DEPARTMENT OF PATHOLOGY

1982 - 1983

N. Kaufman, M.D. G.F. Kipkie, M.D. David M. Robertson, M.D. R. Kisilevsky, M.D., Ph.D. H.D. Steele, M.D. T.F. McElligott, M.D. A.F. Clark, Ph.D. W.E.N. Corbett, M.D. R.S. Kerbel, Ph.D. S. Ludwin, M.B. R.S. Prentice, M.D. S.M. Wasan, M.D. J.C. Wyllie, M.D. A.J. de Bold, Ph.D. A.R. Giles, M.B., B.S. J.W. Dennis, Ph.D. B.E. Elliott, Ph.D. J.T. Feltis, M.D. W.A. Fletcher, M.D. A.E. Lagarde, Ph.D., D.Sc. P.N. Manley, M.D. S. Nag, M.D., Ph.D. M.J. Raymond, Ph.D. D.F. Dexter, M.D. S.E. Ford, M.B., B.S. R. Bell, M.D. S.A. Bencosme, M.D., Ph.D. J.C. Kennnedy, M.D., Ph.D. P.M. Ford, M.D.

Emeritus Professor Emeritus Professor Professor and Head Professor Professor Professor Associate Professor Assistant Proofessor Clinical Assistant Lecturer (Joint Appointment) Sessional Appointment Sessional Appointment Assistant Professor (Cross Appointment)

PERSONNEL

Dr. G.F. Kipkie, Director of Laboratories, Department of Pathology, retired on June 30, 1982, after thirty-three years of consecutive service in the department. Dr. Kipkie was appointed to the Honorary Staff at Kingston General Hospital and was granted the title of Professor Emeritus at Queen's University effective from the date of his official retirement.

On July 1, 1982, two new pathologists joined the staff in the department. Dr. Sally E. Ford, a graduate of London School, trained in Pathology in England University Medical Kingston General Hospital, and at the University of Ontario in cardiovascular pathology. Western Dr. Ford's prime responsibility is in cardiovascular pathology. Timothy Feltis, a graduate of Queen's University, in this department and spent one year as a Medical Research Council Fellow at the Mount Sinai School of Medicine in New York. Feltis's main responsibility is general Dr. surgical pathology, and pathology of the kidney.

Dr. A.J. de Bold and Dr. A.R. Giles were both promoted from Assistant Professor to Associate Professor in the department effective July 1, 1982.

Dennis was appointed Assistant Professor in Dr. James W. the Department of Pathology effective April 1, 1983. Dennis received both his M.Sc. and Ph.D. from Queen's Dennis did his postdoctoral training in the University. Dr. Group, Department of Pathology, Queen's Cancer Research the German Cancer Research Centre, Heidelberg, University, West Germany, the University of Toronto and the Hospital for Children. Dr. Dennis spent 1982-1983 as a Senior Fellow of the National Cancer Institute. Postdoctoral is currently a member of the Cancer Research Group of the Department of Pathology.

Mr. W.M. Hill, Administrative Assistant in the department since July 1973, retired on July 30, 1982. Mr. Hill gave almost a decade of service to the department.

Mr. Norman Meyers was appointed Administrative Assistant in the department effective August 1, 1982. Mr. Meyers has been in the department since 1961, and Chief Technologist since 1955.

AWARDS

Sukriti Nag, Dr. David M. Robertson and Dr. Henry B. Dinsdale of the Departments of Pathology and Medicine were awarded first prize for their Poster entitled, "Permeability Immunohistochemical Studies in Chronic Hypertension" at the Fifth International Symposium on Brain Edema Groningen, the Netherlands. The Poster was prepared and presented by Dr. Nag. This work is part of continuing studies on the mechanism of brain damage in hypertension.

Dr. Donald Ho, a resident in the Department of Pathology, was awarded the Desmond Magner Award and took up this award in March of 1983. The purpose of the Desmond Magner Award is to enable Canadian pathology residents to spend up to one month at the Canadian Tumour Reference Center in Ottawa studying tumour pathology and diagnosis, with a view to establishing a high standard of tumour pathology in Canada.

Dr. David Munoz-Garcia, a resident in the Department of Pathology, division of neuropathology, won the Mary Tom Award for the best presentation by a resident at the annual meeting of the Canadian Association of Neuropathologists held in September 1982 in Montreal.

Dr. Robert Kerbel of the Cancer Research Group of the Department of Pathology was awarded the Basmajian Award in January 1983. This award is made to the member of the full time staff of the Faculty of Medicine at Queen's University who is "judged to have made the most meritorious contribution to medical research during the previous year or several years". It is the only award made by the Faculty of Medicine to recognize excellence in medical research by members of staff.

RESEARCH

Adolfo J. de Bold, Assistant Professor of Pathology, who is located at Hotel Dieu Hospital, has focussed international attention on the Department of Pathology with the discovery substance produced by the heart. This substance - a peptide - is a powerful diuretic and natriuretic agent, i.e. it has the ability to induce the kidneys to excrete increased amounts of water salt. and This new substance, named cardionatrin, is of interest to researchers investigating clinical entities such as hypertension and congestive heart failure. It is also interest to the pharmaceutical of industry who recognize the potential in modelling diuretic drugs after the newly discovered substance.

Recently Dr. de Bold was invited to the Philadelphia headquarters of the pharmaceutical company, Smith, Kline & French, to present a seminar and participate in round table discussions dealing with topics related to his research. In addition, the American Heart Association invited Dr. de Bold to act as a discussant at the 1982 Fall meeting in Cleveland, where United States and Canadian laboratories were presenting material relating to this area of research.

discovery of cardionatrin is the culmination of fourteen of uninterrupted research into the significance of certain features of the heart which hinted that this organ, addition to its function in blood pumping, also produced an internal secretion. Data gathered up to 1979 indicated that the mentioned of the heart might be features regulation of body fluids and kidney function. Further research is being carried out in collaboration with Drs. T.G. Flynn, P.L. Davies, and J.C.C. Roder, all of Queen's University.

CANCER RESEARCH GROUP

Dr. Robert Kerbel was appointed Director of the Cancer Research Group in the Department of Pathology effective April 1, 1983. Dr. Kerbel has been a member of the Cancer Research Group since 1975, and co-director since 1979. Under his imaginative and enthusiastic leadership, the Cancer Research Group has continued to expand its research potential. With the addition of another member of senior staff, Dr. J. Dennis, on April 1, 1983, this productivity should be further enhanced.

VISITING LECTURERS

A complete list of Visiting Lecturers, indicating the titles of their seminar presentations, is outlined in Appendix I.

PAPERS AND ABSTRACTS

During the year 27 papers were published. A complete list of these published papers is contained in Appendix III.

PATHOLOGY COURSE REHABILITATION SCIENCE

Several members of the Department of Pathology again participated in the lecture schedule of the School of Rehabilitation Therapy. Forty-seven students from the School of Rehabilitation Therapy received a total of eleven lectures in pathology. Dr. Dexter and several of the residents from the Department of Pathology shared the lecturing responsibility, and Dr. Dexter was in charge of the overall organizational aspect.

TEACHING

Postgraduate Eighteen housestaff were registered in the postgraduate training program in the Department of Pathology for 1982-1983. In addition, two residents from the Department of Obstetrics and Gynecology, one resident from Surgery, and four residents from the Department of Radiology were on rotation in the department. During 1982-1983 four residents in the department were successful in passing their American Board of pathology examinations.

A Departmental Postgraduate Committee, whose function is to develop and carry out departmental and faculty policies on in-training evaluation, resident program evaluation and other matters relating to the department, meets at regular intervals. This committee is composed of the Head of the department, six senior staff members, and one resident representative.

Graduate Two Master of Science students, D. Munoz-Garcia and F. Nestel, and two Ph.D. students, D. Carlow and R. Walker, were registered as graduate students in the department. One student, Nestel, successfully completed and defended his Master of thesis in February 1983. Science Another student, successfully completed and defended his Ph.D. thesis in April One graduate student, K. Wong, although registered in the Department of Biochemistry, worked under the supervision of Dr. Kisilevsky in the Department of Pathology, and successfully defended his Ph.D. thesis in November 1982.

The Department of Pathology will be introducing a new graduate course, Pathology 823, Cancer Biology, commencing January 1984. This course has been designed to consider cancer in the broadest possible perspective. The course is geared to graduate students who do not necessarily have an M.D., although medical graduates engaged in a graduate program are not excluded.

Undergraduate Seventy-seven second medical year undergraduates took General Pathology and Special Pathology during the academic year 1982-1983. Eleven medical undergraduates were in the department during the summer of 1982 working either as summer interns or engaged in research. Three medical undergraduates took electives in the department during 1982-1983.

Fellows Two postdoctoral fellows, Dr. Robert G. Liteplo, and Dr. Suzanne Laferte, were appointed to the Cancer Research Group of the Department of Pathology. Dr. Kerbel is Dr. Liteplo's supervisor, and Dr. Elliott is Dr. Laferte's supervisor.

CLINICOPATHOLOGICAL CONFERENCES

A total of twenty-five Clinicopathological Conferences were presented. There were sixteen from the Department of Medicine; six from the Department of Surgery; two from the Department of Pediatrics; and one from the Department of Obstetrics and . Gynecology.

RESEARCH GRANTS

Research grants held by senior members of staff for the current academic year are listed in Appendix II. Operating grants during 1982-1983 totalled \$1,177,215 and direct, competitive personal suport was \$143,300.

FUTURE PLANS

During the past year the Planning Committee of the Department of Pathology, under the chairmanship of Dr. Steele, participated with the architects engaged by Kingston General Hospital the planning of new facilities for biochemistry and the autopsy suite, and renovations of the remainder of the hospital laboratories.

The next major change, presently in the planning stage, development of a laboratory computing system. Currently systems are available commercially which provide specimen identification, direct capture of data from automated equipment, quality control procedures, and both cumulative and statistical data reports. At present the laboratory generates over a million reports a year, all of which are handled manually, present information in an optimal fashion for patient not care. The development of a laboratory computer system is ideally part of a total hospital patient care data system. It is hoped that during the coming year significant progress will be made in developing the specifications required for such a system.

PAPERS DELIVERED AT CONGRESSES, INVITED LECTURESHIPS, AND OTHER ACTIVITIES

During the year several mmembers of senior staff delivered papers at meetings, were invited lecturers and visiting professors at various universities. This information is contained in Appendix IV and Appendix V.

EXTRAMURAL ACTIVITIES OF NATIONAL AND INTERNATIONAL IMPORTANCE

DR. A.F. CLARK Dr. Clark is member of both the Ontario a Treatment and Research Foundation Advisory Research Committee, and the Working Party on CEA and Estrogen Receptors. is also a Scientific Officer of the Medical Research Council Maintenance Grants Panel. On university committees, Dr. Clark is a member of the Principal's Advicory Committee; a member the Animal Care Committee; a mmember of the Radiation Safety Committee; a member of the Ethics Committee of Queen's University; a of the Hazardous Chemicals Committee; member member of the Faculty of Medicine Student Appeals Committee and a member of the Faculty of Medicine Council.

DR. W.E.N. CORBETT Corbett is Consultant Pathologist for Dr. the Canadian Tumour Reference Centre of the National Cancer Institute of Canada, on the diagnostic panel for lymphoreticular malignancies. Dr. Corbett is a member of the Residency Training the Canadian Association of Pathologists. Committee of also a Reference Pathologist, National Cancer Institute of Canada (Malignant Lymphoma). Dr. Corbett is also a Trials the Hematology Subcommittee, School Terminology, St. Lawrence College, and a member of the Curriculum of Committee of the Faculty of Medicine at Queen's University.

Panel of the Canadian Tumour Reference Center. At Hotel Dieu Hospital, Dr. Dexter is Secretary-Treasurer of the Medical Staff. He is also a member of the curriculum committee for Rehabilitation Medicine.

DR. B.E. ELLIOTT Dr. Elliott is a member of the National Cancer Institute of Canada Hematology and Immunology Panel B. Dr. Elliott is also Chairman of the Animal Care Committee of Queen's University.

DR. W.A. FLETCHER Fletcher is Secretary-Treasurer of the Dr. Society of Cytology; a member of the Canadian Association of Pathologists Commission on Continuing Education; a of the Toronto Institute of Medical Technology Advisory Council - Cytotechnology, and a member of the Council, Section on Laboratory Medicine, Ontario Medical Association. Dr. Fletcher of the Medical Audit Committee at Kingston General member Hospital. Fletcher is Chairman of the Infection Control Dr. Committee and the Medical Audit Committee at the Lennox & County General Hospital. He is also a member of the Perinatal Mortality Committee at Moose Factory Hospital.

- DR. P.M. FORD Dr. Ford is Chairman of the Protocol Committee for Study of Apheresis in Rheumatoid Arthritis; a member of the Arthritis Society Medical and Scientific Manpower Development Committee; Ontario Medical Association representative on the Faculty of Medicine Continuing Medical Committee and Chairman of the Safety Committee for Etherington Hall.
- DR. A.R. GILES Dr. Giles is Chairman of the Ontario Hemophilia Study Group; a member of the Canadian Hemophilia Medical Scientific Advisory Committee; a member of the Ontario Factor VIII Supplier/User/Fractionator Group; a member the Canadian Plasma Exchange Study Group and a member of the Canadian Plasma Exchange Study Group Rheumatology Protocol Dr. Giles also Chairman of the Therapeutic is Pheresis Committee at Kingston General Hospital.
- DR. R.S. KERBEL Dr. Kerbel is a member of the Study Section Pathology B, National Institutes of Health, U.S.A. He is also a member of the Ad Hoc Committee on MRC Biohazards Regulation Changes.
- DR. R.S. KISILEVSKY Dr. Kisilevsky is a Scientific Officer of the Medical Research Council Pathology and Morphology Committee. He is also a member of the Canadian Arthritis and Rheumatism Society Research Grants Panel. Dr. Kisilevsky has also been appointed to the Editorial Board of Laboratory Investigation.
- DR. S.K. LUDWIN Dr. Ludwin is a member of the Medical Advisory Board of the Multiple Sclerosis Society of Canada. He is also Chairman of the Royal College of Physicians and Surgeons of Canada Committee on Neuropathology. Dr. Ludwinn is a member of the Editorial Advisory Board, Journal of Neuropathology and Applied Neurobiology.
- DR. P.N. MANLEY Dr. Manley serves on the following committees Canadian Association of Pathologists: Chairman, Commission on Continuing Education, member of the Central Scientific Planning Committee, and member of the Membership Committee. Dr. Manley was also an examiner in anatomical pathology for the Royal College of Physicians and Surgeons of Canada.

- DR. T.F. McELLIGOTT McElligott is a member of both the Dr. Advisory Medical Board and the Standing Committee on Records and Statistics Ontario Cancer Treatment and of the Foundation. also Secretary-Treasurer of the Canadian He is Association Pathologists and representative from the CAP to both the Canadian Blood Committee and the International Council Laboraotory Medicine of Canada. At Hotel Dieu Hospital Dr. McElligott is Chairman of the Infection Control Committee, the HDH Planning Committee and the Outpatient Committee. At Queen's University Dr. McElligott is a mmember of the Faculty Promotion Committee, Chairman of the Dean's Curriculum Task Force, and a member of the Life Sciences Review as well as being an ex officio member of both the Curriculum Committee and the Awards Committee.
- DR. R. PRENTICE Dr. Prentice is a member of Council of the Ontario Association of Pathologist, and a reference pathologist for the Canadian Tumour Reference Center Skin Tumour Panel. At Hotel Dieu Dr. Prentice is also Chairman of the Medical Education Committee, and a member of the Medical Advisory Committee and the Tissue and Audit Committee.
- DR. M.J. Raymond Dr. Raymond is a member of the Ontario Council of Health Task Force on High Technology Diagnostic Laboratory Procedures and Equipment.
- DR. D.M. ROBERTSON Dr. Robertsonn is a Scientific Officer for the Neuroscience Committee, Medical Research Council; a member of Committee in Neuropathology, Test American Board Pathology; a member of the Editorial Board of Laboratory Investigation; a member of the Ontario Council of Health Advisory Panel; Consultant in Pathology of the Ontario Cancer Fouundation, Kingston Clinic; a member of the National Advisory Committee of the Canadian Brain Tissue Bank; a member of the Advisory Board of Neuropathology An International President-Elect of the International Academy of Pathology (United States-Canadian Division); Consultant Neuropathologist of the Canadian Tumour Reference Center and Chairman of the Ontario Treatment and Research Foundation Research Personnel Committee. Dr. Robertson is Chairman of the Biohazards Committee Queen's University and Chairman of the Faculty Postgraduate Education Committee. At Kingston General Hospital he is Chairman of the Ad Hoc Budget Committee, and Vice-Chairman of the Medical Advisory Committee.
- DR. H.D. STEELE Dr. Steele is a member of the Ambulatory Care Committee, the Clare Nelson Committee, and the Utilization Committee at Kingston General Hospital. He is a member of the Medical Advisory Committee at St. Mary's of the Lake Hospital, and Chairman of the Infection Control Committee. Dr. Steele is also a member of the Royal College of Physicians and Surgeons Test Committee in Anatomical Pathology.

RESEARCH

Dr. A.F. Clark Dr. Clark's research is concerned with androgen metabolism. He has been studying androgen metabolism in the rat especially as it related to the prostate gland. Prostatic enzymes involved in androgen metabolism are being studied so as to understand their role in controlling the expression of androgenic activity. The androgen dependence of the prostatic enzyme, acid phosphatase, is being studied. Prostate cell culture studies are being utilized to investigate androgen metabolism, indicators of androgen actions and the mechanism of androgen actions in normal cells. He is also associated with Dr. C. Bird of the Department of Medicine in studies on the kinetics of androgen metabolism in humans.

Dr. A.J. de Bold Dr. de Bold's research has concentrated on the study of atrial natriuretic factor. This factor is a naturally occurring diuretic heart peptide first described and isolated in Dr. de Bold's laboratory. Extensive collaborative work has been established to continue this line of research. The possible pharmaceutical use of atrial natriuretic factor is being explored in collaboration with pharmaceutical companies.

Dr. D.F. Dexter Dr. Dexter, in collaboration with Dr. evaluating a new method of tumour cell transplantationusing preculture with lung tissue cubes and evaluating the pathology of human melanoma metastasizing tumour cell lines in nude mice. Dexter's research with Dr. Roder is in various areas including assessment of induced and spontaneous tumours in NK deficient mice the relationship to impaired immune surveillance. a study of the characteristics of various human addition, hybridomas is ongoing. In collaboration with Dr. C. Bird and Clark, Dr. Dexter is assessing the estrogen status and receptor protein in patients with carcinoma of the and currently is investigating the potential of the demonstration of estrogen receptor binding sites on tissue by fluorescent techniques. In collaboration with Dr. E.E. Dexter is also correlating pathological prognostic factors against isotope clearance rates in patients with breast cancer versus actual follow-up data.

Dr. B.E. Elliott The long term objective of Dr. Elliott's programme obtain an understanding of host T cell is to immuno-surveillance and how this system can be used in defense against neoplasia. A fundamental question in tumor immunology is spontaneous human tumors express antigens recognized as foreign by the host immune system. Three main projects currently underway in Dr. Elliott's laboratory are: a) the biochemical and genetic properties regulating the expression of tumor antigens are being studied; b) immunoregulatory steps required in the induction an optimal CTL response against the tumor are being studied by establishing in vitro tumor specific T cell clones and c) a human tumor system is being developed, analogous to the murine tumor model, to determine whether tumor antigens can be recognized on the parent tumor by autologous T lymphocytes immunized in vitro against immunogenic variants derived from the original tumor.

RESEARCH (continued)

Dr. P.M. Ford Dr. Ford is doing research on a study of the interaction rheumatoid factor with immune complexes in the of pathogenesis of immune complex associated diseases. grant started July 1982 and will run for two years. research Ford is also a co-investigator of a clinical trial of the calcium blocker Diltiazem in patients with Raynaud's phenomenon. Dr. also chairman of a multi-center Ford is Plasmapheresis Protocol Study Group for Rheumatoid Arthritis which is being supported by Health and Welfare.

Dr. A.R. Giles Dr. Giles research activities are as follows: 1) investigation of the thrombogenicity of prothrombin complex concentrates, 2) investigation of the association between thrombocytopenic bleeding and antibiotic therapy, development of a Factor VIII bypassing therapy for hemophilics with a Factor VIII inhibitor, 4) combined in vitro and in vivo study of the interaction of specific clotting factors and their inhibition by their natural inhibitors with particular reference to Protein-C and Factors V and VIII, 5) investigation the role of plasmapheresis in the treatment of severe rheumatoid arthritis.

Dr. R.S. Kerbel Dr. Kerbel's research program is concerned the cell biology of tumor progression, heterogeneity, and cancer metastasis. A major part of his current program is devoted to an analysis of the possibility that cancer cell populations can diversify and progress towards of malignancy increased (metastasis) spontaneous somatic cell hybridization in vivo with normal host cells, such as macrophages or fibroblasts. Definitive evidence process has been obtained in an experimental mouse this tumour system, using so-called lectin-resistant membrane mutant sublines of the tumour. This program is being done collaboration with Dr. A.E. Lagarde. In a collaborative study with Dr. Dennis, mutants, hybrids, and parental cell lines J. being used in a comparative manner to study features of cells and host responses which are relevant to the metastatic process. A third area of investigation, collaboration with Dr. P. Frost, California, and Dr. concerns new approaches to specifically immunotherapy of established metastases, and the study of tumor cell specific During the past year considerable associated antigens. has been achieved towards developing a new model to progress metastasis and tumor progression from the perspective of human cancer cell populations. This involves the growth of human tumors in athymic 'nude' mice.

RESEARCH (continued)

- Dr. R. Kisilevsky Dr. Kisilevsky's research concerns 1) the protein synthesizing apparatus of liver cells, and the manner in apparatus is upset in induced disease states. particular problems at the moment are a) modulation of ribosome structure b) an examination of several enzymes involved in ribosomal protein phosphorylation c) mRNA metabolism d)initiation factor phosphorylation - all during induced cell injury and 2) pathogenesis of experimental murine amyloidosis.
- Dr. A.E. Lagarde Dr. Lagarde is using somatic cell genetic approaches and tissue culture techniques to study tumor-host hormonal immune interactions and during cancer progression in The objective is to analyzse the cellular animal models. responsible for the successive chromosome alterations mechanisms lead somatic cells to acquire increasing malignant and to examine the role played by host immune defence potential, mechanisms during the stepwise selection of tumoral variants. lines have been successfully established in cloned cell which retain the functional characteristics of natural culture, killer (NK) lymphocytes. They will provide us with a unique tool study the molecular basis of the tumor recognition and lysis by NK cells, as well as to explore the possibility of using them in adoptive immunotherapy of cancer. The natural progression of hamster fibroblastic cell line toward the production fibrosarcomas in nude mice offers another tumor-host experimental where the response of the thymus-independent immune system to tumor xenografts can be validly examined.
- Dr. S.K. Ludwin Dr. Ludwin's project deals with the mechanisms of remyelination in the central nervous system. This study involves the use of Cuprizone to cause demyelination in the central nervous system of young mice. Through the use of electron microscopy, radio-autography and immunohistochemistry, is attempting to elucidate the cellular mechanisms Ludwin in remyelination. In addition, a project involving oligodendrocyte mitogenesis in tissue culture explants of the nervous system has been started under funding from the PSI Foundation.
- <u>Dr. P.N. Manley</u> Dr. Manley's research activities involve the diagnostic specificity of prostatic acid phosphatase, an analysis by immunohistochemistry and radioimmunoassay.
- <u>Dr. T.F. McElligott</u> Dr. McElligott, in collaboration with his graduate student, continues to study the morphologic aspects of hepatotoxicity of drugs with the support of the Canadian Liver Foundation.

- RESEARCH (continued)
- Dr. S. Nag Dr. Nag's research concerns the following: 1) studies of cerebral findings in experimental acute and chronic hypertension at the light and electron microscopic level. In addition, immunoperoxidase studies of both human and animal brains is underway to localise extravasation of endogenous serum albumin; 2) studies of cells obtained from isolated cerebral microvessels is ongoing.
- Raymond has continued the development and Dr. M. Raymond Dr. immprovement of the methodologies employed in the clinical chemistry laboratory. His research interest is investigation of the potential application for computers within the clinical laboratories. This ongoing study is concerned with possible impact of computerization on the handling of patient data, laboratory management and resident programs within the department. In addition, a new study has undertaken to investigate the applications computer-aided diagnosis to laboratory medicine.
- Dr. D.M. Robertson Dr. Robertson is studying models experimental diabetic neuropathy. In collaboration with Dr. H. Dinsdale of the Department of Medicine, Dr. Robertson is studying the effects of and chronic hypertension on acute cerebral flow and permeability. blood Dr. Robertson, co-investigators Drs. Kerbel, Elliott and Lagarde, of the Cancer Research Group, Department of Pathology, are jointly carrying out research in tumor biology and immunogenetics.
- Dr. H.D. Steele Dr. Steele, with Dr. H. Gorwill of the Department of Obstetrics and Gynecology, are using a mouse model to study the effects of certain hormones on cervico-vaginal development, and the relationship of these to neoplasia. With co-investigator Dr. J. Carmichael of the Department of Obstetrics and Gynecology, Dr. Steele is reviewing the cytologic history and findings of recently diagnosed cases of carcinoma of the cervix.
- Dr. S. Wasan Dr. Wasan's research involves the following areas: 1) study of corneal lesions by light and scanning electron microscopy in association with Dr. W.E. Willis of the Department of Ophthalmology, Hotel Dieu Hospital, and 2) study of contact lens and Timolol induced corneal lesions in rabbits, in collaboration with Dr. W.E. Willis, and funded by PSI.
- <u>Dr. J.C. Wyllie</u> Dr. Wyllie's research activities conducted during the past year consisted of a light microscopic study of subarticular (epiphyseal) lesions in rheumatoid disease.

VISITING LECTURERS

DEPARTMENT OF PATHOLOGY

1982 - 1983

- Dr. Marc Lalande, Department of Pediatrics, Children's Hospital Medical Center, Boston, Mass., presented a research seminar entitled, "Applications to Flow Cytofluorometry to Cell Surface and Chromosome Analysis and Sorting" in the Cancer Research Laboratories, Botterell Hall, on June 28, 1982.
- <u>Dr. Suzanne Laferte</u>, McGill Cancer Center, McGill University, presented a special seminar in Botterell Hall 3rd Floor Conference Room entitled, "Biochemical Studies of Cross-Reactive Carcinoembryonic Antigens from Neoplastic and Normal Tissues" on July 7, 1982.
- <u>Dr. Curtis Gemmel</u> Senior Lecturer in Bacteriology, University of Glasgow, presented a special seminar entitled, "Streptococcal M Protein and the Effects of Antibiotics" on August 4, 1982, in Richardson Laboratory.
- <u>Dr. Kenneth Pritzker</u>, Assistant Professor, Department of Pathology, Mount Sinai Hospital and University of Toronto, presented a special seminar entitled, "Crystals and Joint Disease" in the departmental library on August 12, 1982.
- Dr. F. Sharkey Assistant Professor, Department of Medicine, M.S. Hershey Medical Center, Pennsylvania State University, Hershey, Pennsylvania, presented a special seminar entitled, "Morphometric Grading of Human Breast Carcinoma" in the departmental library on August 26, 1982.
- Dr. S.N. Huang Chairman, Department of Pathology, Memorial University, St. John's, Newfoundland, presented a seminar entitled, "The Histogenesis and Significance of Alcoholic Hyaline" in the departmental library on September 13, 1982.
- Dr. Thierry Boon Director, Cellular Genetics Unit,, Brussels, presented a research seminar in conjunction with the Queen's Quest Visiting Scholar program entitled, "Immunological Alteration of Tumor Cells by Chemical Mutagenesis: Implications for Immune Surveillance Theories of Cancer" in the conference room of Botterell Hall on September 14, 1982.

- Dr. Hanna M. Pappias Department of Neurology and Neurosurgery, McGill University, presented a seminar in conjunction with Queen's Neurosciences Seminar Series entitled, "Functional Disturbances in Brain Following Injury: Search for Underlying Mechanisms" in the departmental library on September 22, 1983.
- Dr. Horatio T. Enterline Professor of Pathology, University Hospital, University of Pennsylvania School of Medicine, presented a seminar entitled, "Sarcomas of the Gastrointestinal Tract" in the departmental library on October 20, 1982.
- Dr. M. Nesheim Mayo Clinic, Rochester, New York, presented a special seminar entitled, "Aspects of the Structure and Function of the Prothrombinase Complex" on November 9, 1982, in the departmental library.
- <u>Dr. R. Losito</u> Centre Hospitalier Universitaire, University of Sherbrooke, presented a special seminar entitled, "The Isolated Liver Studies Related to Hemostasis" in the departmental library on November 11, 1982.
- Dr. Alexandre Duncan Ludwig Institute for Cancer Research, Toronto, presented an informal research seminar entitled, "What are Sister Chromatid Exchanges" in the conference room of Botterell Hall on December 13, 1982.
- Dr. Peter L. Carlen Associate Professor, Medicine (Neurology) Toronto Western Hospital, Department seminar in conjunction presented with the Neurosciences Seminar Series entitled, "Calcium, Gaba, and the Mechanism of Inhibition by Sedative Hypnotic Drugs". Neuronal Dr. Carlen is an Ontario-Quebec Neurobiology Exchange Speaker. took place in the departmental library on December 7, 1982. The seminar
- <u>Dr. F. Richmond</u> Department of Physiology, Queen's University, presented a seminar in conjunction with the Neuroscience Seminar Series entitled, "Structural Variations in the Muscle Spindle Family: Consideration for Proprioceptive Behaviour" in the departmental library on January 11, 1983.
- Dr. T. Reader Neuroscience Research Group, University of Montreal, presented a seminar at the Neurosciences Seminar Series on January 26, 1983. The title of his seminar was "Electrophysical and Biochemical Studies of Cortical Monoamine Innervation".

<u>Dr. Monroe W. Cohen</u>, Department of Physiology, McGill University, presented a seminar in conjunction with the Queen's Quest Visiting Scholar program entitled, "Neuromuscular Synaptogenesis: Localization of Acetylcholine Receptors and Cholinesterase" in the departmental library on February 2, 1983.

<u>Dr. M. Deschens</u>, of Laval University presented a seminar in conjunction with the Queen's Quest Visiting Scholar program entitled, "The Physiological Basis of Thalamic Rhythmicity" in the departmental library on February 16, 1983.

Dr. Kresimir Krnjevic, department of Physiology, McGill University presented a seminar in conjunction with the Queen's Quest Visiting Scholar program entitled "The Physiological Role of Acetylcholine in the Cortex" in the departmental library on February 23, 1983.

Dr. Peter M. Davies, Department of Pathology, Albert Einstein College of Medicine, New York, presented a seminar in the departmental library on March 2, 1983 in conjunction with the Queen's Quest Visiting Scholar program entitled "The Neurochemistry of Alzheimer's Disease"

Dr. Robert L. Reid, Department of Obstetrics and Gynecology, Queen's University, presented a seminar to the Neurosciences group on March 9, 1983 in the departmental library entitled "Neuroendocrine Regulation of Gonadotropin Secretion".

Dr. David M. Goldberg, Professor and Chairman, Department of Clinical Biochemistry, University of Toronto, Biochemist-in-Chief, Hospital for Sick Children, was a Queen's Quest Visiting Scholar. He was sponsored by the Department of Pathology and supported by Queen's Quest. Dr. Goldberg gave a presentation March 10 in accordance with the Medical Sciences Lecture Series entitled "Clonal Aspects of Liver Microsomal Enzyme Induction". On March 11, Dr. Goldberg lead a discussion with Clinical Pathology residents (completed clinical pathological conference with laboratory data). He then gave a departmental seminar to staff and residents in the departmental library entitled "Discriminant Function Analysis and Utilization of Laboratory Tests for the Diagnosis of Liver Disease"

Dr. Carol Petito, Department of Pathology, Cornell University Medical College, New York, visited the department March 30, 1983 and presented the Neurosciences Seminar. The title of her seminar was "Mechanisms of Ischemic Brain Damage". Dr. Petito also participated in the Neuropathology Conference in the department March 31 and presented a Neuropathology Slide Seminar.

Dr. M.J. Phillips, Pathologist-in-Chief, Hospital for Sick Children, Toronto, presnted a Slide Seminar to the residents in the department on April 5, and also a Special Seminar in the departmental library entitled "What is Actin Doing in the Liver".

Dr. Donald M. Price, Department of Pathology and Neurology, Johns Hopkins University School of Medicine, Baltimore, presented the Neurosciences Seminar in the department on April 6, 1983. The title of his seminar was "Neurobiology of Alzheimer Disease".

Dr. William G. Tatton, Playfair Neuroscience Unit, Toronto Western Hospital, presented the Neurosciences Seminar in the department on April 20, 1983. The title of his seminar was, "Postnatal Development of the Corticospinal System".

Dr. Klaus Lewin Dr. Lewin, Professor and Vice-Chairman, Department of Pathology, UCLA School of Medicine, Los Angeles, visited the department May 10, 1983. He presented a seminar entitled, "Gastrointestinal Manifestations of AIDS". In addition, Dr. Lewin presented a Gastrointestinal Slide Seminar to the residents and staff.

Dr. J. Hirsh Dr. Hirsh, Professor and Chairman, Department of Medicine, McMaster University, was a Medical Research Council Visiting Professor May 18 and 19, 1983. Dr. Hirsh participated in case presentations by the resident staff in the Departments of Medicine and Pathology. Dr. Hirsh gave the Medical Sciences Lecture; the title of his talk was, "The Principles and Management of Anticoagulation Therapy". In addition, Dr. Hirsh gave a Research Presentation to the staff and residents and presented a seminar entitled, "Investigation of Thromboembolic Disorders" to the residents in Radiology, Medicine and Pathology. Dr. Hirsh also participated in Grand Medical Rounds and presented Venous Thrombosis in a Patient with Antithrombin III Deficiency.

(i)

APPENDIX II

RESEARCH GRANTS IN PROGRESS

DEPARTMENT OF PATHOLOGY

APRIL 1, 1982 - MARCH 31, 1983

NAME	GRANTING BODY	AMOUNT OF GRANT	TITLE OF PROJECT
Dr. A. Clark	National Cancer Institute	32,880	Hormones in the control of growth and function of rat prostate cells
Dr. A. Clark	Medical Research Council	72,660	Steroid Metabolism and Actions
Dr. A.J. deBold	Ontario Heart Foundation	34,312	Studies on a Natriuretic Factor Isolated from Heart Atria
Dr. A.J. deBold	J.P. Bickell Foundation	15,000	Investigations on a Diuretic (Natriuretic) Factor Isolated from Atrial Myocardium
Dr. A.J. deBold	Medical Research Council	29,000	Isolation and Characterization of Atrial Natriuretic Factor
Dr. B.E. Elliott	Medical Research Council	43,700	Clonal Analysis of Ctyolytic lymphoreticular cells in host defense: Physiology, serology and biochemistry of effector and target interactions
Dr. A.R. Giles	Alpha Therapeutic Corporation	79,275 (1982-84)	Developemnt of Factor VIII Bypass
Dr. A.R. Giles	Health and Welfare Canada	71,757	An Investigation of Mechanisms Responsible for the Thrombo- genicity of Prothrombin Complex Concentrates in Patients with Liver Disease

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NAME	GRANTING BODY	AMOUNT OF GRANT	TITLE OF PROJECT
Dr. A.R. Giles	Medical Research Council	28,000	The Role of Phospholipid in Bypassing Factor VIII (Anti-hemophilic Factor) Activity and/or Inhibition in vivo
Dr. R.S. Kerbel	Medical Research Council	42,624	Detection, significance and applied use of membrane-associated antigen and receptor alterations on activated lymphocytes and macrophages
Dr. R. Kisilevsky	Medical Research Council	55,611	Molecular Pathology - the protein synthesizing apparatus of liver cells in an induced pathological state: a biochemical dissection of pathological reactions
Dr. R. Kisilevsky	Medical Research Council	79,587	Amyloidogenesis: An analysis of the causative factors in an experimental murine model
Dr. S.K. Ludwin	Medical Research Council	43,067	Studies in Central Nervous System Remyelination
Dr. S.K. Ludwin	P.S.I. Foundation	31,700	Tissue Culture Study of Oligodendrocyte Mitogenic Factors
Dr. P. Manley	National Cancer Institute	20,875	Diagnostic Specificity of Prostatic Acid Phosphatase: An Analysis by Immuno- histochemistry and Radio- immunoassay

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NAME	GRANTING BODY	AMOUNT OF GRANT	TITLE OF PROJECT
Dr. T.F. McElligott	Canadian Liver Foundation	10,000	Morphological Aspects of Drug-Induced Hepatotoxicity
Dr. S. Nag	Ontario Heart Foundation	30,000	Mechanisms of Cerebral Damage in Hypertension
Dr. D. Robertson	Medical Research Council	49,470	Maintenance Cost of Electron Microscopic Unit for the Study of Molecular Pathology
Dr. D. Robertson (Dr. H. Dinsdale)	Medical Research Council	58,275	Research in Cerebrovascular Disease
Dr. D. Robertson (Dr. R. Kerbel, Dr. B. Elliott Dr. A. Lagarde)	National Cancer Institute	313,609	A Program in Tumour Biology and Immunogenetics
Dr. D. Robertson (Dr. R. Kerbel, Dr. B. Elliott, Dr. A. Lagarde, Dr. J. Dennis, Dr. J. Roder	Medical Research Council	36,886	Maintenance Grant for Fluorescence Activated Cell Sorter
Dr. H.D. Steele (Dr. R.H. Gorwill)	Medical Research Council	10,155	Studies on the Effect of Clomiphane Citrate on Vaginal Differentiation in the Mouse
Dr. T.F. McElligott	Atkinson Charitable Foundation	20,802	Purchase of Ultracentrifuge

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- 638. Structural Requirements for Cyclic AMP to Bind to a Rat Liver Receptor(s). (ABSTRACT)

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- 639. Effect of DL-Ethionine on Rat Liver Cyclic AMP Levels.
 (ABSTRACT)

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- A New Method for the Preparation of Solid-Phase Immunoadsorbents
 Edwin R. Phillips, James W. Dennis, Bruce E. Elliott, Robert S. Kerbel
 Analytical Biochem. 121:83, 1982
- The Role of Androgen Metabolism in the Control of Androgen Action in the Rat Prostate

 M. Tenniswood, C.E. Bird, A.F. Clark

 Mol. & Cell. Endocrinol. 27:89, 1982
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 Workshop on Diabetes, October 1981, Toronto, Canada. (ABSTRACT)
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 S. Ford and Malcolm D. Silver
 IN: The Coronary Artery, Edited by Stanley Kalsner,
 Croom Helm Ltd., London, 1982, p. 596
- An Enzyme-Linked Immunosorbent Assay (Elisa) for Detergent Solubilized Ia Glycoproteins Using Nitrocellulose Membrane Discs
 Roger G.E. Palfree and Bruce E. Elliott
 J. Immunol. Methods 52:395, 1982
- 650. Further Characterization of Amyloid-Enhancing Factor M.A. Axelrad, R. Kisilevsky, J. Willmer, S.J. Chen M. Skinner Lab. Invest. 47:139, 1982
- Stroma Free Human Platelet Lysates Potentiate the In Vivo Thrombogenicity of Factor Xa by the Provision of Coagulant-Active Phospholipid

 A.R. Giles, M.E. Nesheim, H. Hoogendoorn, P.B. Tracy
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 Acta Morphologica 3:49, 1982
- Facilitation of Tumour Progression by Cancer Therapy R.S. Kerbel, A.J.S. Davies The Lancet, October 30, 1982, p. 977

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- An Electron Microscopic Study of Heme Uptake by Rat Duodenum.

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 M.P. Tenniswood, P.P. Abrahams, C.E. Bird, A.F. Clark
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- Tuberous Sclerosis in an Infant of 28 Weeks Gestational Age
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 Danuta Kozbor, David Dexter, John C. Roder
 Hybridoma Volume 2, Number 1:7, 1983
- 661. Kinetics of Amyloid Deposition: I. The Effects of Amyloid-Enhancing Factor and Splenectomy R. Kisilevsky, L. Boudreau Lab. Invest. 48:53, 1983
- 662. Kinetics of Amyloid Deposition: II. The Effects of Dimethylsufoxide and Colchicine Therapy R. Kisilevsky, L. Boudreau, D. Foster Lab. Invest. 48:60, 1983

PAPERS DELIVERED AT MEETINGS AND CONFERENCES

- Dr. A.F. Clark (With J. Orlowski, J. Downey and C.E. Bird) presented a paper at the New England Endocrine Conference meeting in North Holyoke, Mass. in October 1982. The paper was entitled, "Changes in Acid Phosphatase Characteristics of the Rat Ventral Prostate During Sexual Maturation".
- Dr. W.E.N. Corbett Dr. Corbett presented two papers at the annual meeting of the Canadian Association of Pathologists in Vancouver in June 1982. They were entitled, "Variant Acute Promyelocytic Leukemia" (with Dr. A. Packer) and "Fulminant Cystococcosis with Pathologic Splenic Rupture Complicating Chronic Lymphocytic Leukemia" (with Dr. D. Lillicrap).
- Dr. A.J. de Bold Dr. de Bold presented a paper at the American Society of Experimental Biology meeting in April 1982, the title of which was, "The Relationship between Atrial Natriuretic Factor and Specific Atrial Granules".
- Dr. D.F. Dexter Dr. Dexter presented a paper at the Ontario Association of Pathologists meeting in Peterborough in September 1982 entitled, "Tumour Cell infiltrated Lung Cubes A Novel Method for Tumour Transplantation".
- Dr. P.M. Ford Dr. Ford presented a paper at the PanAmerican Congress of Rheumatology in Washington in June 1982. The title of his paper was, "In Situ Reactivity of Human IgM Rheumatoid Factor (RF) with Glomerular Immune Complexes in Experimental Chronic Serum Sickness".
- Dr. A.J. Giles Dr. Giles presented "Factors Influencing the Reproductibility and Standardization of Animal Models of Thrombosis" at the International Committee on Thrombosis and Hemostasis in Bergamo, Italy, July, 1982. Dr. Giles also presented "Measurement of Coagulent-Active Phospholipid Content as a Predictor of In Vivo Thrombogenicity" at the same meeting. At the American Heart Association meeting in Dallas in November 1982 Dr. Giles presented a paper entitled, "A Canine Model for Evaluating the Interactions Between the Intrinsic and Extrinsic Pathways of Coagulation In Vivo".
- Dr. R. Kisilevsky Dr. Kisilevsky presented two papers at the Federation of Biological Societies meeting in Edmonton in June 1982. The titles of these papers were, "Structural Requirements for Cyclic AMP to Bind to a Rat Liver Receptor(s)"(with K.H. Wong) and "Effect of DL-Ethionine on Rat Liver Cyclic AMP Levels" (with K.H. Wong). Dr. Kisilevsky also "Inflammation Associated Amyloidosis" Experimental Pathology Symposium which was part of the Canadian Association of Pathologists meeting in Vancouver in June 1982.

- Dr. A.E. Lagarde Dr. Lagarde presented a paper entitled, "Long Term Murine Cloned Cell Lines Exhibiting Spontaneous Killing Activity" at the Canadian Federation of Biological Societies meeting in Ottawa in June 1983, and at the 15th International Leukocyte Culture Conference at Asilomar, California, in December 1982.
- Dr. T.F. McElligott McElligott (with R.M. Dr. Walker) two papers at the Canadian Federation of Biological presented annual meeting in Edmonton in June 1982. Societies "Evidence for a Central Action of the Parent Compound They were, Acetaminophen-Induced Hypothermia in Mice" and "Enhanced Acetaminophen Toxicity Mice Following Chronic in Consumption". Dr. McElligott (with R.M. paper entitled, "Acetaminophen-induced Hepatic Congestion in Walker) presented a Mice" at the Society of Toxicology meeting in February 1983.
- <u>Dr. P. Manley Dr.</u> Manley (with Dr. F. Swaine) presented a paper "Lymph Node Infarction" at the annual meeting of the Canadian Association of Pathologists in June 1982.
- Dr. S. Nag Dr. Nag presented a paper entitled, "Permeability and Immunohistochemical Studies of Brain in Chronic Hypertension" at the Fifth International Symposium on Brain Edema in Holland in June 1982, and at the annual meeting of the Canadian Association of Neuropathologists in Montreal in September 1982.
- <u>Tr. R.S. Prentice</u> Dr. Prentice presented a paper entitled, "Malignant Melanoma" at the Symposium on Tumours of the Eye and Orbit at the Donald Gordon Centre, Queen's University, in May 1982.
- Dr. H.D. Steele Dr. Steele presented a paper at the Canadian Congress of Laboratory Medicine in Vancouver in June 1982 entitled, "The Effect of Clomiphene Citrate on Vaginal Differentiation in the Mouse".
- Dr.S.M. Wasan Dr. Wasan presented, "The Ultrastructural and Immunofluorescent Effects of Topical Timolol on the Rabbit Corneas" at the Association for Research in Vision and Ophthalmology in Sarasota in May 1982. Dr. Wasan also presented "Timolol Induced Lesions in Human and Rabbit Corneas" at the Canadian Ophthalmological Society meeting in Toronto in June 1982.
- <u>Dr. J.C. Wyllie</u> Dr. Wyllie presented, "Histopathology of the Subchondral Bone Lesion in Rheumatoid Arthritis" at the 1st Edward Dunlop Scientific Symposium 'Mechanisms of Connective Tissue Destruction and Repair in Articular Tissues' held at Kingston in October 1982.

INVITED LECTURESHIPS AND VISITING PROFESSORSHIPS

Dr. A.J. de Bold Dr. de Bold was an invited lecturer in Argentina in October 1982. He gave a talk entitled, "Presence of a Peptide with Diuretic and Natriuretic Properties in the Atrial Myocardium" to the Biology Society in Cordoba. Dr. de Bold also gave a talk entitled, "The Use of HPLC in the Clinical Laboratory" in the Department of Clinical Chemistry, Central Laboratory Hospital Nacional de Clinicas in Cordoba. In San Juan de Bold presented "Therapeutic Drug Monitoring" to the Society of Clinical Chemists. At the Institute of Experimental Biology and Medicine, Buenos Aires, Dr. de Bold gave a talk entitled "Presence of a Peptide with Potent Diuretic and Natriuretic Properties in the Atrial Myocardium. Relationship with Atrial Specific Granules".

Dr. P.M. Ford Dr. Ford was an invited lecturer in the Department of Medicine at McMaster University in December 1982 and presented a lecture entitled, "Lupus Nephritis". Dr. Ford also presented a lecture entitled, "Plasmapheresis in Rheumatoid Arthritis - A Double-Blind Crossover Controlled Study" to the Haemonetics Research Institute Tenth International Advanced Apheresis Seminar in Boston in May 1983.

Dr. A.R. Giles Dr. Giles presented a paper entitled, "Hemophilia Related Research" at the Advances in Hemophilia Symposium sponsored by the Ontario Chapter of the Canadian Hemophilia Society, Toronto, in September 1982. Dr. Giles also presented a paper "Hemostatic Complications of Surgery - Their Diagnosis and Management" at the Canadian Anesthetists Society in North Bay, September, 1982.

Dr. R.S. Kerbel Dr. Kerbel presented a lecture entitled, "Impact of Tumor Heterogeneity on Tumor Marker Studies" at the Colonic Cancer meeting, sponsored by the U.S. National Cancer Institute, held in September, 1982, in Maine. Dr. Kerbel also presented a lecture entitled, "Somatic Cell Hybridization in Relation to Metastasis and Tumor Progression" at the National Cancer Frederick Cancer Research Facility, Institute Frederick, Md. in October 1982. At the Ontario Cancer Institute in Toronto in October, 1982, Dr. Kerbel presented, "Somatic Cell Hybridization in Relation to Metastasis and Tumor Progression". In November 1982 Dr. Kerbel presented a lecture to the Department of Microbiology at McGill University. The title of this lecture was "The Biology of Cancer Metastasis and Tumor Heterogeneity Studied with Lectin Resistant Membrane Mutant Tumor Sublines". In March 1983 Dr. Kerbel was an invited lecturer at New York University Bellevue Hospital, Department of Pathology, and presented a talk entitled, "Origin and

Dr. R.S. Kerbel (continued): Implications of Tumor Heterogeneity". Dr. Kerbel gave a lecture entitled, "Spontaneous Fusion In Vivo Between Tumor Cells and Normal Host Cells as a Possible Means of Generating Tumor Progression and Metastatic Variants" in March, 1983, at the M.C. Anderson Symposium on Fundamental Cancer Research: Invasion and Metastasis and in May, 1983, at the Bat Sheva Rothschild Conference on Metastasis in Tiberius, Israel.

Dr. D.M. Robertson In October 1982 Dr. Robertson attended the XIV International Congress of Pathology sponsored by the International Academy of Pathology and held in Sydney, Australia. Dr. Robertson attended this Congress as one of the North American Vice-Presidents of the I.A.P. Dr. Robertson was an invited participant in the Neuropathology Symposium on 'Cerebral Tumours' and his presentation was entitled, "Differential Diagnosis of Small Round Cell Tumors in the Central Nervous System". In March 1983 Dr. Robertson was invited to be a member of the Royal College of Physicians and Surgeons of Canada On Site Survey Team evaluating laboratory medicine specialties at the University of Toronto and Affiliated Teaching Hospitals.