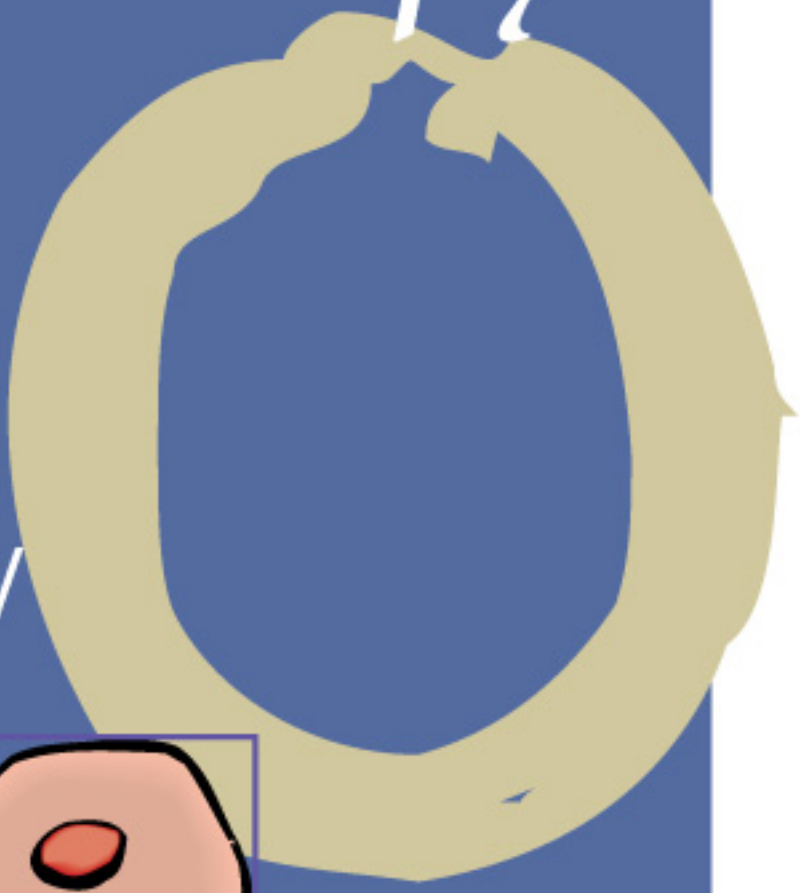
Pharmacotherapy of Obesity:

Targets and Tools for the 21st Century



Friday, April 16, 2004

Renaissance Hotel Congressional Hall B

Washington, DC

The ASPET-Ray Fuller Symposium Series

Sponsored by:

ASPET

American Society For Pharmacology and Experimental Therapeutics

The ASPET-Ray Fuller Symposium Series

ASPET

AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS

Pharmacotherapy of Obesity:
Targets and Tools for the 21st Century

Organized by:

Kenny J. Simansky, *Drexel University College of Medicine*
and
Timothy H. Moran, *Johns Hopkins University School of Medicine*

April 16, 2004
Congressional Hall B
Renaissance Washington, D.C. Hotel
999 Ninth Street, N.W., Washington D.C.

Pharmacotherapy of Obesity: Targets and Tools for the 21st Century

Friday, April 16, 2004
Renaissance Washington, D.C. Hotel
999 Ninth Street, N.W., Washington, D.C.
Congressional Hall B

7:00 am	**Continental Breakfast**
8:15 am	**Welcome and Introduction** Kenny J. Simansky, Ph.D., *Drexel University College of Medicine*
8:30 am	**Framing the problems for research in obesity and the role of NIH in progress toward solutions** Philip F. Smith, *Ph.D., National Institute of Diabetes & Digestive & KidneyDiseases (NIDDK), National Institutes of Health (NIH)*
9:00 am	**A clinical view of the obesity epidemic and current pharmacologic treatments** F. Xavier Pi-Sunyer, M.D., *St. Luke's/Roosevelt Hospital*
9:30 am	**The new neuroendocrinology of energy homeostasis** Michael W. Schwartz, M.D., *University of Washington*
10:15 am	**Break**
10:45 am	**The pharmacology of melanin concentrating hormone-1 receptor antagonists in the regulation of eating and body weight** Timothy J. Kowalski, Ph.D., *Schering Plough Research Institute*
11:15 am	**Melanocortin receptors as targets for the development of novel anti-obesity agents** Russell J. Sheldon, Ph.D., *Procter & Gamble Pharmaceuticals*
11:45 am	**Discussion**
Noon	**Lunch**

1:30 pm **Welcome back and afternoon framework**
Timothy H. Moran, Ph.D., *Johns Hopkins University School of Medicine*

1:45 pm **Molecular physiology of adipocyte signaling and fuel utilization**
Sheila Collins, Ph.D., *Duke University Medical College*

2:15 pm **Fatty acid metabolism and energy regulation: New pharmacological strategies for obesity therapy**
Francis P. Kuhajda, M.D., *Johns Hopkins University School of Medicine*

2:45 pm **Serotonergic mechanisms regulating eating and satiation**
Kenny J. Simansky, Ph.D., *Drexel University College of Medicine*

3:15 pm **Serotonergic 5-HT_{2c} receptor agonists as novel therapeutic agents for obesity**
Keith Miller, Ph.D., *Bristol-Myers Squibb*

3:45 pm **Break**

4:15 pm **Peripheral peptidergic mechanisms regulating food intake**
Timothy H. Moran, Ph.D., *Johns Hopkins University School of Medicine*

4:45 pm **CCK-1 receptor agonists: A promising approach for the treatment of obesity**
Jerzy Szewczyk, Ph.D., GlaxoSmithKline

5:15 pm **Discussion**

Organizing Committee

Kenny J. Simansky, *Drexel University College of Medicine*
and **Timothy H. Moran**, *Johns Hopkins University School of Medicine*

Support for this symposium was provided by Bristol-Myers Squibb, Drexel University, Eli Lilly and Company, and GlaxoSmithKline

ASPET gratefully acknowledges the support for the ASPET-Ray Fuller Symposium Series of the following organizations: Abbott Laboratories, Bristol-Myers Squibb, DuPont Pharmaceutical Company, Eli Lilly and Company, Johnson and Johnson, Schering-Plough Research Institute, GlaxoSmithKline, and Wyeth Ayerst Research.

SPEAKER ABSTRACTS

Framing the Problems for Research in Obesity and the Role of NIH in Progress Towards Solutions

Philip F. Smith, Ph.D.
NIDDK/NIH

Abstract not available

A Clinical View of the Obesity Epidemic and Current Pharmacological Treatments

F. Xavier Pi-Sunyer, M.D.
St. Luke's-Roosevelt Hospital Center
Columbia University College of Physicians and Surgeons
New York, N.Y.

The prevalence of overweight in the United States has increased dramatically in the last decade. Data from the third National Health and Nutrition Survey (NHANES III), conducted from 1988-1991, showed that 33.4% of Americans were obese. This is an 8% increase over a decade earlier. Americans are moving into the obese category at the rate of 1% a year. Overweight and obesity are more prevalent in certain ethnic groups of the U.S. population such as Mexican men, African American women, and Native Americans. Obesity is increasing not only in adults, but also in children and adolescents. This is despite the fact that obesity is very much in the minds of Americans. In fact, they are spending over $40 billion yearly on weight reduction products and services. The discrepancy between effort and result has led to inspection of our treatment methods, to see where they may be coming short.

For the past three decades, behavior modification has been used to treat obesity. No single definition of behavior modification exists. Definitions range from the applications of operant conditioning, classical conditioning, or principles of learning theory, to more broadly based cognitive behavioral models. The primary goal is to change an obese individual's eating and physical activity habits. Changes are gradual. Following achievement of a weight that is maintainable without excessive exercise or overly restrictive eating limitations, relapse prevention training is used to teach the individual how to cope with emotional and social situations associated with eating relapse. Unfortunately, in the few studies available, three to five year follow-ups show gradual return to baseline.

Because of the relative lack of success of behavior modification, diet, and exercise, there is an interest in drug therapy for obesity.

For patients with a body mass index (BMI) =>30 or for those with a BMI of 27-30 with two or more risk factors, however, who have failed on diet and exercise alone, pharmacotherapy is an option.

The New Neuroendocrinology of Energy Homeostasis

Michael W. Schwartz, M.D.
University of Washington

The homeostatic regulation of adiposity involves humoral mediators that circulate at levels proportional to body fat stores and, acting through neuronal receptors, elicit behavioral and metabolic responses over time that promote stability of body fat content. In recent years, our understanding of how information regarding body energy stores is communicated to the brain and subsequently integrated into behavioral and metabolic responses has greatly improved. Much of this progress is due to the identification of specific neurons in the arcuate nucleus of the hypothalamus that serve as sensors of whole-body energy status, and initiate downstream responses designed to maintain fuel stores at a constant level. While many regions of the brain are involved in energy homeostasis, circuits that begin in the arcuate nucleus are some of the best understood at a molecular level. New information regarding the roles played by two adiposity-related hormones – insulin and leptin -- in the control of discrete subsets of arcuate nucleus neurons, and the cellular pathways that mediate these effects, provides a model for understanding how energy homeostasis is achieved.

Contained within the arcuate nucleus are neurons that potently stimulate food intake via the release of both neuropeptide Y (NPY) and agouti-related peptide (AgRP), and these neurons are inhibited by input from insulin and leptin. Opposing the effects of these NPY/AgRP neurons are adjacent melanocortin-containing neurons that reduce food intake and are stimulated by insulin and leptin. Both subsets of arcuate neurons in turn project to other key hypothalamic areas, including the paraventricular nuclei and lateral hypothalamic area, where "second order" neurons in a food intake-regulatory circuit are found. Ultimately, signaling via this pathway is linked to hindbrain areas that sense and respond to meal-related signals involved in the perception of satiety and meal termination.

Efforts to delineate the mechanisms whereby changes of body fat content are transduced into compensatory adjustments of food intake provide a framework for understanding how genetic and dietary factors can disrupt energy homeostasis signals and thereby lead to obesity, and identify new targets for drug development in the treatment of obesity and related disorders.

References

Schwartz MW, Woods SC, Seeley RJ, Porte D Jr., and Baskin DG: Central nervous system control of food intake. Nature 404:661-671, 2000.

Schwartz MW, Morton GJ: Keeping hunger at bay. Nature 418:595-596, 2002

Barsh GS, Schwartz MW: Genetic approaches to studying energy balance: Perception and integration. Nature Reviews Genetics 3:589-600, 2002.

The Pharmacology of Melanin Concentrating Hormone-1 Receptor Antagonists in the Regulation of Food Intake and Body Weight

Timothy J. Kowalski, Ph.D.
Schering Plough Research Institute

Pharmacological experiments and studies with genetically modified mice have shown that melanin-concentrating hormone (MCH) plays a role in feeding and energy homeostasis. In the central nervous system, MCH expression is limited to the lateral hypothalamus and the zona incerta. Two MCH receptors have been identified; MCH1-R, which is expressed throughout the brain of rodents and higher mammalian species and MCH2-R, which is not expressed in rodents but is widely expressed in the brain of higher mammalian species. In rodents, acute central infusion of MCH increases food intake, while chronic central infusion or transgenic MCH over-expression promotes hyperphagia, increased adiposity and insulin resistance. Genetic ablation of *mch* or *mch1-r* produces a lean phenotype in mice. This evidence, along with reports showing that small molecular weight MCH1-R antagonists decrease food intake and body weight in rodents, suggests that MCH1-R antagonists may be efficacious for the treatment of obesity and metabolic syndrome.

The effects of MCH1-R antagonists on food intake and metabolic syndrome abnormalities (elevated adiposity, impaired insulin sensitivity, and hyperlipidemia) in rodent models of diet-induced obesity will be presented.

Melanocortin Receptors as Targets for the Development of Novel Anti-Obesity Agents

Russell J. Sheldon, Ph.D.
Procter & Gamble Pharmaceuticals, Mason, OH

Pathways involving melanocortin peptides and their receptors constitute one of the most exciting areas of obesity research. Melanocortin signaling involves the interplay among four agonist ligands (α-MSH, β-MSH, γ-MSH, and ACTH) that are all derived from a common precursor protein (pro-opiomelanocortin [POMC]), two antagonist ligands (agouti and agouti-related protein [AgRP]), and five melanocortin receptors (named MC1-R thru MC5-R). Of the potential receptor targets, the MC4-R and MC3-R have been associated with pathways involved in energy intake, energy expenditure and nutrient partitioning. Studies of mice with null mutations in the MC4-R and MC3-R and the more recent identification of loss-of-function mutations in these receptors in obese humans provide part of the rationale for the development of MC4-R and/or MC3-R agonists to lower food consumption and to enhance energy expenditure in obese humans.

MT-II is a synthetic, cyclic melanocortin peptide that exhibits high affinity and full agonist activity at the MC1-R, MC3-R, MC4-R and MC5-R. Our group and others have used MT-II as a tool to explore the pharmacology of MC4-R and MC3-R agonism, using assays and endpoints that are relevant to the use of melanocortin drugs for weight loss. Our research has focused on understanding the *in vivo* activity of MT-II and other MC agonists when delivered by peripheral routes of administration, which is relevant to the eventual mode of delivery of melanocortin drugs in humans. MT-II produces a strong suppression of 24-hour food intake when given either intraperitoneally (IP) or subcutaneously (SC) to lean rats. Repeated or continuous dosing of MT-II to obese rats for up to 28 days leads to a reduction of body weight that is proportional to the reduction of cumulative food intake over the duration of dosing. MT-II treatment of DIO rats also causes lower levels of fat mass and reduces plasma levels of leptin, triglycerides and free-fatty acids. These findings provide encouraging support for the further development of MC4-R and MC3-R agonists for the treatment of obesity.

Our group has also explored the aversive properties of peripherally dosed MT-II using acute and subchronic conditioned-taste aversion (CTA) paradigms. Findings from acute dosing studies led to the general conclusion that strong suppression of food intake by acute, peripheral delivery of MT-II is associated with a positive CTA response, while lower levels of food intake reduction are not. We have extended these findings to repeated dosing of MT-II where continuous dosing of rats with MT-II for 7 days also supported a positive CTA response, suggesting an inability to extinguish the aversive stimulus with continuous exposure of MT-II. The progression of peptide and small molecule melanocortin drugs toward clinical trials will help to dimension the physiological basis and human relevance of these preclinical findings.

Aside from the typical challenges of designing compounds with high affinity and efficacy at the appropriate melanocortin receptors, more intangible properties (e.g, relative level of MC4-R and MC3-R activity, blood-brain barrier transport properties) may dictate the weight loss efficacy or side-effect profile observed with a given drug in the clinic. Despite these challenges, melanocortin drugs continue to show promise as an approach for treatment of human obesity and its comorbidities.

References

1. Gantz, I. and T.M. Fong, The melanocortin system. Am. J. Physiol. 284: E468-E474, 2003

2. Benoit, S.C. et al., Assessment of the aversive consequences of acute and chronic administration of the melanocortin agonist, MT-II. Int. J. Obesity, 27: 550-556, 2003

3. Sebhat, I. et al., Melanocortin-4 receptor agonists and antagonists: chemistry and potential therapeutic utilities. Ann. Rep. Med. Chem. 38: 31-40, 2003

Peripheral Peptidergic Mechanisms Regulating Food Intake

Timothy H. Moran,
Department of Psychiatry and Behavioral Sciences
Johns Hopkins University School of Medicine, Baltimore, MD, 21205

During and following a meal, the physical and chemical properties of ingested food evoke a variety of feedback signals that can serve to module current and future food intake. Food accumulates in the stomach resulting in gastric distention and a significant portion of ingested nutrients pass quickly from the stomach into the proximal intestine contacting receptive elements sensitive to both the volume and chemical character of the digestion products. Gastrointestinal peptide release is altered and neural elements are activated. Meal-released peptides such as cholecystokinin (CCK) and pancreatic glucagon have documented actions in meal termination. In contrast, the release of ghrelin, a gastric peptide that stimulates food intake through actions involving hypothalamic sites, is inhibited by nutrients entering the intestine. As digestion continues, nutrient digestive products contact receptive elements in the lower intestine, stimulating the release of additional peptides that may have effects in modulating food intake over the longer term. These peptides include GLP-1, peptide YY (3-36) and pancreatic polypeptide (PP). Various roles for these peptides in modulating hypothalamic feeding circuits have been proposed. Together, these feedback signals play important roles in modulating both within and across meal food intake and as such are potential targets for the development of antiobesity agents.

Key words: cholecystokinin, gut peptides, satiety

Molecular Physiology of Adipocyte Signaling and Fuel Utilization

Sheila Collins, Ph.D.
Duke University Medical College

The primacy of the catecholamines and the β-adrenergic receptors (βARs) in the control of adipocyte lipolysis and thermogenesis are well established. The βARs are recognized as the predominant force in the mobilization of metabolic energy, which is stored largely in the form of triglycerides, through their activation of the cAMP and PKA signaling cascade. While key targets of PKA have been identified such as hormone sensitive lipase and perilipin, we have shown that certain MAP kinase pathways, including ERK and p38 MAPK, are also triggered in adipocytes in response to βAR activation. We have now established that ERK activation contributes to lipolysis and investigating a novel mechanism of direct recruitment of components of the Src signaling cascade to βAR intracellular domains by proteomic approaches. We also find that cAMP-dependent PKA activation in brown adipocytes leads to activation of p38 MAPK, and is required for UCP1 and PGC-1α gene transcription and brown fat thermogenesis. Moreover, this pathway appears to be preferentially used in brown adipocytes by a number of different cAMP-responsive genes, suggesting that it is a major 'traffic' route for cAMP sensing in this cell type. But the identity of the components and their hierarchy in this pathway has been unknown. We now find selective activation of p38α MAPK in brown adipocytes, despite the greater overall abundance p38β MAPK in brown fat, and the preferential recruitment of several novel signaling proteins.

Fatty Acid Metabolism and Energy Regulation: New Pharmacological Strategies for Obesity Therapy

Francis P. Kuhajda, MD, Gabriele V. Ronnett, MD, PhD

Obesity is a world-wide health issue. Fatty acid synthase (FAS) is a lipogenic enzyme that catalyzes the NADPH condensation of acetyl-CoA and malonyl-CoA to generate long-chain fatty acids. We and others have demonstrated that inhibition of FAS using synthetic FAS inhibitors such as C75, administered centrally or peripherally, was able to reduce food intake and induce a profound loss of body weight. FAS is expressed in a number of brain regions, including arcuate and paraventricular nuclei (PVN) within regions that comprise the arcuate-PVN pathway. FAS co-localizes with neuropeptide Y (NPY) in neurons in the arcuate nucleus, suggesting that C75 may alter food intake via interactions within the arcuate-PVN pathway mediated by NPY. Indeed, C75 inhibits fasting-induced increases in NPY, supporting this hypothesis. Moreover, chronic C75 treatment affects the expression of both anorexigenic and orexigenic hypothalamic neuropeptides leading to reduced food intake. More recently, we have investigated the cellular mechanisms of C75's action to show *in vitro* and *in vivo* that at least part of the anorexic effect of C75 may be due to modulation of AMP-activated protein kinase (AMPK), a known peripheral energy-sensing kinase.

In addition to reduction in food intake, we have also observed that C75 treated diet-induced obese mice lose more weight than pair-fed controls. Paradoxically, whole animal calorimetry and *in vitro* studies of fatty acid oxidation revealed that C75 acted to increase energy production as fatty acid oxidation. During FAS inhibition, there is an accumulation of the FAS substrate, malonyl-CoA. Malonyl-CoA is known to *inhibit* fatty acid oxidation through the inhibition carnitine palmitoyl-transferase-1 (CPT-1) activity, the rate-limiting enzyme of fatty acid oxidation on the outer membrane of the mitochondria. While C75 does inhibit FAS, it concomitantly *stimulates* CPT-1 activity, even in the presence of inhibitory concentrations of malonyl-CoA leading to *increased* fatty acid oxidation. Thus, at least one component of the mechanism leading to increased fatty acid oxidation in C75 treated mice is the direct activation of CPT-1. While acute treatment of C75 alters FAS and CPT-1 activity, chronic C75 treatment alters the expression fatty acid metabolism genes, further promoting a lean phenotype. Thus, C75 decreases food intake by altering the expression of hypothalamic neuropeptides leading to an overall anorexigenic signal. In addition, C75 also stimulates fatty acid oxidation, in part by stimulating CPT-1, and altering fatty acid metabolism gene expression. Together, these actions lead to profound weight loss in diet induced obese mice.

Recently, our collaborators have developed a series of compounds that selectively inhibit FAS or stimulate fatty acid oxidation *in vitro*. Both of these classes of compounds lead to weight reduction in diet induced obese mice, albeit through different mechanism of action. Collectively, these data suggest a role for the pharmacological manipulation of fatty acid metabolism as a means to treat obesity.

References:

Loftus T, Jaworsky D, Frehywot G, Townsend C, Ronnett G, Lane M and Kuhajda F. Reduced food intake and body weight in mice treated with fatty acid synthase inhibitors. *Science* 288: 2379-2381, 2000.

Thupari JN, Landree LE, Ronnett GV and Kuhajda FP. C75 increases peripheral energy utilization and fatty acid oxidation in diet-induced obesity. *PNAS* 99: 9498-9502, 2002.

Kim EK, Miller I, Landree LE, Borisy-Rudin FF, Brown P, Tihan T, Townsend CA, Witters LA, Moran TH, Kuhajda FP and Ronnett GV. Expression of FAS within hypothalamic neurons:a model for decreased food intake after C75 treatment. *Am J Physiol Endocrinol Metab* 283: E867-E879, 2002.

Landree LE, Hanlon AL, Strong DW, Rumbaugh G, Miller IM, Thupari JN, Connolly EC, Huganir RL, Richardson C, Witters LA, Kuhajda FP, and Ronnett GV. C75, a fatty acid synthase inhibitor, modulates AMP-activated protein kinase to alter neuronal energy metabolism. *J Biol Chem* 279: 3817-3827, 2004.

Thupari JN, Kim EK, Moran TH, Ronnett GV, and Kuhajda FP. Chronic C75 Treatment of Diet-Induced Obese Mice Increases Fat Oxidation and Reduces Food Intake to Reduce Adipose Mass. *Am J Physiol Endocrinol Metab*, 2004.

Serotonergic Mechanisms Regulating Eating and Satiation

Kenny J. Simansky, Ph.D.
Department of Pharmacology and Physiology
Drexel University College of Medicine, Philadelphia, PA 19102

Four decades ago, the drug fenfluramine was shown to reduce food intake in animals and humans. Early evidence that this agent released neuronal serotonin (5-HT) and blocked its reuptake suggested that this monoamine served a physiological role to inhibit eating. 5-HT is synthesized by enterochromaffin cells in the gastrointestinal mucosa and by neurons within the enteric and central nervous systems. This distribution places 5-HT in position to mediate diverse processes involved in regulating food intake. Such processes range from the endocrine and paracrine signaling functions of the gut, to modulating the impact of sensory information in the brainstem, to recruiting neuropeptide circuits in the forebrain that inhibit eating. Drugs that activate 5-HT receptors postsynaptically on neurons, or on gut smooth muscle, reduce food intake. These drugs can act indirectly by releasing 5-HT or preventing its reuptake (as with fenfluramine), or directly by stimulating the receptors (as with the active metabolite of fenfluramine and numerous other agents). Seven families of 5-HT receptors containing at least 14 subtypes have been cloned and the cellular transduction mechanisms identified for at least 12 of these. In the periphery, 5-HT itself and several of its structural analogs reduced food intake in rats. These actions involved two subtypes of receptors (probably 5-HT_{2A} and a 5-HT_1-family receptor). The specific physiological roles of these peripheral mechanisms remain to be determined and it is premature to consider them targets for drug development. Suggestions that 5-HT_{2B} and 5-HT_6 receptors regulate eating are similarly premature. Considerable evidence does exist, however, that 5-HT_{2C} and 5-HT_{1B} receptors in the brain play significant roles to inhibit consumption of food. The evidence is primarily pharmacological but also comes from bioengineered mutants in which the receptor genes have been deleted. The cooperative action of these two receptors in normally developed adults may be necessary for complete expression of all aspects of satiety.

References

Bickerdike MJ. 5-HT2C receptor agonists as potential drugs for the treatment of obesity. Current Topics in Medicinal Chemistry. 3(8):885-97, 2003

Heisler LK. Cowley MA. Kishi T. Tecott LH. Fan W. Low MJ. Smart JL. Rubinstein M. Tatro JB. Zigman JM. Cone RD. Elmquist JK. Central serotonin and melanocortin pathways regulating energy homeostasis. Annals of the New York Academy of Sciences. 994:169-74, 2003

Hoyer D. Hannon JP. Martin GR. Molecular, pharmacological and functional diversity of 5-HT receptors. Pharmacology, Biochemistry & Behavior. 71(4):533-54, 2002

Simansky, K. J. and Nicklous, D. M. Infusion of d-fenfluramine into the parabrachial nucleus inhibits feeding: Blockade by the 5-HT_{1B} antagonist SB216,641. Pharmacology Biochemistry and Behavior, 2002, 71:681-690.

Serotonergic 5-HT_{2C} Receptor Agonists as Novel Therapeutic Agents for Obesity

Keith J. Miller, Ph.D.
Principal Scientist
Metabolic Diseases Research, Bristol-Myers Squibb

Serotonin has long been known to participate in feeding behavior. For a number of years it remained a mystery as to which serotonin receptor or receptors participated in the regulation of food intake as the available pharmacological tools were relatively non-selective. Evidence for the involvement of the 5-HT_{2C} receptor in feeding, using compounds such as mCPP and MK212, was developing but it took the advent of receptor knockout technology to provide the strongest evidence. Tecott and colleagues generated a 5-HT_{2C} knockout mouse that developed a late onset obesity syndrome. Additionally these animals were relatively insensitive to the 5-HT releasing agent fenfluramine. These data suggested that a selective 5-HT_{2C} agonist would be useful in reducing food intake and body weight.

A few years after Tecott's seminal discovery, data implicating the chronic use of fenfluramine in the development of heart valve hyperplasia emerged. Subsequently it was determined that activation of serotonin 5-HT_{2B} receptors by a metabolite of fenfluramine, norfenfluramine, may play a role in the development of the heart valve lesion. These data have had major impact on the development of 5-HT_{2C} agonists for obesity in that selectivity vs. other serotonin receptors has become paramount.

Agonist-based therapy has the inherent risk of tolerance. Thus the questions of partial vs. full agonism and the potential for chronic therapy must be assessed. Vickers and colleagues have presented data with various compounds that the feeding effects of agents such as mCPP and Ro 60-0175 do not tolerate with chronic administration, however highly selective compounds with varying intrinsic activities have not been similarly examined.

The ability to surmount the hurdles mentioned above will be put into context utilizing the 5-HT_{2C} agonist IL639. The compound is a highly selective 5-HT_{2C} receptor agonist relative to other serotonin receptors, including 5-HT_{2A} and 5-HT_{2B}. IL639 has been shown to be chronically effective in reducing food intake and body weight gain in rats. Examination of c-Fos expression in the brain has revealed the compound activates feeding centers in the brain, including those regions known to be activated by other anorectics, highlighting the potential for complex interplay among other mediators of food intake.

References

Tecott, L.H. et al. Eating disorder and epilepsy in mice lacking 5-HT2C serotonin receptors. Nature (1995) 374; 542-546.

Fitzgerald, L.W. et al. Possible role of valvular serotonin 5-HT2B receptors n the cardiopathy associated with fenfluramine. Mol. Pharmacol. (2000) 57; 75-81.

Vickers, S.P. et al. Comparative effects of continuous infusion of mCPP, Ro 60-0175 and d-fenfluramine on food intake, water intake, body weight and locomotor activity in rats. Br. J. Pharmacol. (2000) 130; 1305-1314.

Peripheral Peptidergic Mechanisms Regulating Food Intake

Timothy H. Moran,
Department of Psychiatry and Behavioral Sciences
Johns Hopkins University School of Medicine, Baltimore, MD, 21205

During and following a meal, the physical and chemical properties of ingested food evoke a variety of feedback signals that can serve to module current and future food intake. Food accumulates in the stomach resulting in gastric distention and a significant portion of ingested nutrients pass quickly from the stomach into the proximal intestine contacting receptive elements sensitive to both the volume and chemical character of the digestion products. Gastrointestinal peptide release is altered and neural elements are activated. Meal-released peptides such as cholecystokinin (CCK) and pancreatic glucagon have documented actions in meal termination. In contrast, the release of ghrelin, a gastric peptide that stimulates food intake through actions involving hypothalamic sites, is inhibited by nutrients entering the intestine. As digestion continues, nutrient digestive products contact receptive elements in the lower intestine, stimulating the release of additional peptides that may have effects in modulating food intake over the longer term. These peptides include GLP-1, peptide YY (3-36) and pancreatic polypeptide (PP). Various roles for these peptides in modulating hypothalamic feeding circuits have been proposed. Together, these feedback signals play important roles in modulating both within and across meal food intake and as such are potential targets for the development of antiobesity agents.

Key words: cholecystokinin, gut peptides, satiety

CCK-1 Receptors Agonists: A Promising Approach for the Treatment of Obesity

Jerzy R. Szewczyk

Department of Medicinal Chemistry, GlaxoSmithKline,
Five Moore Drive, PO Box 13398, Research Triangle Park, North Carolina 27709-3398.
Phone (919) 483-6283 Fax (919) 315-5668 E-mail george.r.szewczyk@gsk.com.

Over 30 years have passed since Gibbs, Young, and Smith [1] demonstrated the ability of exogenously administered cholecystokinin (CCK) to inhibit food intake in rats. This observation was the beginning of very extensive studies into the role CCK plays in the regulation of food intake in mammals. CCK is a brain-gut peptide, which exists in multiple forms. CCK peptides exert their action on two distinct receptor subtypes: CCK-A (Alimentary) now called the CCK1R, mostly expressed peripherally; and CCK-B (Brain), renamed the CCK2R, which is primarily present in the brain. Through the use of subtype-selective agonists and antagonists for the CCK receptor, it was determined that the effect of CCK on feeding was dependent on agonist induced activation of peripheral CCK1 receptors[2,3]. This discovery was followed by intense research with the goal of identifying small molecule agonists on the CCK1 receptor as potentially useful agents for the treatment of obesity. This presentation will attempt to summarize the results of this research.

References

[1] Gibbs, J.; Young, R.C.; Smith, G.P. Cholecystokinin decreases food intake in rats. J. Comp. Physiol. Psychol. **1973**, 84, 488-495.

[2] Moran, T. H.; Kornbluh, R.; Moore, K.; Schwartz, G. J. Cholecystokinin inhibits gastric emptying and contracts the pyloric sphincter in rats by interacting with low affinity CCK receptor sites. Regul. Pept. **1994**, 52(3), 165-72.

[3] Schwartz, G. J.; McHugh, P. R.; Moran, T. H. Pharmacological dissociation of responses to CCK and gastric loads in rat mechanosensitive vagal afferents. Am. J. Physiol. **1994**, 267(1, Pt. 2), R303-R308

SPEAKER DISCLOSURES

FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY
DISCLOSURE POLICY

ASPET- Ray Fuller Symposium: "Pharmacology of Obesity: Target and Tools for the 21st Century"

The Federation of American Societies for Experimental Biology is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. The Federation designates this educational activity for up to 8 credit hours in Category 1 credit towards the AMA Physician's Recognition Award. The Federation requires that audiences at FASEB sponsored educational programs be informed of a presenter's (speakers, faculty, authors, and contributors) academic and professional affiliations, and the disclosure of the existence of any significant financial interest or other relationship a presenter has with the manufacturer(s) of any commercial product(s) discussed in an educational presentation. This policy allows the listener/attendee to be fully informed in evaluating the information being presented.

*Disclosure should include **any relationship that may bias your presentation** or which, if known, could give the perception of bias.* These situations may include, but are not limited to:

1) stock options or bond holdings in a for-profit corporation or self-directed pension plan
2) research grants
3) employment (full or part-time)
4) ownership or partnership
5) consulting fees or other remuneration
6) non-remunerative positions of influence such as officer, board member, trustee, spokesperson
7) receipt of royalties
8) speakers bureau
9) other _____

For full time employees of industry or government, the affiliation listed in the program will constitute full disclosure.

The following speakers have disclosed relationships. The nature of the relationship and the associated commercial entity are listed.

Speaker	Description	Institution(s)
Collins, Sheila	5 5, 6	Merck Research Labs EAS Corporation
Kowalski, Timothy	1, 3	Schering-Plough Research Institute
Kuhajda, Francis	1, 2, 4,5	FASgen, Inc
Miller, Keith	3	Bristol-Myers Squibb
Pi-Sunyer, Xavier	2, 3 5	J & J, Sanofi Lilly, Roche, Novo, Weight Watchers
Schwartz, Michael	5	Abbott Laboratories, Tularik, Inc., Amylin, Inc., Sanofi

SPEAKER ROSTER

Ray-Fuller Symposium

Pharmacotherapy of Obesity: Targets and Tools for the 21st Century

Speakers

Sheila Collins, Ph.D.
Duke University Med College
028 Clinical & Research Labs
Box 3557 Medical Center
Durham, NC 27710
(919) 684-8991
Fax: (919) 684-3071
colli008@mc.duke.edu

Timothy J. Kowalski, Ph.D.
Schering Plough Research Inst
2015 Galloping Hill Road
K15-3-3600
Kenilworth, NJ 07033
(908) 740-4956
Fax: (908) 740-3294
Timothy.Kowalski@spcorp.com

Frank P. Kuhajda, M.D.
John Hopkins Bayview Med Ctr
Department of Pathology
Room 154A
4940 Eastern Avenue
Baltimore, MD 21224
(410)550-0671
Fax: (410) 550-0075
Fkuhajda@jhmi.edu

Keith Miller, PhD
Bristol Myers Squibb
Metabolic Diseases
Bristol-Myers Squibb-PRI 311
Pennington & Rocky Hill Rd
Pennington NJ 08534
(609) 818-5497
Fax: (609) 818-3239
Keith.Miller@bms.com

Timothy H. Moran, Ph.D.
Johns Hopkins University Sch of Med
Dept Psychiatry & Behavioral Sci
720 Rutland Ave, Ross Bldg, Rm 618
Baltimore, MD 21205
(410) 955-2344
Fax: (410) 614-0013
tmoran@jhmi.edu

F. Xavier Pi-Sunyer, M.D.
St. Luke's/Roosevelt Hospital
Obesity Research Center WH-10
1111 Amsterdam Avenue
New York, NY 10025
(212) 523-4161
Fax: (212) 523-4830
fxp1@Columbia.Edu

Michael W. Schwartz, M.D.
University of Washington
Div of Metab, Endocrin & Nutrition
Harborview Medical Center
325 Ninth Avenue
Seattle, WA 98104
(206) 341-5288
Fax: (206) 341-5293
Mschwart@U.Washington.edu

Russell J. Sheldon, Ph.D.
Proctor & Gamble Pharmaceuticals
8700 Mason Montgomery Road
Mason, OH 45040-9317
(513) 622-2867
Fax: (513) 622-1195
sheldon.rj@pg.com

Kenny J. Simansky, PhD
Drexel University College of Med
Dept Pharmacology & Physiology
MS 488, NCB 8808, 245 N 15th St
Philadelphia, PA 19102
(215) 762-8141
Fax: (215) 762-2299
simansky@drexel.edu

Philip F. Smith, Ph.D.
NIDDK/NIH
Div Diabetes, Endocrin & Metab Disorders
Room 693, MSC5460
6707 Democracy Blvd.
Bethesda, MD 20892-5460
(301) 594-8816
Fax: (301) 480-3503
SmithP@Extra.NIDDK.NIH.Gov

Jerzy R. Swewczyk, Ph.D.
GlaxoSmithKline
Research Triangle Park, NC 27709
(919) 483-6283
Fax: (919) 315-5668
George.R.Szewczyk@gsk.com

REGISTRANTS

Ray-Fuller Symposium
Pharmacotherapy of Obesity: Targets and Tools for the 21st Century

Registrants

Nika Adham
Forest Research Institute
Harborside Financial Center
Jersey City, NJ 07303
Phone: (201) 427-8993
Fax: (201) 427-8993
nika.adham@frx.com

Susan Aja
Johns Hopkins Univ Sch of Med
Dept Psychiatry & Behavioral Sci
720 Rutland Ave
Ross Bldg, Room 618
Baltimore, MD 21205
Phone: (410) 955-2996
Fax: (410) 614-0013
saja1@jhmi.edu

Fred Alavi
FDA/DMEDP
5600 Fishers Lane
Rockville, MD 20857
Phone: (301) 827-6405
Fax: (301) 443-9282
alavif@cder.fda.gov

Jeff Anderson
Cypress Bioscience, Inc.
4350 Executive Drive, Suite 325
San Diego, CA 92121
Phone: (858) 452-2323, x109
Fax: (858) 453-1222
janderson@cypressbio.com

Christian Asbrand
DeveloGen AG
Rudolf-Wissell St 28
D-37979 Goettingen
Germany
Phone: 49 55 150558611
Fax: 49 55 150558588
asbrand@develogen.com

Hibah Awwad
University of Houston
4800 Calhoun Rd, SR Bldg II
Houston, TX 77054
Phone: (713) 743-1775
Fax: (713) 743-1229
hawwad@uh.edu

Katharine Barnes
Trends in Pharmacol Sci, Elsevier
84 Theobald's Road
London WC1x 8RR
UK
Phone: 44-20-761-14159
Fax: 44-20-761-14485
katharine.barnes@elsevier.com

Charles Baum
Alexian Brothers Med Ctr
25 E. Schaumburg, Ste 110
Schaumburg, IL 60194
Phone: (847) 472-2145
baumc@alexaian.net

Sheng Bi
Johns Hopkins University
720 Rutland Ave, Ross 618
Baltimore, MD 21205
Phone: (410) 955-2996
Fax: sbi@jhmi.edu
sbi@jhmi.edu

Jarol Boan
Duke University
762 9th St #511
Durham NC 27705
Phone: (919) 660-6677
Fax: (919) 660-8802
jarol.boan@duke.edu

Linda Bristow
Merck Research Labs San Diego
3535 General Atomics Court
San Diego, CA 92121
Phone: (858) 202 5457
Fax: (858) 202 5815
Linda_bristow@merck.com

Michael Brune
Abbott Laboratories
R47M AP13A-2
200 Abbott Park Road
Abbott Park, IN 60064-3537
Phone: (847) 937-9215
Fax: (847) 938-1656
michael.e.brune@abbott.com

Kevin Burris
Palatin Technologies
4-C Cedar Brook Drive
Cranbury, NJ 08512
Phone: (609) 495-2208
Fax: (609) 495-2202
kburris@palatin.com

Lynne Butler
Pfizer Inc.
Eastern Point Rd, MS-8274-1337
Groton, CT 06340
Phone: (860) 441-5133
Fax: (860) 715-3577
lynne_d_butler@groton.pfizer.com

Boe-Gwun Chun
Korea University Col of Med
Pharmacology Department
Dongdaemoon PO Box 46
Seoul, South Korea
Phone: 82-2-920-6236
Fax: 82-2-927-0824
bgchun@korea.ac.kr

Rebecca Corwin
Penn State University
Nutritional Sciences Dept
126 S. Henderson
University Park, PA 16802
Phone: (814) 865-6519
Fax: (814) 863-6103
rxc13@psu.edu

Gaylen Edwards
University of Georgia
Dept of Physiol & Pharm
2223 Vet Med - 1
Athens, GA 30602-7411
Phone: (706) 542-5854
Fax: (706) 542-0261
gedwards@uga.edu

Jeri El-Hage
Food & Drug Admin/DMEDP
5600 Fishers Lane, Rm 14B-45
Rockville, MD 20857
Phone: (301) 827-6369
Fax: (301) 443-9282
elhagej@cder.fda.gov

Paul Ernsberger
Case Western Reserve Univ
Department of Nutriton
10900 Euclid Ave.
Cleveland, OH 44106
Phone: (216) 368-4738
Fax: (216) 368-6644
pre@cwru.edu

Antonio J. Farre
Laboratorios DR. Esteve, S.A.
Av. Mare de Deu de Montserrat
221 - 08041 Barcelona
Spain
Phone: +34 934466000
Fax: +34 934504899
afarre@esteve.es

Tung Fong
Merck
R80M-213, PO Box 2000
Rahway, NJ 07065
Phone: (732) 594-3337
Fax: (732) 594-3337
tung_fong@merck.com

Carlos Forray
Synaptic Pharmaceutical Corp
215 College Rd
Paramus NJ 07652
Phone: (201) 261 1331
Fax: (201) 261 0623
CAFO@Lundbeck.com

Masanori Fukazawa
Chugai Pharmaceutical Co., Ltd.
Fuji Gotemba Research Laboratories
1-135 Komakado
Gotemba,Shizuoka 412-8513
Japan
Phone: +81-550-87-5219
Fax: +81-550-87-6716
fukazawamsn@chugai-pharm.co.jp

Aarti Gokhale
University of Houston
4800 Calhoun Rd
SR II Room 521F
Houston, TX 77054
Phone: (713) 743-1227
Fax: (713) 743-1229
aartigd@hotmail.com

Suman Gupta
Ranbaxy Research Labs
R& D Sector-18, Plot 20
Udyog Vihar Industrial Area
Gurgaon, India
Phone: 91-124-5194776
Fax: 91-124-2343545
suman.gupta@ranbaxy.com

John Hadcock
Pfizer
Eastern Point Road
Groton, CT 06340
Phone: (860) 715-4058
Fax: (860) 715-4608
john_r_hadcock@groton.pfizer.com

Amer Hakam
Univ of Houston
Dept of Pharmacol & Pharmaceut
4800 Calhoun Building, S & R II
Houston, TX 77204-5037
Phone: (713) 743-1295
Fax: (713) 743-1229
ahakam@uh.edu

Stephan Hjorth
AstraZeneca R&D, Integrative
Pharmacology
Pepparedsleden
SE-43183 Mölndal
Sweden
Phone: +46-31-7762048
Fax: +46-31-7763767
Stephan.Hjorth@astrazeneca.com

Gi-Hyun Hong
Korea University Col of Med
Pharmacology Department
Dongdaemoon PO Box 46
Seoul, South Korea
Phone: 82-2-920-6236
Fax: 82-2-927-0824
hgihyun@netian.com

Ali Iranmanesh
V. A. Medical Center
R & D Office
1970 Roanoke Blvd
Salem, Virginia 24153
Phone: (540) 983-1015
Fax: (540) 855-3448
ali.iranmanesh@med.va.gov

Varsha Iyer
University of Houston
Dept of PPS
4444 Cullen Blvd , Apt # 1104
Houston, TX 77004
Phone: 713-743-1775
varshaiyer@hotmail.com

Janis Jibrin
Self Magazine
2122 "O" St., N.W.
Washington, D.C. 20037-1007
Phone: (202) 667-7387
Fax: (202) 833-3831
jjibrin@aol.com

David Johnson
Duquesne University
Grad School of Pharmaceut Sci
Pittsburgh, PA 15282
Phone: (412) 396-5952
Fax: (412) 396-4660
johnsond@duq.edu

Jens Jordan
Charité, Franz Volhard Clinic
Wiltbergstr. 50
D-13125 Berlin
Germany
Phone: +49-30-94172581
Fax: +49-30-94172265
jordan@fvk.charite-buch.de

Dong-Hoon Kim
Korea University Col of Med
Pharmacology Department
Dongdaemoon PO Box 46
Seoul, South Korea
Phone: 82-2-920-6236
Fax: 82-2-927-0824
ldhkim@korea.ac.kr

Kimberly Kinzig
John Hopkins University
720 Rutland Ave, Ross 618
Baltimore, MD 21205
Phone: (410) 955-2996
Fax: (410) 614-0014
kkinzig1@jhmi.edu

Catherine Kotz
University of Minnesota
Mpls VA Medical Center
One Veterans Drive
GRECC (11G)
Mpls, MN 55417
Phone: (612) 467-3312
Fax: (612) 725-2084
kotzx004@umn.edu

Elaine Lanza
NCI, NIH
6116 Executive Blvd, Ste 702
Bethesda, MD 20892
Phone: (301) 594-2933
Fax: (301) 402-1259
EL33T@NIH.GOV

James L. Leach
Ross Products Div of Abbott Labs
625 Cleveland Ave
Columbus OH, 43215-1724
Phone: (614) 624-7115
james.leach@abbott.com

Evelyn Lobo
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285
Phone: (317) 651-9099
Fax: (317) 433-6661
loboev@lilly.com

Gustavo Lonnig
Academia Mexicana para el
Estudio de la Obesidad
Tuxpan 39-502
Col Roma, C.P. 96760
Mexico
Phone: (55) 52640788
Fax: (55)52645268
glonngi@obesiweb.com

Cathy Mahle
Bayer
400 Morgan Lane
West Haven CT 06516
Phone: (203) 812-5456
Fax: (203) 812-2686
cathy.mahle.b@bayer.com

Luciano Manara
Sanofi Midy Res. Center
Via Piranesi 38
20137 Milan
ITALY
Phone: +39 02 73942257
Fax: +39 02 73942452
lluciano.manara@sanofi-synthelabo.com

Stacy Markison
Neurocrine Bioscoiences
10555 Science Center Drive
San Diego, CA 92121
Phone: (858) 320 7561
Fax: (858) 658 7696
smarkison@neurocrine.com

Aditi Marwaha
University of Houston
4800 Calhoun Rd, SR II
Houston, TX 77054
Phone: (713) 743-1230
Fax: (713) 743-1232
aditikhera@yahoo.com

Cheryl Miller
Hill's Pet Nutrition
786 N. 988 Road
Topeka, KS 66601
Phone: (785) 748-0322
Fax: (785) 286-8014
cmillerbalster@yahoo.com

Dennis Miller
Univ of Missouri
208 McAlester Hall
Dept of Psychol Sci
Columbia, MO 65211
Phone: (573) 884-8141
Fax: (573) 882-7710
millerden@missouri.edu

Judith Moreines
Wyeth Consumer Healthcare
5 Giralda Farms
Madison, New Jersey 07940
Phone: (973) 660-6952
Fax: (973) 660-7390
moreinj@wyeth.com

Raul Morin
Academia Mexicana
para el Estudio de la Obesidad
Tuxpan 39-502
Col Roma, C.P. 96760
Mexico
Phone: (55) 52640788
Fax: (55)52645268
glonngi@obesiweb.com

John Nelson
ASPET
9650 Rockville Pike
Bethesda, MD 20814
Phone: (301) 634-7918
Fax: (301) 634-7061

Nomeli Nunez
National Cancer Institute
Executive Plaza North, Ste 3109
Bethesda, MD 20892-7361
Phone: (301) 496-8640
Fax: (301) 402-4863
nunezn@mail.nih.gov

Eva O'Tanyi
Bristol Myers Squibb
PO Box 5400
Princeton, NJ 08543-5400
Phone: (609) 818-5523
Fax: (609) 818-3239
eva.otanyi@bms.com

Mike Overton
Florida State University
236 Biomedical Research Facility
Tallahassee, Fl. 32306-4340
Phone: (850) 644-7217
Fax: (850) 644-0989
overton@neuro.fsu.edu

Jorgen Soberg Petersen
Zealand Pharma A/S
Smedeland 26B
DK-2600 Glostrup
Denmark
Phone: 45 4328 1207
Fax: +45 4328 1212
jsp@zp.dk

Lavanya Rajachandran
Neurogen Corporation
35 N.E. Industrial Road
Branford, CT 06405
lrajachandran@nrgn.com

Herman Rhee
Food and Drug Admin/DMEDP
5600 Fishers Lane, Rm 14B-45
Rockville, MD 20857
Phone: (301) 827-6386
Fax: (301) 443-9282
rheeh@cder.fda.gov

Matt Ricci
Research Diets, Inc
20 Jules Lane
New Brunswick, NJ 08901-3642
Phone: 732-247-2390
Fax: 732-247-2340
ricci@researchdiets.com

Karin Rimvall
Molecular Pharmacology Dept
Novo Nordisk A/S
Novo Nordisk Park
DK2760 Måløv
Denmark
Phone: +45 44434757
Fax: +45 44663939
KRim@novonordisk.com

Chantal Rivera
Baylor College of Medicine
1100 Bates, Suite 6014
Houston, Texas 77030-2600
Phone: 713-798-0314
Fax: chantalr@bcm.tmc.edu
chantalr@bcm.tmc.edu

Kenneth Rohrbach
Bristol-Myers Squibb Company
PO Box 5400, HW21-2.03
Princeton, NJ 08543-5400
Phone: (302) 818-5541
Fax: (302) 818-3239
kenneth.rohrbach@BMS.com

Julie Satterwhite
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285
Phone: (317) 276-9845
Fax: (317) 433-6661
jhs@lilly.com

Milan Schmidt
New Prague Clinic
301 East Main Street
New Prague, MN 56071
Phone: (952) 758-4461
Fax: (952) 758-5011
milanschmidt@mchsi.com

Gulnar Shahid
Univ of Houston
Dept of Pharmacol & Pharmaceut
4800 Calhoun Building
S & R II, 532C
Houston, TX 77204-5037
Phone: (713) 743-1295
Fax: (713) 743-1229
gulnarshahid@hotmail.com

Harry Smith
ASPET
9650 Rockville Pike
Bethesda, MD 20905
Phone: (301) 634-7790
Fax: (301) 634-7989

Jihyun Song
NIH, Korea
Nokbun dong #5
Eunpyung Ku, Seoul, 122-701
South Korea
Phone: 82-2-380-1530
Fax: 82-2-354-1057
jssong@nih.go.kr

Pamela Starke-Reed
National Institutes of Health
6707 Democracy Blvd., Rm 633
Bethesda, MD 20817
Phone: (301) 594-8805
Fax: (301) 480-3768
ps39p@nih.gov

Michael A. Statnick
Eli Lilly and Company
Endocrine Research
Lilly Corporate Center
Indianapolis, IN 46285-0403
Phone: (317) 277-1123
m.statnick@lilly.com

Alain Stricker-Krongrad
Athersys, Inc.
3201 Carnegie Avenue
Cleveland, OH 44115
Phone: (216) 431-9900
Fax: (216) 361-1478
astricker-krongrad@athersys.com

Carina Tan
Merck & Co
Box 2000, 80Y-300
Rahway, NJ 07065
Phone: (732) 594-5723
Fax: (732) 594-6708
carina_tan@merck.com

Jennifer Teske
Unniversity of Minnesota
13256 Owatonna Ct, NW
Blaine, MN 55449
Phone: (612) 270-2776
teskeja@umn.edu

Marc Thibonnier
Bayer
400 Morgan Lane
West Haven, CT 06516
Phone: (203) 812-2229
Fax: (203) 812-5033
marc.thibonnier.b@bayer.com

Jagan N. Thupari
Johns Hopkins Medical Inst
R:215, Alpha Center
5210 Eastern Avenue
Baltimore MD-21224
Phone: (410) 550-7422
Fax: jthupari@jhmi.edu
jthupari@jhmi.edu

Meghna Trivedi
Heart and Kidney Inst
4800 Calhoun Rd
Science and Rsch Bldg II, Rm 521
Houston, TX 77204
Phone: (713) 743-1230
Fax: (713) 743-1232
meghnat@hotmail.com

Pedro Velasquez
University of Tennessee
8819 Bredbury Cv E
Cordova, TN 38016-6498
Phone: (901) 572-5202
Fax: (901) 572-5834
pvelasquez@utmem.edu

Philip Wahl
Novo Nordisk A/S
Novo Nordisk Park
DK-2760 Måløv
Denmark
Phone: +45 44 434 429
Fax: +45 44 434 417
pwa@novonordisk.com

Birgitte Wulff
Novo Nordisk A/S
Novo Nordisk Park
C9.S.27
2760 Maaloev
DK-Denmark
Phone: +45 44 434 545
Fax: +45 44 434 587
bsw@novonordisk.com

Susan Z. Yanovski
NIDDK, NIH
Obesity and Eating Dis Prog
6707 Democracy Blvd
Bldg II, Rm 665
Bethesda, MD 20892-5450
Phone: (301) 594-8882
Fax: (301) 480-8300
sy29f@nih.gov

Ray W. Fuller
1935-1996

The ASPET-Ray Fuller Symposium is an annual series of sponsored meetings to bring together academic, government and industry scientists to focus on an emerging area of drug discovery, spanning basic to clinical considerations.

Ray Fuller was born in 1935 and grew up on a farm in Southern Illinois in a fairly isolated area without electricity, telephones, or indoor plumbing. Despite never expecting to attend high school when he was growing up, Ray Fuller received a B.A. in chemistry from Southern Illinois University. He helped put himself through college by working at the Anna State Hospital and it was during this job that he developed his interest in the brain and the idea that a better understanding of the central nervous system could lead to better treatments for the mentally ill. Following graduation from SIU with an M.A. in microbiology, Ray got his Ph.D. in 1961 in biochemistry from Purdue University. In 1963 he moved to Eli Lilly and Company where he was a member of the scientific triad responsible for the discovery of fluoxetine (Prozac). He served as an adjunct faculty member at Southern Illinois University and Indiana University School of Medicine and was a Visiting Lecturer at the Massachusetts Institute of Technology.

Ray Fuller was an active member of the American Society for Pharmacology and Experimental Therapeutics (ASPET). He served as a Councilor of the Society as well as a member of the Board of Publications Trustees, the Long Range Planning Committee, several awards committees, and a member of the executive committee of the then Section on Neuropharmacology. He received numerous honors, including two honorary doctorates and the Pharmaceutical Manufacturers Association's Discoverers Award, for his work on fluoxetine.

In the commencement address that he gave to the graduates of the Southern Illinois University in 1994, Ray Fuller provided three points of advice: "First is, be yourself. Nobody else can do that. Second is, don't let the fear of making mistakes keep you from finding out what you can accomplish. And third is, keep learning—continue your education—throughout life." As a tribute to the breadth of his contributions to pharmacology, ASPET Council has permanently named the symposium series to honor the late Ray W. Fuller.