CURRICULUM VITAE

Part I:

Date Prepared:	April 19, 2005
Name:	Rona Stephanie Carroll
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Email:	rcarroll@rics.bwh.harvard.edu Fax: (617)232-9029
Place of birth:	Boston

Education:

1982 B.A.	Pitzer College
1984 M.S.	Massachusetts Institute of Technology (Neuroscience)
1987 Ph.D	Massachusetts Institute of Technology (Neuroscience)

Postdoctoral Training:

1987 –1991	Research Fellow in Medicine, Endocrine Division, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

Academic appointments:

1991-2000	Instructor in Surgery, Harvard Medical School, Boston, MA
2000-2002	Instructor in Neurosurgery, Harvard Medical School, Boston, MA
2002-	Assistant Professor in Surgery, Harvard Medical School, Boston,

Hospital appointments:

1987-present	Department of Medicine, Brigham and Women's Hospital, Boston
1991-present	Department of Surgery, Brigham and Women's Hospital, Boston
1991-present	Department of Neurosurgery, Children's Hospital, Boston, MA

Major Administrative Responsibilities:

1991-present	Associate Director, Laboratory of Neurosurgical Oncology, Department of Neurosurgery, Brigham and Women's; and Children's Hospital, Boston, MA
2001-present	Director, Brigham and Women's Hospital Brain Tumor bank

Professional Societies:

1988	The Endocrine Society
1989	Society of Neuroscience
1994	American Association for Cancer Research
1997	American Association for Neurosurgeons
2003	Society of Neuro-oncology

Community Service Related to Professional Work:

1996-2004	Teacher	Science Education	Burbank School, Belmont
2000-present	Teacher	Science Education	Winsor School, Boston

Editorial Boards:

1999-present	Ad hoc reviewer	Neurosurgery
1999-present	Ad hoc reviewer	Journal of Neurosurgery
2000-present	Ad hoc reviewer	Journal of Neuro-Oncology
2002-present	Ad hoc reviewer	Clinical Cancer Research
2002-present	Ad hoc reviewer	Cancer Research

Awards and Honors:

1989	Nichols Institute New Investigator Award, The Endocrine Society

Part II:

A. Narrative Report

The laboratory that I direct in the Department of Neurosurgery provides a unique environment for basic science researchers, medical students, international research fellows and neurosurgeons to take a multidisciplinary approach to understanding basic biology, and to developing new therapies to treat brain tumors. The laboratory is focused on developing novel, local therapeutic strategies for the treatment of malignant gliomas. Microencapsulation, Alzet minipumps, and nanoparticles are the three types of delivery systems we are presently researching.

Malignant gliomas are highly aggressive tumors with a median survival time of 12 to 18 months. Angiogenesis, tumor cell proliferation and migration are the hallmarks of solid tumors, such as gliomas. Human endostatin (hES) an angiogenic agent is rapidly cleared from the blood. To achieve significant tumor regression, 2.5mg/kg recombinant endostatin was administrated once daily for 16 days. The quantities of protein needed for this therapy, the purification procedure for large-scale production, and the attendant costs of these processes, suggest that alternative delivery methods may be required for efficient therapeutic use of endostatin. We developed an alginate-poly L- (lysine) microcapsules system The alginate- poly L- (lysine) membranes allow the free exchange of nutrients and oxygen between the implanted cells and the host while preventing the escape and elimination of encapsulated cells. More importantly, this approach provides a prolonged sustained delivery of recombinant protein produced by the cells, thus maintaining high levels of the agent. A single local injection of encapsulated endostatin-secreting cells resulted in a 72% reduction in subcutaneous human gliomas. Continuous local delivery of endostatin may offer a novel therapeutic approach to the treatment of a variety of tumor types. These studies were published in the journal *Nature Biotechnology*. In collaboration with Dr. Marcelle Machluf at the Technion in Israel we are developing other novel delivery systems including nanoparticles for use in our intracranial nude mice model.

In collaboration with Dr. Lorenzo Bello at University of Milan and Dr. Andreas Bikfalvi at University of Bordeaux we have demonstrated that a fragment derived from the autocatalytic digestion of MMP-2, called PEX, acts simultaneously as an inhibitor of glioma angiogenesis, cell proliferation and migration. PEX is detected in the cultured media of various human glioma, endothelial, breast and

prostate carcinoma cell lines. PEX is purified from the media of glioma cell lines by chromatography. In human glioma tissue, PEX expression correlates with histological subtype and grade, and with alphavBeta3 integrin expression to which it is bound. Systemic administration of PEX to subcutaneous and intracranial human glioma xenografts results in a 99% suppression of tumor growth with no signs of toxicity. Delivery of PEX directly into the site of the tumor in the brain also results in significant tumor suppression with a lower concentration of protein. Thus, PEX is a very promising candidate for the treatment of human malignant gliomas. These results were published in two manuscripts in *Cancer Research, 2001*.

B. Funding Information

Past:

9/82-5/85 NIMH training grant
9/85-8/87 National Research Predoctoral Fellowship Award
Behavioral and endocrine control of LH secretion
6/88-5/91 National Research Postdoctoral Fellowship Award
Hormonal Regulation of Gonadotropin Biosynthesis
7/00-6/01 Center for Innovative Minimally Invasive Therapy
1998-2000 Ospedale Maggiore di Milano

6/01-6/03 NIH Co-investigator NIH 2R44CA86768-02, Co-PI 15% Effort
$864,373
Neural stem cells target gene therapy to brain tumors

Current:

6/03-6/05 Brain Science Foundation, PI
Novel Local Therapies for meningiomas
$138, 280
The goal of this project is to develop new therapies for meningiomas.

6/03-6/05 Brain Science Foundation, PI
Development of a meningioma model
$168,960
The goal of this project is to develop new models to study meningiomas

6/02-7/05 Dana Fund, Co-PI
A Human Brain Tumor Cell Culture and Tumor Bank Facility

10/01-9/06 NIH 1RO1 NS-40069-01A (PI: Leviton) Co-PI, 20% Effort
$13,926, 499
Molecular Antecedents of Brain Damage in Pre-term Infants

10/04-9/07 United States Israel Binational Science Foundation (Co-PI)
New local delivery approaches for brain tumor therapy

C. Report of Current Research Activities

Project	Role
Use of stem cells to target human gliomas	Co-investigator
MRI assessment of brain tumors	Co-investigator
Novel delivery systems for brain tumors	Co-investigator

Development of novel therapeutics Co-investigator
Role of steroid hormone receptors in meningiomas Co-investigator

D. Report of Teaching

1. Local contributions

1990-present Each year in laboratory on average I have taught two-three Neurosurgery residents from abroad. They come as research fellows with little laboratory experience. I am responsible for training and supervising these people including design of experiments, analysis of data and preparation of manuscripts.

1990-present Each year in laboratory on average we have two medical students working in the laboratory part time during the school year and full time in the summer. . I am responsible for training and supervising these people including design of experiments, analysis of data and preparation of manuscripts.

Seminars

September 2000	University of Milan
February 2001	Brain Tumor Support Group
September 2001	University of Bordeaux
October 2001	DF/HCC Neuro-Oncology Program
November 2001	Tumors of the Central Nervous System
November 2002	Tumors of the Central Nervous System

Part III:

Bibliography:

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2. Carroll RS, Erskine MS, Doherty PC, Lundell LA, Baum MJ. Coital stimuli controlling LH secretion and ovulation in the female ferret. Biology of Reproduction 1985; 32:925-933.

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6. Carroll RS, Corrigan AZ, Gharib SD, Vale W, Chin WW. Inhibin, activin and follistatin: Regulation of follicle stimulating hormone messenger ribonucleic acid levels. Molecular Endocrinology 1989; 3:1969-1976.

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8. Bibeau CE, Tobet SA, Anthony EL, Carroll RS, Baum MJ, King JC. Vaginocervical stimulation of ferrets induces release of luteinizing hormone-releasing hormone. J. Neuroendocrinology 1990; 3:953-960.

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19. Carroll RS, Zhang J, Dashner K, Sar M, Wilson EM, Black PM. Androgen receptor expression in meningiomas. J. Neurosurgery 1995; 82; 453-460.

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