations, providing ample space for our labs in a single facility set amid the picturesque landscape of upstate New York.

Once fully operational at our new location, we began work on research that remains central to our program: healthspan extension through methionine restriction. OFAS has been at the forefront of this research for nearly 20 years. During this time, we have found that a diet low in the essential amino acid methionine increases lifespan and decreases the incidence of age-related diseases such as diabetes and dyslipidemia. Having produced more than a dozen publications on the topic and formed active collaborations with other organizations pursuing this study, OFAS enters its second half-century exploring the mechanisms by which this dietary intervention extends healthy lifespan. Once our findings are complete, we can look forward to translating this basic metabolic phenomenon into a preventive or therapeutic intervention that is practical and convenient for humans.

# Dermatology



Photomicrograph of human sebaceous and sweat gland.

Dermatologic conditions, while not often life-threatening, profoundly affect an individual's psychological and emotional well-being. After developing hair transplantation in the 1950s, Dr. Orentreich directed OFAS research to seek ways to cure or relieve a variety of these conditions.

Our focus has typically been on the pilo-sebaceous apparatus (the sebaceous glands and hair) and its disorders. We developed the mouse model for **andro(chrono)genetic alopecia (AGA)** and modified the ear sebaceous gland model of the Syrian golden hamster. Throughout the '80s and into the '90s, we utilized these and other models to investigate potential topical anti-androgen treatments for hair loss and acne. We found that compounds inhibiting the  $5\alpha$ -reduction of testosterone to dihydroxytestosterone (DHT) and preventing DHT from binding to its intracellular receptor had many beneficial implications for acne and baldness therapies.



Teddy bear hamster, a model we developed for use in hirsutism research.

In our investigations for **acne treatments**, we found that combinations of anti-androgens at very low concentrations are more effective than the same combinations at higher concentrations, reducing the risk of systemic side effects while maintaining efficacy, and that adding microdoses of other compounds such as triamcinolone acetone or Vitamin D3 further reduced sebaceous gland size. We determined that methyl caprate, a fragrant oil found in apricots and pineapples, increases the skin's

penetrability and, thus, the effectiveness of these topically-applied drugs.

We screened a wide range of compounds for efficacy using the sebaceous gland in the AGA model; we also screened anti-hypertensive drugs, including Minoxidil. Minoxidil proved quite effective in retarding the progression of androgen-dependent hair loss in this model. Later, we looked at the ability of nonbalding AGA mouse skin to metabolize major and minor androgens and found that there was no unusual androgen metabolic profile, *i.e.*, its skin was similar to human skin, therefore providing a useful model for AGA.

We transplanted both bald (miniaturized) and nonbald human hair follicles from the same donors (male and female) onto immunodeficient mice. The nonbald follicles continued to produce hair successfully and the miniaturized follicles returned to producing full-bodied hairs. These findings elevated this mouse model from being a simple screening tool to serving as an effective means for studying the mechanism of hair loss in both men and women.

## The AGA Mouse Model

In the 1980s, a large portion of our research was devoted to androgen-dependent conditions such as alopecia, hirsutism, and acne. Macaques, the most-studied nonhuman model for common baldness, are scarce and expensive to maintain. By selective breeding and routine testing for androgen-mediated cutaneous responses, we developed a substrain of the B6CBA mouse that expresses andro(chrono)genetic alopecia (AGA) when treated exogenously with testosterone. Our studies demonstrated that hair loss in the AGA mouse was androgen-dependent; the new model was appropriate for the screening of compounds that might influence the balding process in humans.



# Disease Prevention



One of some two dozen species of *Helicobacter* that reside in the intestinal tract of animals and human beings, *H. pylori* is between 2.5 and 5.0 microns long and lives beneath the mucus layer of the stomach. Courtesy of Luke Marshall, *Helicobacter* Foundation

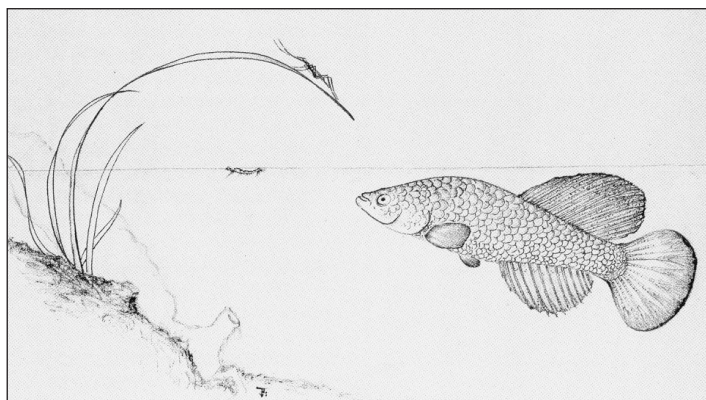
OFAS has always had a focus on preventive medicine. Two of our most interesting areas of research involved a common bacterium and a crafty killifish.

*Helicobacter pylori* (*H. pylori*) is the bacterium responsible for most stomach ulcers and many cases of chronic gastritis. It can weaken the stomach's protective coating, allowing digestive juices to irritate the sensitive stomach lining. As much as half of the world's population may be infected with *H. pylori*. Most infections occur in persons living in developing countries or crowded, unsanitary conditions where bacteria are passed from person to person. Usually contracted in childhood, *H. pylori* grow only in the stomach.

OFAS has performed research in a series of collaborations with Kaiser Permanente Division of Research and Stanford University Medical School Department of Health Research and Policy (1995-2007) linking this bacterium to more than ulcers. Infection with *H. pylori* is associated with an increased risk of **gastric adenocarcinoma** and might be a cofactor in its pathogenesis with certain substrains playing different roles. *H. pylori* infection is also associated with non-Hodgkin's lymphoma affecting the stomach.

Interestingly, the absence of *H. pylori* infection, independent of cigarette smoking and body mass index (BMI), is associated with a marked increase in risk of developing **esophageal adenocarcinoma**, but results suggest that *H. pylori* infection is not associated with the development of pancreatic cancer.

We began studying the annual fish *Nothobranchius guentheri* for potential use as an aging model but found that its greatest use might lie in the field of disease prevention. These fish have adapted to extreme environments by entering a dormant phase during drought conditions. In a cooperative study with the World Health Organization, OFAS staff conducted **malaria** field control trials in Sri Lanka and Zambia. The embryos of these fish survived in dried-up ponds until the rains returned, at which point they resumed development and feasted on the newborn larvae of malaria-bearing mosquitoes. Fewer larvae achieving maturity means fewer disease-bearing adult mosquitoes and, subsequently, fewer malaria infections in the human population.



*Nothobranchius guentheri* eating mosquito larvae.

# Cancer



Cancer has been a significant topic of research at OFAS, including numerous collaborations, since the early 1980s. As with other diseases, the majority of our efforts have been preventive in nature, directed toward discovering reliable methods both to predict and to lower the risk of tumor development. Many of these studies have been accomplished through the use of the OFAS-Kaiser Permanente Serum Treasury.

One in six men in the US will develop **prostate cancer** in his lifetime. In collaboration with researchers at Duke University and Kaiser Permanente Medical Care Program (KPMCP), we have found that, for older men, low levels of serum Vitamin D are associated with increased prostate cancer risk. Increasing Vitamin D intake or getting more through modest sun exposure may help to decrease this risk. However, higher levels of Vitamin D may be associated with increased development of **basal cell carcinoma**. In a study conducted with Duke University, Harvard School of Public Health, and KPMCP, no protective effect was found between Vitamin D and breast cancer incidence in women, but high levels of HDL-cholesterol might increase risk of **breast cancer** in post-menopausal women.

We determined, in partnership with Hoffmann-La Roche and KPMCP, that of the two dietary sources of Vitamin A, the vegetable-sourced  $\beta$ -carotene offers protection against **lung cancer**; lower levels are strongly associated with increased risk of developing lung cancer. The animal-sourced form, retinol, was not associated with lung cancer risk, according to the finding of a study OFAS performed in conjunction with KPMCP, Columbia University, and the National Cancer Institute.

In collaboration with scientists at Stanford University, the University of Michigan, and KPMCP, we have studied gastrin, a hormone secreted in the stomach, in relation to gastric and colorectal cancers. Higher than normal serum gastrin levels are associated with a marked increased risk for **colorectal carcinoma**. These high levels, when combined with low serum pepsinogen, are also a powerful predictor of future **gastric cancer** risk.

# Diet and Healthspan



*Laboratory technicians have a rat run on a rotarod treadmill, which measures motor function and is a useful tool in assessing aging in laboratory animals.*

OFAS began research on methionine because it is a major contributor to the protein in hair; we showed that hair production is more than doubled by just a small increase in methionine intake by the long-haired hamster. But far more important results came from restricting methionine intake.

Research revealed that dietary methionine restriction (MR) produces profound effects on aging and development. Specifically, rats develop at a slower rate and live about 50% longer when fed a low-methionine diet. The metabolic profile of these animals remains 'youthful' well into old age. Notably, the MR diet leads to lower body weight, less fat accumulation, improved insulin sensitivity, and reduced incidence of age-related diseases such as diabetes and dyslipidemia.

Having discovered these remarkable effects of the MR diet, we now seek to determine and understand the mechanisms by which MR works. Our research has shown that the reduced fat accumulation is not from caloric restriction; indeed, MR rodents eat more than their control-fed counterparts. Results indicate that adiposity resistance is associated with mitochondrial biogenesis in fat and with increased mitochondrial aerobic capacity in liver and skeletal muscle. In relation to its effects on dyslipidemia, MR disrupts the lipogenic/lipolytic balance, contributing importantly to adiposity resistance in Fisher F344 rats.

We have recently engaged in collaborative research based on results from the Hordaland Homocysteine Study showing a direct correlation between cysteine (a metabolite derived from methionine) and obesity in humans.

Supplementation of MR diets with cysteine reversed MR's effects on decreased adiposity in rodents, confirming that cysteine is a key component in fat mass accumulation. Cysteine is used by the body for the synthesis of two important antioxidants, glutathione and taurine, levels of which are also decreased by MR in rats. Taurine has been reported to control adiposity in humans; therefore, taurine supplementation studies were also conducted and showed that taurine was not associated with the desirable MR effects on adiposity. Because cysteine supplementation does not restore methionine levels in rats, we are currently examining whether the lifespan extension effects of MR are a consequence of reduced methionine or its metabolite, cysteine.



*This B6C3F1 Hybrid mouse is a model we use for our methionine restriction studies. This type of mouse is used for a broad range of research applications, including aging studies.*

# Medical Devices



Therapeutic Silicone Technologies, Inc. (TST), a clinical research subsidiary of OFAS, focuses on preventing complications common in the diabetic population. Its purpose is to conduct human studies and engage in collaborative research with other institutions. TST also seeks licensing opportunities for our medical devices as a means to fund research at OFAS.

Diabetes incidence is increasing rapidly in the United States. Between 1980 and 1995, the number of diabetes patients in this country was a relatively stable 5 to 8 million; by 2010, the number had risen dramatically to 25.8 million, or 8.3% of our population, according to CDC statistics released January 26, 2011. The American Diabetes Association says that the disease could actually lower average life expectancy of Americans for the first time in a century.

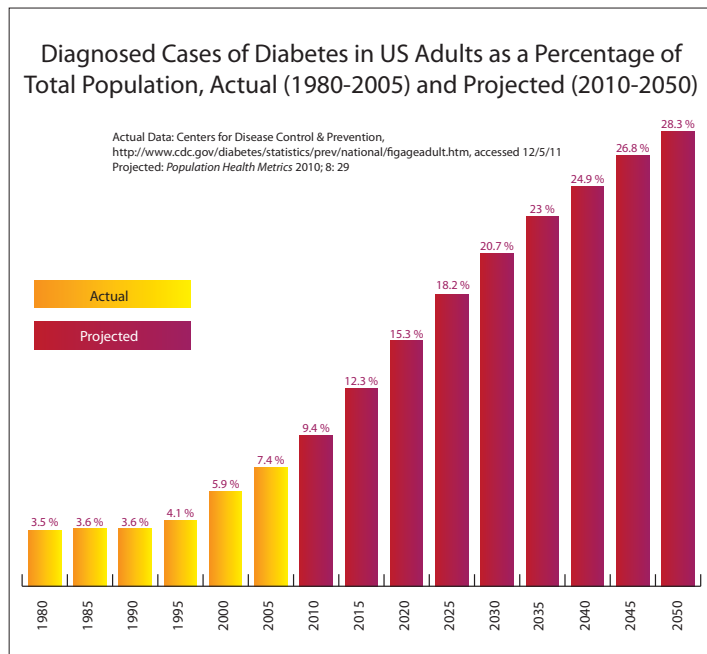
Common and dreaded complications of diabetes are lower extremity ulceration and amputation. There is currently no satisfactory treatment to deal with this enormous public

health problem. As a result, physicians continue to seek new tools to prevent pre-ulcerative foot lesions.

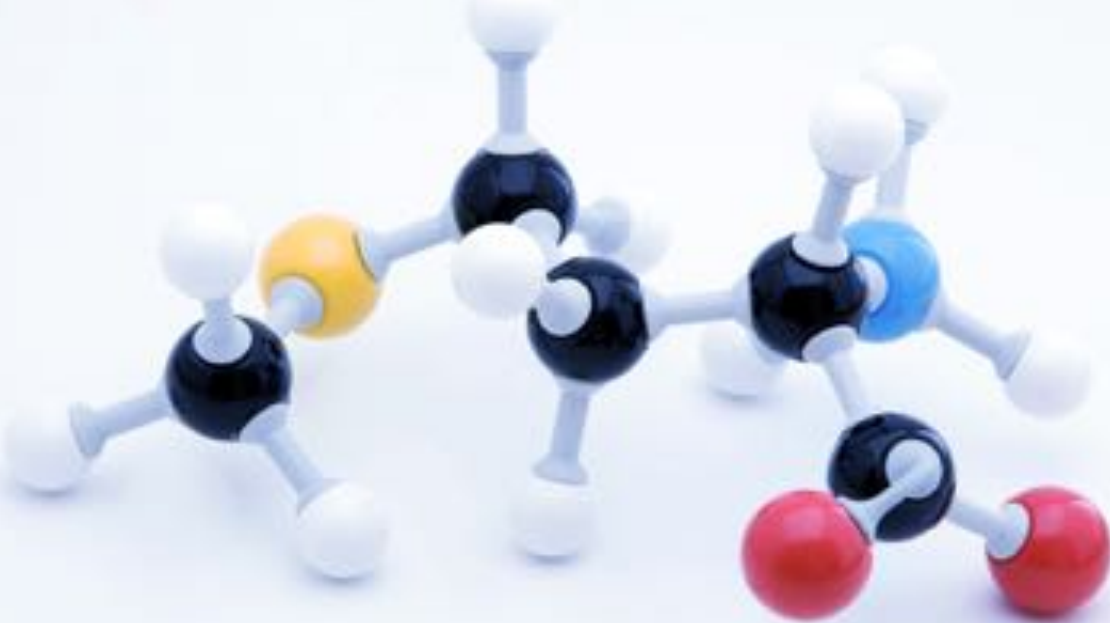
The goal of TST is to launch a clinical trial to evaluate the efficacy of a liquid injectable silicone, OrthoSil™, for the

prevention of foot ulcers in the high-risk population of diabetic patients. High risk is defined by the presence of diabetes, neuropathy, and history of ulceration, all independent risk factors for lower extremity ulceration/re-ulceration and subsequent amputation. It is expected that OrthoSil would not only reestablish the internal 'padding' of the diabetic foot at high-pressure sites by decreasing the pressure responsible for the wounds but would also significantly reduce reliance on patient foot care compliance, often a challenge in disease management.

OrthoSil would serve as a permanent "internal orthotic," a stable, cushion-like soft tissue prosthesis augmenting and simulating natural tissue padding.



# Future Directions



*3D representation of the Methionine molecule*

Improvements in public health and medical technology have extended average human lifespan dramatically in the past century. As good as these extra years can be, they are all too often marred by age-related disorders such as metabolic syndrome X, diabetes, dyslipidemia, and cardiovascular disease. Our studies in animals thus far have shown that methionine restriction (MR) not only increases lifespan but also delays or prevents these conditions of advancing age; however, the mechanisms behind this action are unclear. Continuing our studies in animal models of aging, obesity, and diabetes, we seek to elucidate the various metabolic and signaling pathways affected by MR. Other methods of dietary intervention will also be relevant to advancing knowledge in the study of obesity and diabetes. We hope these studies will lead to identification of a novel molecule as a potential target for treating some of the risk factors of these age-associated diseases.

Even as we work toward identifying the mechanisms by which MR extends healthspan, we are beginning the process of moving to clinical trials to determine MR's efficacy in humans. If MR shows the promise we believe

it will, we can move forward to work with nutritionists and other medical experts on developing human dietary interventions that mimic methionine restriction in rodents.

As we embark on the next phase of our mission—to prevent, halt, or reverse those disorders that decrease the quality or length of life—by translating our years of animal research into effective human applications, we are also working to expand OFAS in other ways. We seek to grow internally with the addition of new scientists; to broaden our collaborations with medical and academic institutions; to institute community involvement and internship programs; to recreate our facilities in the form of energy efficient, sustainable laboratories; and always to maintain the high standard of laboratory practices and research methods that have brought us to this 50<sup>th</sup> anniversary year.

# Collaborations



## Oxford University and the University of Oslo

Since 2008 OFAS has been conducting collaborative work with investigators at Oxford University and the University of Oslo. Because methionine restriction (MR) reduces fat mass in rats, studies were conducted to determine the effects of MR on obesity. In collaboration with Drs. Helga Refsum (University of Oslo), and Amany Elshorbagy (formerly at Oxford University, now at University of Alexandria, Egypt), we examined whether methionine or products from methionine metabolism regulate fat mass accumulation. Our continuing collaborations will also provide information to confirm or refute hypotheses postulating that obesity is a key modulator of lifespan.

## Penn State University

MR not only extends lifespan and reduces adiposity in rodent; it also produces favorable health effects by improving glucose sensitivity and reducing cholesterol. A crucial aspect of our MR research is the question of whether it can be translated to humans. We are currently collaborating with Dr. John Richie, Professor in the Public Health Sciences Department of the College of Medicine, Penn State University, who joined OFAS as a consultant, to develop protocols to extend MR studies to humans. Dr. Richie recently directed a human MR study to examine the effects of this dietary intervention on antioxidants such as glutathione.

# Energy Efficient Laboratories



Although architecturally striking—constructed in the 1910s as an English-style barn—the building that houses the OFAS laboratories presents challenges when it comes to energy performance. With its low-efficiency envelope and heating and cooling systems nearing the end of their design life, the design of the structure adversely affects operations and maintenance costs, as well as systems reliability.

In 2010-11, in an effort to move toward best energy practices, OFAS underwent a comprehensive energy audit resulting in a schedule for program development. The study, conducted by L&S Energy Services in collaboration with the New York State Energy Research and Development Authority (NYSERDA), resulted in a plan for energy conservation measures (ECMs) that could reduce consumption up to 30%.

This year we have begun implementing various recommended measures, such as installing variable air volume systems, an energy-efficient cooling system, temperature setbacks, and replacement of lighting units. The payback period for these measures ranges from 0.4 to 3 years; rebates from NYSERDA contribute to the cost savings. We have already noticed increased energy efficiency owing to these measures.

In the years ahead, OFAS will continue to implement its green laboratory program to reduce energy consumption and eliminate energy inefficiencies.

# Publications

## 2011 Publications

Dietary methionine restriction increases fat oxidation in obese adults with metabolic syndrome.

Plaisance EP, Greenway FL, Boudreau A, Hill KL, Johnson WD, Krajcik RA, Perrone CE, Orentreich N, Cefalu WT, Gettys TW. *Journal of Clinical Endocrinology and Metabolism*, 2011; 96(5):E836-40.

In preclinical reports, restriction of dietary methionine intake was shown to enhance metabolic flexibility, improve lipid profiles, and reduce fat deposition. Collaborating with researchers at Pennington Biomedical Research Center, we performed this 'proof of concept' study to evaluate the efficacy of dietary methionine restriction (MR) in humans with metabolic syndrome. Sixteen weeks of dietary MR in subjects with metabolic syndrome produced a shift in fuel oxidation that was independent of the weight loss, decreased adiposity, and improved insulin sensitivity that was common to both diets.

Circulating angiopoietins-1 and -2, angiopoietin receptor Tie-2 and vascular endothelial growth factor-A as biomarkers of acute myocardial infarction: a prospective nested case-control study.

Iribarren C, Phelps BH, Darbinian JA, McCluskey ER, Quesenberry CP, Hytopoulos E, Vogelmann JH, Orentreich N. *BMC Cardiovascular Disorders* 2011; 11:31.

With scientists at Kaiser Permanente Division of Research and Aviiir, Inc., we examined the association between circulating levels of markers of angiogenesis with risk of incident acute myocardial infarction (AMI) in men and women. Our data support a role of angiopoietin-2, a protein growth factor that promotes the formation of blood vessels, as a biomarker of incident AMI independent of traditional risk factors such as educational attainment, hypertension, diabetes or smoking.

2011 blueberry health study report: memory scores continue to improve; power milestones bring personalized research closer. (abstract)

Burns DJ, Doiron DL, Raphaelson HA, Hull K, Kokesh AD,

Kristal BS, Pruchnicki A, Sachs BS, Schnoll R, Vogelmann JH, Wetherell A, Martin R

**40<sup>th</sup> Annual Meeting of the American Aging Association, June 3-6, 2011, Raleigh, NC, #121.**

In a collaborative effort with a number of institutions, including Brigham & Women's Hospital (Boston, MA), we have been investigating the effects of blueberry consumption on memory. Since 2002, the data have shown continually increasing scores on memory tests by persons consuming wild blueberries on a daily basis.

Dietary glycine supplementation mimics lifespan extension by dietary methionine restriction in Fisher 344 rats.

Brind J, Malloy V, Augie I, Caliendo N, Vogelmann JH, Zimmerman JA, Orentreich N

*The FASEB Journal*, 2011; 25:528.2.

Dietary methionine restriction (MR) extends lifespan in rodents by 30–40% and inhibits growth. Since glycine is the vehicle for hepatic clearance of excess Met, we hypothesized that dietary glycine supplementation (GS) might produce biochemical and endocrine changes similar to MR and also extend lifespan. In GS rats, both median and maximum lifespan increased. Body growth reduction was less dramatic. Long-term GS resulted in reductions in mean fasting glucose, insulin, IGF-1, and triglyceride levels. Adiponectin, which increases with MR, did not change in GS.

## Manuscripts in Preparation

- Genomic and metabolic responses to methionine restriction in Fisher 344 rats
- Methionine restriction protects against diet-induced obesity and insulin resistance in C57BL/6J mice
- Methionine restriction prevents and reverses steatosis in the obese mouse
- Review: Methionine Restriction



# Staff



**Bernardita P. Calinao, PhD**  
**Deputy Director**

Dr. Calinao has over 20 years of management experience. She served as a consultant for OFAS in 2007 prior to her appointment as Deputy Director in 2008. She is responsible for general financial operations and those of research and other projects, such as the implementation of a facility-wide energy program. Dr. Calinao is a Human Ecologist and holds a doctoral degree in Environmental Planning from the State University of New York College of Environmental Science and Forestry.

**Carmen E. Perrone, PhD**  
**Assistant Director of Scientific Affairs & Director of Cell Culture Laboratory**

After receiving her doctorate in Cellular Biology from the University of California, Los Angeles (UCLA), Dr. Perrone conducted post-doctoral research at Brown University and the American Health Foundation. In 2000 she was appointed Research Assistant Professor in Pathology at New York Medical College. Dr. Perrone joined OFAS in August 2005 as Director of the Cell Biology Laboratory; in 2009, she accepted the additional position of Assistant Director of Scientific Affairs. While overseeing research efforts in all of our labs, she continues to conduct her own experiments and is directly involved in many of our methionine-restriction diet projects.

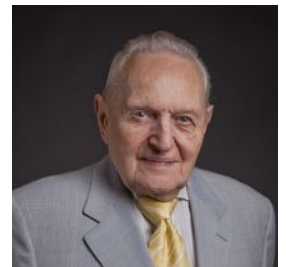


**Gene Ables, PhD**  
**Director of Animal Sciences Laboratory**

Dr. Ables received his doctorate in Veterinary Medicine from Hokkaido University (Japan). His post-doctoral research in preventive medicine and nutrition at Columbia University focused on obesity, specifically liver lipid metabolism. In 2006, he was appointed Associate Research Scientist at the Columbia University Medical Center. Dr. Ables joined OFAS in April 2011 as a Senior Scientist and was recently appointed Director of the Animal Sciences Laboratory where he is currently leading staff in investigations of the methionine-restricted diet's effects on lipid and glucose metabolism, as well as its effects on the immune system.

**Joseph H. Vogelmann, DEE**  
**Senior Scientist**

Prior to joining OFAS, Dr. Vogelmann was a senior manager in the United States Air Force for defense research and development projects and a senior corporate executive for management of research and development. At OFAS, Dr. Vogelmann has served as Technical Director of the Advanced Clinical Blood Laboratory since 1975 and as the designer of the computer system and creator of the computer software for cataloguing, locating, and indexing the more than 1 million samples in the OFAS-KP Serum Treasury. He also serves as the OFAS-designated principal investigator for all collaborations that use the OFAS-KP Serum Treasury.



**Virginia L. Malloy, MS**  
**Safety & Compliance Officer**

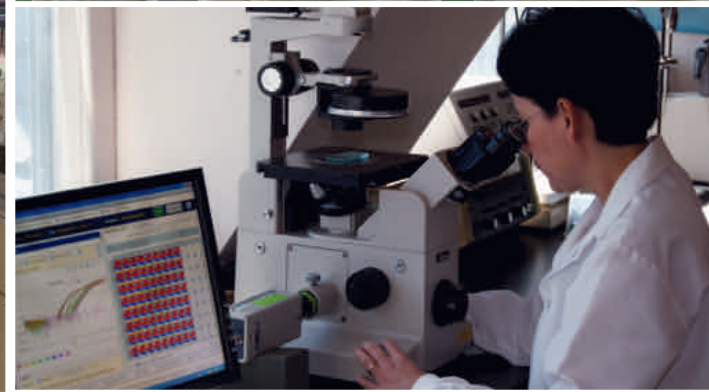
Ms. Malloy began her tenure at OFAS shortly after receiving her Master's degree in Biology from St. John's University (NY). Her early research involved potential antiandrogen therapies for the treatment of dermatoses such as acne and androgenetic alopecia; later, her focus moved to aging, specifically studying biomarkers responsible for the increased lifespan on the methionine-restricted diets. Making use of her exquisite rigorous attention to detail, she has recently been appointed as Safety & Compliance Officer, overseeing all aspects of the radiation and chemical safety programs at OFAS.



**Cell Culture Laboratory:**  
*Jason Plummer,  
Carmen Perrone, Dwight Mattocks*



**Biochemistry Laboratory:**  
*Joseph Vogelman, Frantz Perodin,  
Stephen Massardo, Ines Augie*



**Animal Sciences Laboratory:**  
*Mark Peffers, Heidi Seymour,  
Nicholas Caliendo, Virginia Malloy,  
Jay Zimmerman, Gene Ables*





**Front row:** *Bernardita Calinao, Virginia Malloy, Gene Ables, Ines Augie, Norman Orentreich, David Orentreich, Joseph Vogelman*

**Second row:** *Sylvia Duffy, Angela Tremain, Jay Zimmerman, Carmen Perrone, Frantz Perodin, Nancy Durr, Dwight Mattocks, Heidi Seymour, Raeanne Davis*

**Back row:** *Joel Brind, Stephen Massardo, Jason Plummer, Herb Burack, Mark Peffers, Nicholas Caliendo*

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