



Mayo Clinic  
Department of Medical Genetics  
and the  
VHL Family Alliance  
Present the

# Fourth International Symposium on von Hippel-Lindau Program and Attendee List for **VHL Care in the New Millennium** *July 20-23, 2000*

**Thursday, July 20, 2000**

**7:30-8:30 Registration, Continental Breakfast**

## **Basic Science Day**

### **8:30 Welcome**

Hugh C. Smith, M.D. Chair, Mayo Clinic-Rochester  
Board of Governors

### **8:45 Keynote: Gene Therapy for Brain Tumors.**

Corey Raffel, M.D., Pediatric Neurosurgery, Mayo  
Clinic

### **9:10 Structure of the VHL Gene and Protein**

Molecular Image of the VHL Gene Product, *Charles E. Stebbins, Ph.D., Yale University School of Medicine, New Haven, Connecticut*

Nuclear/cytoplasmic localization of the VHL tumor suppressor gene and its importance for tumor suppression activity. *Stephen Lee, Ph.D., Assistant Professor, Faculty of Medicine, University of Ottawa, Ontario, Canada.*

Q&A with Drs. Stebbins and Lee

### **9:50 Break**

### **10:10 Function of the VHL Protein**

The VHL gene is involved in cross-talk between cell-ECM and cell-cell signaling. *Eliot J. Davidowitz, Ph.D., Postdoctoral Fellow, Albert Einstein College of Medicine of Yeshiva University, Comprehensive Cancer Research Center, Bronx, New York*

The von Hippel-Lindau tumor suppressor is a component of an SCF-like E3 Ubiquitin protein Ligase complex. *Joanna Lisztwan, B.Sc., Friedrich-Miescher Institut, Novartis Pharmaceuticals, Basel, Switzerland.*

Molecular Pathogenesis of the von Hippel-Lindau Hereditary Cancer Syndrome. *William Kaelin, M.D., Dana Farber Cancer Institute, Boston, Massachusetts*

Q&A with Drs. Davidowitz, Lisztwan and Kaelin

### **11:30 VHL-regulated Gene Expression**

Serial Analysis of Gene Expression to identify targets for therapeutic use. *M. Craig Caldwell, Ph.D., Intramural Research Training Award (IRTA), Gerontology Research Center, LBC, National Institute on Aging, Baltimore, Maryland*

The Role of the VHL gene in Neuronal differentiation in human neuroblastoma. *Hidetoshi Murata, M.D., Department of Neurosurgery, Yokohama City University, Yokohama, Japan*

The role of the VHL protein in control of oxygen-regulated VEGF gene expression. *James Gnarra, Ph.D., Associate Professor, Louisiana State University Medical Center, New Orleans, Louisiana*

The von Hippel-Lindau tumour suppressor: role in oxygen regulated gene expression. *Patrick Maxwell, M.D., Ph.D., University of Oxford, England*

Regulation of tyrosine hydroxylase gene expression by von Hippel-Lindau tumor suppressor complex in pheochromocytoma PC12 cells. *Maria F. Czyzyk-Krzeska, M.D., Assistant Professor of Physiology, University of Cincinnati College of Medicine.*

Q&A with Drs. Caldwell, Murata, Gnarra, Maxwell, and Czyzyk-Krzeska

### **1:10 Lunch**

### **1:50 Understanding & Controlling Tumorigenesis**

The VHL knockout mouse: A tool for understanding oxygen-regulated development. *James Gnarra, Ph.D., Associate Professor, Louisiana State University Medical Center, New Orleans, Louisiana*

Progress towards the development of a mouse model for VHL disease. *Laura Schmidt, Ph.D., Senior Scientist, Laboratory of Immunobiology, IRSP, SAIC Frederick, National Cancer Institute-Frederick Cancer Research and Development Center, Frederick, MD.*

Evidence for a Stepwise Progression Model for VHL Tumorigenesis. *Ann Killary, Ph.D., Associate Professor, M. D. Anderson Cancer Research Center, Houston, Texas.*

VHL Gene Targeted by Carcinogens, *Hiltrud B. Brauch, Ph.D., Associate Professor, Oncology Research Coordinator, the Dr. Margarete Fischer-Bosch-Institute of Clinical Pharmacology, Stuttgart, Germany*

Q&A with Drs. Gnarra, Schmidt, Killary, and Brauch

### **3:10 Break**

### **3:30 Toward Gene Therapy**

Cancer Gene Therapy with an Adenoviral Vector Expressing VHL Tumor Suppressor Gene. *Prem Seth, Ph.D., Human Gene Therapy Research Inst, Des Moines, Iowa*

Transmembrane carbonic anhydrases as new targets for cancer treatment. *Sergey Ivanov, Ph.D., NIH, Frederick Monoclonal Antibodies for the treatment of Kidney Cancer: Relationship between VHL and Antigen Expression.*

*Egbert Oosterwijk, Ph.D, Univ Nijmegen, Netherlands.*

Q&A with Drs. Seth, Ivanov, and Oosterwijk

### **5:30 Adjourn for the day**

**6-8pm, Welcome Reception, Kahler Hotel**

*Abstracts and Speaker biographies can be found in the Abstract Book*



## Friday July 21, 2000

7:30 am, Continental Breakfast

### Friday AM Tracks I & II: Genotype/Phenotype Alignment

#### 8:00 Genetic Changes: Cause and Effect

Phenotypic Variability in VHL disease: Allelic Heterogeneity and Genetic Modifiers. *Eamonn R. Maher, M.D., F.R.C.P., Professor of Medical Genetics, and Head Medical and Molecular Genetics, University of Birmingham, England. - Dr. Maher will not be attending.*

First Generation Diagnoses of VHL: New Mutations and VHL Mosaicism. *Gladys M. Glenn, M.D., Ph.D., Medical Officer, Genetic Epidemiology Branch, Cancer Diagnostic Branch, and Clinical Associate, Surgery Branch, National Cancer Institute, Rockville, Maryland.*

Somatic Mosaicism in VHL and its Implication. *Giuseppe Opocher, M.D., Department of Genetics, University of Padua, Italy.*

Is P25L a "real" VHL Mutation? *Paul G. Rothberg, M.D., Director of Genetics, Children's Mercy Hospital, Kansas City, Missouri*

Q&A with Drs. Maher, Glenn, Opocher, and Rothberg

#### 9:20 Break

#### 9:40 Understanding Genotype/Phenotype Alignments

Genotype Studies in France: Medical and Fundamental Implications. *Stéphane Richard, M.D., Ph.D., Professor and Chairman of the Laboratory of Neuro-Oncology at the École Pratique des Hautes Études in Paris.*

Renal lesions in VHL disease : toward genotype-phenotype correlation. *Dominique Chauveau, M.D., Ph.D., Nephrology, Hôpital Necker, Paris.*

Roles of genetic polymorphisms in the incidence and prognosis in Japanese patients with sporadic RCC. *Eijiro Nakamura, M.D., Ph.D., Department of Urology, Faculty of Medicine, Kyoto University, Japan*

Pheochromocytomas in VHL Patients. *Sophie Giraud, M.D., Ph.D., Geneticist, Hôpital Edouard Herriot, Paris, France.*

Q&A with Drs. Richard, Chauveau, Nakamura and Giraud

#### 11:10 Finding All VHL Mutations

VHL Testing. *Alessandra Murgia, M.D., Ph.D., Director, Laboratory of Molecular Genetics, University of Padua, Italy.*

Genetic Diagnostic Testing for von Hippel-Lindau Disease. *Catherine Stolle, Ph.D., Managing Director, Genetic Diagnostic Laboratory, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania.*

Q&A with Drs. Murgia and Stolle

### Friday AM Track II: VHL 101

#### 8:00 Introduction to Terminology and Concepts.

Siebens building, room 406

For attendees relatively new to VHL, or who have not previously attended a Conference. *Joyce Graff, Editor, VHL Family Forum, and Founder Emeritus of the VHL Family Alliance*

#### 12:00 Lunch

### Friday PM General Session: Tracks I, II, & III VHL Care in the New Millennium

#### 1:00 Welcome to Mayo Clinic

Goals for the Meeting, Introduction of Conference Hosts from Mayo. *By Virginia Michels, M.D., Professor, Department of Medical Genetics, Mayo Clinic, Rochester, Minnesota.*

#### 1:10 Welcome, The VHLFA Story.

Introduction of Board Members, Chapter Chairpersons, and Conference Hosts. *Lois Erickson, Co-Chairman of the Symposium and Minnesota Chapter Chair, VHL Family Alliance, Bloomington, Minnesota.; Kelly Heselton, VHLFA Treasurer, Lakeville, Minnesota; Peggy Marshall, Chair VHL Family Alliance, Corinth, Mississippi*

#### 1:30 Keynote: VHL Care in the New Millennium: the Role of Genetics

Virginia Michels, M.D., Mayo Clinic

#### 1:50 VHL Clinical Care Centers

Who is Participating, Goals of the Program. *Joyce Graff, Editor and CCC Chair, VHL Family Alliance, Brookline, Massachusetts*

Summarization of 4-year activity of Polish VHL Registry. *Karol Krzystolik, Ph.D., Department of Genetics, Pomeranian Academy of Medicine, Szczecin, Poland*

Q&A with speakers Graff and Krzystolik

#### 2:30 Ethical, Legal, and Social Issues

Insurance and Legal Issues. *Thomas D. Rodenberg, Esq., Jeter, Rains, and Byrn, Blue Springs Missouri*  
Putting the House in Order, *Patricia Rasmussen, B.S.W., L.P.N., Minnesota*

Q&A with speakers Rodenberg and Rasmussen

#### 3:45 Break

#### 4:00 DNA Testing

DNA Testing Methods and Applications. *Catherine Stolle, Ph.D., Assistant Professor, Managing Director, Genetic Testing Laboratory*

Psychosocial, Ethical, and Legal Issues in Genetic Testing for von Hippel-Lindau. *Vicki Couch, M.S., Genetic Counselor, Mayo Clinic, Rochester, Minnesota*

Genetic Discrimination: How much do we know and what are we doing about it? *Lindsay Middleton, M.S., Genetic Counselor and Clinical Research Nurse, National Institute of Human Genome Research, National Institutes of Health, Bethesda, Maryland.*

Q&A with speakers Stolle, Couch and Middleton

#### 5:30 Adjourn for the afternoon

#### 6:30 Dinner

## Saturday July 22, 2000

### Saturday General Session: Optimal Clinical Care

#### 8:00 Keynote: Identification of the VHL Gene: Clinical and Basic Implications

McClellan M. Walther, M.D., U.S. National Cancer Institute

#### 8:30 Clinical Research Programs

Clinical Evaluation and Molecular Genetic Diagnosis of VHL. *Gladys M. Glenn, M.D., Medical Officer, Genetic Epidemiology Branch, Cancer Diagnostic Branch, and Clinical Associate, Surgery Branch, National Cancer Institute, Rockville, Maryland*

Molecular Diagnosis of VHL disease in Brazilian families. *José Cláudio Casali da Rocha, M.D., Instituto Ludwig de Pesquisa sobre o Câncer, São Paulo, Brazil*

Q&A with Drs. Glenn and Casali

#### 9:30 Break

#### 9:45 Clinical Research Programs, Continued

Characteristic features in the VHL disease from a survey to urologists and neurosurgeons in Japan. *Taro Shuin, M.D., Ph.D., Professor of Genetics, Kochi Medical School, Nan-koku Kochi, Japan.*

Screening for VHL in patients with CNS Hemangioblastomas. *Sven Gläsker, University of Freiburg, Germany*

VHL in Italy. *Giuseppe Opocher, University of Padua, Padua, Italy*

Results of VHL gene mutation analysis in the Netherlands. *Frederick Hes, M.D., Ph.D., Genetics, University of Utrecht, the Netherlands.*

Q&A with Drs. Shuin, Opocher, and Hes

### 10:45 Clinical Issues

#### 10:45 Preserving Organ Function: Adrenals

Plasma Free Metanephrines in VHL Patients: A Promising new neuro-chemical test for pheochromocytoma in VHL patients. *Jacques Lenders, M.D., Department of General Internal Medicine, St. Radboud University Hospital Nijmegen, the Netherlands.*

Surgery for Adrenal Tumors in VHL: Traditional and Laparoscopic approaches. *Geoffrey Thompson, M.D., Associate Professor, Department of Surgery, Mayo Clinic.*

Q&A with Drs. Lenders and Thompson

#### 11:25 Intraoperative Imaging

Exploring the Benefits of High-Field Strength Intraoperative Magnetic Resonance Imaging. *Walter A. Hall, M.D., Professor of Neurosurgery, Radiation Oncology, and Radiology, University of Minnesota, Minneapolis, Minnesota.*

#### 11:45 Achieving a Diagnosis

Strategies for Finding the Undiagnosed Patient with VHL. *Hartmut P.H. Neumann, M.D., Dept. of Nephrology, Albert-Ludwigs University, Freiburg, Germany, and head of the German Prevention Study on VHL*

Improving Outcomes in VHL Families, *Jane Green, Ph.D., Genetics, Memorial Hospital, Newfoundland*  
Q&A with Drs. Neumann and Green

#### 12:30 Lunch

#### 1:30 Preserving Organ Function: Kidney & Pancreas

Organ Sparing Surgery: Kidney Cancer, Adrenal Tumors. *McClellan Walther, M.D., Staff Physician, Urologic Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.*

Management of neuroendocrine tumors of the pancreas in patients with VHL disease. *Pascal Hammel, M.D., Ph.D., Gastroenterology, Hôpital Beaujon, Clichy, France.*

Nephron-Sparing Surgical Techniques. *David Goldfarb, M.D., Cleveland Clinics Foundation, Cleveland, Ohio*  
Q&A with Drs. Walther, Hammel, and Goldfarb

#### 3:00 Break

#### 3:15 Hemangioblastomas of the CNS and Retina

Central Nervous System Von Hippel-Lindau, Management and Treatment. *Atom Sarkar, M.D., Ph.D., Michael J. Ebersold, M.D., Lynn M. Quast, R.N., Department of Neurosurgery, Mayo Medical Center, Rochester, Minnesota*

Predicting the Development of a CNS Hemangioblastoma. *Tung Nguyen, M.D., National Institute of Neurological Disorders and Stroke, U.S., National Institutes of Health, Bethesda, Maryland*

Hemangioblastomas of the CNS and the retina: impact of VHL and interferon treatment. *Dr. Mika Niemelä, M.D., Ph.D., Attending Neurosurgeon, Helsinki University Central Hospital.*

Retinal Hemangioblastomas in VHL disease: a case-control study. *Hélène Dollfus, M.D., Ph.D., Department of Medical Genetics, Hôpital de Hautepierre, Strasbourg, France.*

The clinical features and genetic mechanisms in hemangioblastoma of the central nervous system. *Hiroshi Kanno, M.D., Department of Neurosurgery, Yokohama City University, Yokohama, Japan*

Q&A with the speakers

#### 4:50 Stereotactic Radiosurgery for Hemangioblastoma

The Role of Stereotactic Radiosurgery in the Management of Patients with VHL. *Bruce Pollock, M.D., Neurosurgery, Mayo Clinic*

Q&A with Drs. Pollock

#### 5:30 Adjourn for the day

Sunday July 23, 2000

**7:30 Continental Breakfast**

**8:00 Sunday Meditation**

**8:00 Keynote: Keeping your Balance, Going the Distance.**

Jay Platt, GySgt USMC, retired, Cartersville, Georgia

**8:30 Tumor Localization and Assessment**

Tumor Assessment using Imaging Techniques. *Peter Choyke, M.D., Chief of MRI, Diagnostic Radiology Department, Clinical Center, National Institutes of Health, Bethesda, Maryland.*

Q&A with Dr. Choyke

**8:50 Radioactive Plaque Therapy for Large Eye Tumors**

Radioactive eye plaque therapy for larger retinal capillary hemangiomas in VHL. *James J Augsburger, M.D, Professor and Chairman of the Department of Ophthalmology and Director of the Ocular Oncology Unit, University of Cincinnati College of Medicine, Cincinnati, Ohio.*

Ruthenium brachytherapy of ocular angioma. *Klaus-Martin Kreusel, M.D., Eye Clinic, Benjamin Franklin Hospital of the Free University of Berlin, Germany.*

Q&A with Drs. Augsburger & Kreusel

**9:30 Break**

**9:45 Innovative Eye Treatments and Clinical Outcomes**

Management of Retinal tumors of VHL disease. *Helmut Buettner, MD & Dennis Robertson, MD, Ophthalmology, Mayo Clinic, Rochester, Minnesota*

Innovative Eye Treatments and Clinical Outcomes, *Emily Y. Chew, M.D., National Eye Institute, National Institutes of Health, Bethesda, Maryland.*

Ophthalmic screening guidelines for VHL and fluorescein-potentiated argon laser treatment of retinal hemangiomas. *Michael B. Gorin, M.D., Ph.D., Associate Professor, Departments of Ophthalmology and Human Genetics, University of Pittsburgh School of Medicine and Graduate School of Public Health.*

Long-term follow-up of retinal angiomas and genotype-phenotype correlation. *Klaus-Martin Kreusel, M.D., Eye Clinic, Benjamin Franklin Hospital of the Free University of Berlin, Germany.*

Q&A with Drs. Buettner, Robertson, Chew, Gorin, and Kreusel

**11:05 Progress in Research**

Capsule Summary of the Thursday Research Meeting.

*Ann Killary, Ph.D., Associate Professor, M. D. Anderson Cancer Research Center, Houston, Texas.*

Progress Toward a Cure: Clinical Trials, Setting Expectations. *William Kaelin, Jr., M.D., Dana Farber Cancer Research Institute, Boston, Massachusetts*

Angiogenic therapy for VHL. *Adrian L. Harris, M.B.Ch.B. F.R.C.P. Ph.D., Professor of Clinical Oncology, Director of Imperial Cancer Research Fund Medical Oncology Unit, Churchill Hospital, Oxford, England.*

Q&A with Drs. Killary, Kaelin, and Harris

**12:05 Symposium Consensus Meeting**

Reaching consensus on Key Issues from this Symposium.

*Led by the Medical Committee: Dr. McClellan M.*

*Walther, Dr. Virginia Michels, Dr. Hartmut Neumann, Dr. Stéphane Richard, Dr. Berton Zbar*

**1:15 Closure**

Thanks and Farewell. Peggy Marshall, Chair, VHLFA; Lois Erickson, Minnesota Chapter; Kelly Heselton, VHLFA Meeting Chair; Tania Durand, Canada; Jennifer Kingston, Australia; Chris Hendrickx, Belgium; and other members of the Conference Committee.

**1:30 Adjourn until Padua 2002!**

**Don't say good-bye  
Say "til next time!"**

**Fifth VHL Symposium,  
Padua, Italy, 2002**

Co-sponsored with the  
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*Chairman: Giuseppe Opocher,  
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