

**DEPARTMENT OF NEUROLOGICAL SURGERY
COLLEGE OF MEDICINE AND PUBLIC HEALTH
THE OHIO STATE UNIVERSITY**

**ANNUAL REPORT OF RESEARCH ACTIVITY:
1 JANUARY THROUGH 31 DECEMBER 2006**

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DEPARTMENT OF NEUROLOGICAL SURGERY
SUMMARY OF RESEARCH ACTIVITY, JANUARY THROUGH DECEMBER 2006

SUMMARY OF DEPARTMENT RESEARCH ACTIVITY

Completing its second full year of operation in 2006, the Department of Neurological Surgery was again recognized by *U. S. News and World Report* among its listing of top-ranked clinical programs in the country.

Three new neurosurgeons, Drs. Mario Ammirati, Ehud Mendel, and Atom Sarkar joined Drs. Chiocca, Caragine, McGregor, and Miller, bringing their respective subspecialty expertise to direct programs and establish research facilities in skull base surgery; spine and spine cancer; and functional neurosurgery and neurological nanomedicine.

We performed 1439 neurosurgical procedures in 2006, including gamma knife radiosurgery, intensity-modulated fractionated stereotactic radiation therapy (IMRT) using a Peacock system, and angiographic procedures (compared to 836 in 2005).

Dr. Mariano Viapiano joined Drs. Saeki, Lawler, and Kaur as research faculty in the Dardinger Laboratory for Neuro-oncology and Neurosciences, sharing an appointment in the Center for Molecular Neurobiology. Dr. Viapiano's research focuses on the functions of the extracellular matrix in the nervous system and the mechanisms whereby brain tumor disrupts this matrix to invade normal brain tissue.

We participated in three clinical trials, received research funding exceeding \$1,600,000, and authored 38 publications, double the number of publications in 2005.

In addition, Department clinicians and researchers were active on a variety of levels in professional organizations and received various institutional, regional, and national awards that recognized their expertise and accomplishments. Dr. Chiocca served as a member of the National Institutes of Health (NIH) Study Section for Developmental Therapeutics (DT) and of the National Cancer Institute (NCI) program project cluster review subcommittees C and D, and Dr. Saeki served on the NIH National Institute of Neurological Disorders and Stroke (NINDS) Neurological Sciences and Disorders B (NSD-B) Study Section.

**DARDINGER LABORATORY FOR
NEURO-ONCOLOGY AND NEUROSCIENCES**

Dr. Chiocca co-directs (with Dr. Herbert B. Newton, Department of Neurology) and oversees the research conducted within the Dardinger Laboratory for Neuro-oncology and Neurosciences.

The Department's strictly research faculty comprises Yoshinaga Saeki, M.D., Ph.D., associate professor and administrative chief of the Laboratory, and assistant professors, Balveen Kaur, Ph.D., Sean Lawler, Ph.D., and Mariano Viapiano, Ph.D.

Drs. Mario Ammirati, Ehud Mendel, and Atom Sarkar, all neurosurgeons, also operate laboratories to explore surgery-related issues related to diseases and disorders of the central nervous system.

- **Dr. Yoshinaga Saeki's** laboratory is interested in the development of therapeutic strategies for neurological, neoplastic, and genetic disorders. Three major ongoing projects employ multidisciplinary research techniques. The first involves the development and applications of herpes simplex virus (HSV)-based amplicon vectors, which are high-capacity plasmid-based vectors with full HSV infection machinery, for gene therapy and neuroscience research. The second research area involves the development and applications of engineered, oncolytic HSV vectors for cancer therapy. The third project involves studying the roles of G protein-coupled receptors that upregulate cAMP signaling in the axonal outgrowth of neurons and neuronal differentiation of neural progenitor cells.
- **Dr. Balveen Kaur's** laboratory group is attempting to understand changes that occur in the microenvironment of gliomas in response to treatment. The ultimate goal is to understand how current treatment strategies can be exploited to their maximum potential. A major focus is investigation of novel mechanisms to disrupt the changes in vascular biology that result from tumor to develop therapeutic strategies that may be used alone or in combination with oncolytic viruses (OV) to augment existing treatment modalities. The laboratory is also studying

the extracellular matrix of tumors to develop ways to enhance viral spread and infection to ultimately enhance therapy. Finally, Dr. Kaur's lab is attempting to identify potential biomarkers in patient serum that will reflect the ongoing OV replication in solid tumors.

- **Dr. Sean Lawler's** laboratory is studying cell signaling mechanisms in disorders of the central nervous system (cancer and neurodegeneration) to ultimately develop novel therapeutic approaches. Using a three-dimensional cell culture system, they are studying the migration and invasion of glioma cells, mechanisms that present a major challenge in brain tumor therapy. They have identified a number of small-molecule drugs that block invasion effectively and are testing these in animal glioma models, and they have identified a number of novel genes that may be important in migration and invasion. In addition, Dr. Lawler's team is examining the role of the microtubule-associated protein, tau, in neurodegeneration in an effort to explore the potential link between amyloid and tau, which may be critical in the progression of Alzheimer's disease.
- **Dr. Mariano Viapiano's** laboratory team studies the composition of the extracellular matrix (ECM) of gliomas. The ECM presents a major barrier to cell movement in the adult central nervous system, but invasive gliomas are impervious to the inhibitory signals from the neural ECM and produce altered versions of matrix molecules that may help their invasive capacity. Dr. Viapiano's group focuses attention on two families of matrix proteins: the lecticans and the link proteins. His lab has begun to characterize the molecular events underlying the pro-invasive role of these proteins in gliomas and started to develop reagents to target and disrupt the interactions of these proteins that promote glioma cell dispersion. By rendering the pro-invasive molecules in the glioma matrix functionally inactive, the Viapiano laboratory aims to design novel targeting strategies that will limit the spread of the disease and render these brain tumors therapeutically accessible.

- **Dr. Mario Ammirati's** microneurosurgical skull base laboratory enables the research and development of innovative surgical approaches to tumors at the base of the brain, educating residents in these techniques and partnering with private and non-private organizations to develop relevant technology for the clinical setting. New surgical approaches that begin with a question in the operating room—"What if this tumor were approached from this angle rather than the conventional one? Could such an approach be better?"—are explored in the lab on anatomical specimens under conditions simulating those in the operating room (same surgical position, operating microscope, instrumentation). Results are then translated to the clinical care of patients when they are used in the operating room and when high-tech tools and techniques can be developed for use in these patients.

Two ongoing projects are the quantification of exposure afforded by the endoscope and microscope in the endonasal-transphenoidal approach to the sella and suprasellar region and the investigation of a navigational system and endoscope to remove the posterior wall of the internal auditory canal (IAC) without disrupting the integrity of the labyrinth via a retrosigmoid approach.

- **Dr. Ehud Mendel's** spine and spine cancer laboratory is evaluating physiologic forces that impact spinal health and methods to optimize the surgical therapy of spinal disorders. They are developing a patient-specific hybrid biomechanical model that uses a patient's muscle recruitment pattern and spinal imaging to predict forces on the various spinal structures, and they are examining the relationship between spinal load and pro-inflammatory cytokine upregulation. In clinical studies, kinematic measures of trunk motion and up-right magnetic resonance imaging are being employed to evaluate biomechanical compromise under physiologic loading and thereby the extent of disorders of the lower back. Studies quantifying the relationship between physical and psychosocial occupational risk factors and low back disorders are also underway.

DARDINGER LABORATORY RESEARCH, continued

- **Dr. Atom Sarkar's** nanomedicine laboratory is investigating the relationship between single-molecule mechanics and disease states, particularly the micromechanical mechanisms that underlie the formation of pathologic fiber in Parkinson's disease and that regulate the migration and spread of glioblastoma multiforme (GBM) tumors. Both projects rely on atomic force microscopy (AFM), which is able to identify single molecules, place them under mechanical stress, and establish their mechanical stability. Such measurements are ultimately important to determine valuable clinically relevant correlations between cell stiffness/elasticity and "aggressive" behavior.

Parkinson's is a disorder of the motor system involving both genetic and environmental factors. The root of the illness is the formation and aggregation of α -synuclein fiber, which is undeniably a multifactorial biochemical and physical chemical process. Because the fundamentals of fibril formation at the single-molecule level are mechanical, understanding the single molecule mechanical behavior for the α -synuclein protein will provide insight into the protein's stability and allow for predictions as to how to prevent fiber formation and ultimately help guide the design for rational molecular therapeutics for Parkinson's.

In the case of the neoplastic cells in glioblastomas, cell motility is unpredictable. The cellular cytoskeleton is a filamentous system of "ropes, cables, and poles" that provides rigidity to the cell and, to a large extent, determines its mechanical properties and motility. Glial fibrillary acidic protein (GFAP) is an important and abundant element of the intermediate filament network, one of the three cytoskeletal components in the malignant astrocytes of these tumors. AFM data from experiments with single molecules can be tailored into a macroscopic model for investigating the role of force in the invasiveness of glioblastoma multiforme.

SELECTED PUBLISHED RESEARCH

(A separate listing of all 38 publications [5 chapters, 33 journal articles] for the year follows this list; impact factors [IF] follow each citation as of 2005 listing).

Research publications for 2006 center around the use of oncolytic viruses for brain tumor models and include two articles in *Cancer Research* (Impact factor = 7.616) and one in the *Proceedings of the National Academy of Sciences USA* (IF 10.231). The respective articles detail research on glioma virotherapy and on angiogenesis.

1. Aghi M, Cohen KS, Klein RJ, Scadden DT, **Chiocca EA**. Tumor stromal-derived factor-1 recruits vascular progenitors to mitotic neovasculature, where microenvironment influences their differentiated phenol types. *Cancer Research* 2006 September; 66(18): 9054-9064. (Impact factor [IF] 7.616)
2. Chakrabarti I, Burton AW, Rhines L, **Mendel E**. Percutaneous vertebroplasty of myelomatous kyphotic wedge fracture in the presence of previous posterior instrumentation: case report. *Journal of Neurosurgery* 2006 August; 5(2): 168-171. (IF 2.446)
3. Friedman A, Tian JP, Fulci G, **Chiocca EA**, Wang J. Glioma virotherapy: effects of innate immune suppression and increased viral replication capacity. *Cancer Research* 2006 February 15; 66(4): 2314-2319. (IF 7.616)
4. Fulci G, Breymann L, Gianni D, Kurozumi K, Rhee SS, Yu J, Kaur B, Louis DN, Weissleder R, Caligiuri MA, **Chiocca EA**. Cyclophosphamide enhances glioma virotherapy by inhibiting innate immune responses. *Proceedings of the National Academy of Sciences USA* 2006 August 22; 103(34): 12873-12878. (IF 10.231)
5. Lamfers ML, Fulci G, Gianni D, Tang Y, **Kurozumi K, Kaur B, Moeniralm S, Saeki Y, Carette JE, Weissleder R, Vandertop WP, van Beusechem VW, Dirven CMF, Chiocca EA**. Cyclophosphamide increases transgene expression mediated by an oncolytic adenovirus in glioma-bearing mice monitored by bioluminescence imaging. *Molecular Therapy* 2006 December; 14(6): 779-788. Epublication 2006 September 22. (IF 5.443)

JOURNAL ARTICLES

6. **Sarkar A**, Caamano S, Fernandez JM. The mechanical fingerprint of a parallel polyprotein dimer. **Epublication** 2006 December 8. *Biophysical Journal* 2007 February; 92(4) (IF 4.507)
7. **Suzuki M, Kasai K, Saeki Y**. Plasmid DNA sequences present in conventional HSV amplicon vectors cause rapid transgene silencing by forming inactive chromatin. *Journal of Virology* 2006 April; 80(7): 3293-3300. (IF 5.178)

ALL DEPARTMENTAL PUBLICATIONS FOR 2006

BOOK CHAPTERS

1. Abbed KM, **Chiocca EA**. Surgical management of cerebellar astrocytomas in adults. In: *Operative Neurosurgical Techniques: Indications, Methods, and Results. Volume I. Fifth edition.* (Schmidek HH, Roberts DW, eds.) Philadelphia, Pennsylvania: Saunders Elsevier, pp 873-880, 2006.
2. **Asadi-Moghaddam K, Chiocca EA**. Chemotherapy-activating gene therapy. In: *Handbook of Brain Tumor Therapy.* (Newton HB, ed.), Philadelphia, Pennsylvania: Academic Press (Elsevier), pp 332-343, 2006.
3. **Asadi-Moghaddam K, Chiocca EA**. Prodrug-activation gene therapy. In: *Gene Therapy in the Central Nervous System.* (Kaplitt MG, Doring MJ, eds.), Philadelphia, Pennsylvania: Academic Press (Elsevier), pp 291-301, 2006.
4. **Lawler SE, Saeki Y, Chiocca EA, Wade-Martins R**: iBAC technologies for neurological disease. In: *Gene Therapy for Neurological Disorders.* (Lowenstein PR, Castro MG, eds.) New York: Taylor & Francis, pp 59-73, 2006.
5. **Saeki Y**. Viral vector delivery to dividing cells. In: *The Cell Cycle in the Central Nervous System.* (Janigro D, ed.), Totowa, New Jersey: Humana Press, pp 477-493, 2006.

(Impact factors (IF), where available, follow each citation as of 2005 listing.)

1. Aghi M, Cohen KS, Klein RJ, Scadden DT, **Chiocca EA**. Tumor stromal-derived factor-1 recruits vascular progenitors to mitotic neovasculature, where microenvironment influences their differentiated phenol types. *Cancer Research* 2006 September; 66(18): 9054-9064. (IF 7.616)
2. Aghi M, **Chiocca EA**. Gene therapy for glioblastoma. *Neurosurgical Focus.* 2006 April 15; 20(4):E18. (no IF given)
3. **Ammirati M**, Perrino F. Symptomatic air trapped in the spine after epidural corticosteroid injection into the lumbar region: Case report. *Journal of Neurosurgery: Spine* 2006 October; 5(4); 559-361. (no IF given)
4. Bronisz A, Sharma S, Hu R, **Godlewski J**, Tzivion G, Mansky K, Ostrowski MC. MITF interactions with 14-3-3 modulate differentiation of committed myeloid precursors. *Molecular Biology of the Cell* 2006 September; 17(9): 3897-3906; Epublication 2006 July 5. (IF 6.520)
5. **Caragine LP Jr**, Halbach VV, Dowd CF, Higashida RT. Intraorbital arteriovenous fistulae of the ophthalmic veins treated by transvenous endovascular occlusion: technical case report. *Neurosurgery* 2006 Feb; 58(1 Suppl): ONS-E170; discussion ONS-E170. (IF 2.587)
6. Chakrabarti I, Burton AW, Rhines L, **Mendel E**. Percutaneous vertebroplasty of myelomatous kyphotic wedge fracture in the presence of previous posterior instrumentation: case report. *Journal of Neurosurgery* 2006 August; 5(2): 168-171. (IF 2.446)
7. Chang S, Vogelbaum M, Lang FL, Haines S, Kunwar S, **Chiocca EA**, Olivi A, Quinones-Hinojosa A, Parsa A, Warnick R. GNOSIS: Guidelines for neuro-oncology: standards for investigational studies—reporting of surgically based therapeutic clinical trials. *Journal of Neuro-oncology.* **Epublication** 2006 December 5. (IF 2.325)

JOURNAL ARTICLES, continued

8. **Cutter JL, Kurozumi K, Chiocca EA, Kaur B.** Gene therapeutics: the future of brain tumor therapy? *Expert Review of Anticancer Therapy*. 2006 July; 6(7): 1053-1064. (No IF given)
9. Dmitrieva NA, Strang CE, Keyser KT. Expression of alpha 7 nicotinic acetylcholine receptors by bipolar, amacrine and ganglion cells of the rabbit retina. *Journal of Histochemistry and Cytochemistry*. **Epublication** 2006 December 22. (IF 2.208)
10. Friedman A, Tian JP, Fulci G, **Chiocca EA**, Wang J. Glioma virotherapy: effects of innate immune suppression and increased viral replication capacity. *Cancer Research* 2006 February 15; 66(4): 2314-2319. (IF 7.616)
11. Fulci G, Breymann L, Gianni D, Kurozumi K, Rhee SS, Yu J, Kaur B, Louis DN, Weissleder R, Caligiuri MA, **Chiocca EA.** Cyclophosphamide enhances glioma virotherapy by inhibiting innate immune responses. *Proceedings of the National Academy of Sciences USA* 2006 August 22; 103(34): 12873-12878. (IF 10.231)
12. **Godlewski J**, Wang S, Wilson TG. Interaction of bHLH-PAS proteins involved in juvenile hormone reception in *Drosophila*. *Biochemical and Biophysical Research Communications* 2006 April; 342(4): 1305-1311. (No IF given)
13. Ino Y, **Saeki Y**, Fukuhara H, Todo T. Triple combination of oncolytic HSV-1 vectors "armed" with interleukin 12, interleukin 18 or soluble B7-1 results in enhanced antitumor efficacy. *Clinical Cancer Research* 2006 January 15; 12(2): 643-652. (IF 5.715)
14. **Kasai K, Saeki Y.** DNA-based methods to prepare helper virus-free herpes amplicon vectors and versatile designing of amplicon vector plasmids. *Current Gene Therapy* 2006; 6(3): 303-314. (No IF given)
15. Koptyra M, Falinski R, **Nowicki MO**, Stoklosa T, Majsterek I, Nieborowska-Skorska M, Blaaiaik J, Skorski T. BCR/ABL kinase induces self-mutagenesis via reactive oxygen species to encode imatinib resistance. *Blood* 2006 July 1; 108(1): 319-327. Epublication 2006 March 9. (IF 10.131)
16. Lamfers ML, Fulci G, Gianni D, Tang Y, **Kurozumi K, Kaur B**, Moeniralm S, **Saeki Y**, Carette JE, Weissleder R, Vandertop WP, van Beusechem VW, Dirven CMF, **Chiocca EA.** Cyclophosphamide increases transgene expression mediated by an oncolytic adenovirus in glioma-bearing mice monitored by bioluminescence imaging. *Molecular Therapy* 2006 December; 14(6): 779-788. Epublication 2006 September 22. (IF 5.443)
17. **Lawler SE, Peruzzi PP, Chiocca EA.** Genetic strategies for brain tumor therapy. *Cancer Gene Therapy*. 2006 March; 13(3):225-233. Epublication 2005 September 2. (IF 3.000)
18. McPherson CM, Suki D, McCutcheon IE, Gokaslan ZL, Rhines LD, **Mendel E.** Metastatic disease form spinal chordoma: a 10-year experience. *Journal of Neurosurgery Spine* 2006 October; 5(4): 277-280. (No IF given)
19. **Mendel E.** Advances in treatment of spinal tumors. *Physicians Practice* 16(8):A-3, 2006 September. (non peer review) (No IF given)
20. Miller B, **Baig M**, Hayes J, Elton S. Injury outcomes in children following automobile, motorcycle, and all-terrain vehicle accidents: an insitutional review. *Journal of Neurosurgery: Pediatrics* 2006 September; 105(3 Suppl):182-186. (IF 2.446)
21. Sachs DC, Inamasu J, **Mendel EE**, Guiot BH. Transoral vertebroplasty for renal cell metastasis involving the axis: case report. *Spine* 2006 November 15; 31(24): E925-E928.
22. **Saeki Y.** Stable CNS gene delivery with Sleeping Beauty armed with a high-capacity HSV virion. *Molecular Therapy* 2006 March; 13(3): 457-458; Epublication 2006 February 7. (IF 5.443)
23. **Sarkar A**, Caamano S, Fernandez JM. The mechanical fingerprint of a parallel polyprotein dimer. **Epublication** 2006 December 8. *Biophysical Journal* 2007 February; 92(4) (IF 4.507)
24. **Sarkar A, Chiocca EA.** Prognostic indicators (editorial). *Journal of Neurosurgery* 2006 August; 105: 161-162. (IF 2.446)

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25. Sasaki T, Kitagawa K, Yagita Y, Sugiura S, Omura-Matsuoka E, **Tanaka S**, Matsushita K, Okano H, Tsujimoto Y, Hori M. Bcl2 enhances survival of newborn neurons in the normal and ischemic hippocampus. *Journal of Neuroscience Research* 2006 November 1; 84(6):1187-1196. (IF 3.239)
26. Slupianek A, **Nowicki MO**, Koptyra M, Skorski T. BCR/ABL modifies the kinetics and fidelity of DNA double-strand breaks repair in hematopoietic cells. *DNA Repair (Amsterdam)* 2006 February 3; 5(2):243-250. **Epublication** 2005 November 14. (IF 5.016)
27. Sasaki T, Kitagawa K, Yagita Y, Sugiura S, Omura-Matsuoka E, **Tanaka S**, Matsushita K, Okano H, Tsujimoto Y, Hori M. Bcl2 enhances survival of newborn neurons in the normal and ischemic hippocampus. *Journal of Neuroscience Research* 2006 November 1; 84(6):1187-1196. (IF 3.239)
28. **Suzuki M, Kasai K, Saeki Y**. Plasmid DNA sequences present in conventional HSV amplicon vectors cause rapid transgene silencing by forming inactive chromatin. *Journal of Virology* 2006 April; 80(7): 3293-3300. (IF 5.178)
29. Terada K, Wakimoto H, Tyminski E, **Chiocca EA, Saeki Y**. Development of a rapid method to generate multiple oncolytic HSV vectors and their *in vivo* evaluation using syngeneic mouse tumor models. *Gene Therapy*. 2006 April 13(8): 705-714. Epublication 2006 January 19. (IF 4.836)
30. **Thoman WJ, Ammirati M, Caragine Jr LP, McGregor JM, Sarkar A, Chiocca EA**. Brain tumor imaging and surgical management: the neurosurgeon's perspective. *Topics in Magnetic Resonance Imaging* 2006 April 17(2): 121-126. (actually published January 2007, but dated 2006) (No IF given)
30. Trojanek J, Croul S, Ho T, Wang JY, Darbinyan A, **Nowicki M**, Del Valle L, Skorski T, Khalili K, Reiss K. T-Antigen of the human polyomavirus JC attenuates faithful DNA repair by forcing nuclear interaction between IRS-1 and Rad51. *Journal of Cellular Physiology* 2006 January; 206(1): 35-46. (IF 4.362)
31. **Viapiano MS**, Matthews RT. From barriers to bridges: chondroitin sulfate proteoglycans in neuropathology. *Trends in Molecular Medicine* 2006 October; 12(10): 488-496 Epublication 7 September 2006
32. **Yamamoto S, Deckter LA, Kasai K, Chiocca EA, Saeki Y**. Imaging immediate-early and late promoter activity during oncolytic herpes simplex virus type 1 infection and replication in tumors. *Gene Therapy* 2006 December; 13(24): 1731-1736. Epublication 27 July 2006. (IF 4.836)

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GRANT/SPONSORED RESEARCH INFORMATION

CLINICAL TRIALS: We participated in three clinical trials in 2006:

- OSU principal investigator (PI): **E. Antonio Chiocca, M.D., Ph.D.**, Department of Neurological Surgery
Sponsor: Neopharm, Inc.
Phase III randomized evaluation of convection enhanced delivery of IL 13-PEQQR compared to gliadel wafer with survival endpoint in glioblastoma multiforme patients at first recurrence.
Description: We enrolled four patients in a Phase III trial testing the infusion by convection of a cytotoxin against malignant glioblastoma. This trial was closed in 2006.
- PI: **E. Antonio Chiocca, M.D., Ph.D.**, Department of Neurological Surgery
Sponsor: Advantagene, Inc.
A Phase 1b study of ADV-tk + Valacyclovir gene therapy in combination with standard radiation therapy for malignant gliomas.
Description: We opened a Phase I trial of gene immunotherapy against newly diagnosed malignant glioma. (We are the primary site for this trial that has also opened at Methodist Neuroscience [formerly Baylor] in Houston, Texas). The trial was completed in January 2006 after 12 patients were accrued; a Phase II trial is pending.
- PI: **John M. McGregor, M.D.**, Department of Neurological Surgery
Sponsor: National Institutes of Health (NIH), Oregon Health and Science University
A Phase II trial involving patients with recurrent PCNSL treated with carboplatin/BBBD, by adding Rituxan (Rituximab), an anti CD-20 antibody, to the treatment regimen. (*BBBD = blood-brain barrier disruption; PCNSL = primary central nervous system lymphoma*)

RESEARCH AND GRANTS

Departmental funding exceeded \$1,600,000, including direct and indirect NIH grant awards that included three R01 and one R21 subprojects.

E. Antonio Chiocca, M.D., Ph.D., professor; department chair; Dardinger Family Endowed Chair in Oncological Neurosurgery

Sponsor: NIH–National Cancer Institute (NCI)–Bioengineering Research Partnership (BRP)

- Interdisciplinary Tumor Complexity Modeling (R01)

Sponsor: NIH–National Institute of Neurological Disorders and Stroke (NINDS)

- Biology of Tauopathies Studied with HSV Amplicons (R01)

Sponsor: NIH–NCI

- Imaging Transcriptional Activation of Gliomas (R21)

Sponsor: NIH–NCI–Massachusetts General Hospital (MGH)

- Gene Therapy for Brain Tumors (P01; sub-contract PI)

Sponsor: NIH–NCI–Case Western Reserve University (CWRU)

- Imaging of Gene Expression in Glioblastoma (R01; sub-contract PI)

Sponsor: NIH–NINDS–Perfusion Technology, LLC

- Dose Response and Dynamics of Ultrasound-Mediated Blood-brain Barrier Opening (STTR; sub-contract PI)

Sponsor: Advantagene, Inc.

- A Phase I b Study of Adv-Tk + Valacyclovir Gene Therapy in Combination with Standard Radiation Therapy for Malignant Gliomas

Sponsor: NeoPharm

- Phase III Randomized Evaluation of Convection Enhanced Delivery of IL13-PEQQR Compared to Gliadel Wafer with Survival Endpoint in Glioblastoma Multiforme Patients at First Recurrence

John M. McGregor, M.D., assistant professor; director, Gamma Knife Radiosurgery; director, Blood-brain Barrier Disruption Program

Sponsor: NIH – NINDS – Oregon Health and Science University (OHSU)

- Two Compartment Models to Improve Brain Tumor Therapy

OTHER AWARDS AND RECOGNITIONS FOR 2006

Departmental clinicians and researchers received various other institutional, regional, and national awards and recognitions in 2006:

Louis P. Caragine, Jr., M.D., Ph.D., associate professor; director, Endovascular Neurosurgery; director, Neurosurgery Intensive Care Unit

- recipient, residents' annual Lawrence Mervis, M.D., Teacher of the Year Award in June 2006
- recognized by the Marquis Who's Who Publications Board by inclusion in *Who's Who in Medicine & Health Care: Sixth Edition 2006-2007*.

E. Antonio Chiocca, M.D., Ph.D., professor; department chair; Dardinger Family Endowed Chair in Oncological Neurosurgery

- selected as one of the "Best Doctors in Ohio" by *Columbus Monthly Magazine*.
- elected to membership in the American Society for Clinical Investigation
- elected to membership in the Society of Neurological Surgeons
- elected as a fellow of the American Association for the Advancement of Science
- became a member of the National Cancer Institute Parent Committee (Scientific Review Council) for program projects grants reviewing clinical/translational studies
- became a member of the Scientific Advisory Committee of the Goldhirsh Foundation Brain Tumor Research Awards Program, October 2006
- invited to faculty, Graduate Program in Neurosciences Graduate Studies, The Ohio State University, October 2006
- became an associate member, Center for Brain and Spinal Cord Repair, The Ohio State University, October 2006
- became a member of the Scientific Advisory Committee of the Neurosurgery Research and Education Foundation (NREF) of the American Association of Neurological Surgeons (AANS)

Clara Raquel Epstein, M.D., second-year resident

- one of seven physicians nationally honored and appointed as a member of the Steering Committee of the American Medical Association (AMA) Minority Actions Consortium Hispanic Physician Outreach Initiative, at the AMA's June 2006 meeting in Chicago. *To improve representation of Hispanic physicians in leadership roles in the AMA and other medical organizations, the AMA has established the Hispanic Physician Outreach Initiative. The Initiative is intended to enhance the position of Hispanic physicians to guide and make policies that affect their practice and the healthcare of the Hispanic population, the largest ethnic minority population in the U.S. The Steering Committee includes members of the Consortium and national leaders. Speaker training, advocacy development, mentoring opportunities, and town meetings are planned.*

Jakub Godlewski, Ph.D., postdoctoral fellow (beginning January 1, 2006), Dardinger Laboratory for Neuro-oncology and Neurosciences

- second recipient, Jeffrey Thomas Hayden Foundation Endowed Fellowship, effective June 1, 2006, awarded as part of a \$250,000 endowment to OSU over a three-year period: The Jeffrey Thomas Hayden Foundation Endowed Fellowship Fund in Pediatric Brain Tumor at the OSU Arthur G. James Cancer Hospital and Richard J. Solove Research Institute. *The endowment is intended to facilitate research and clinical communication between Ohio State and various children's hospitals to encourage physician understanding of the cutting-edge research being conducted at OSU and offer researchers feedback regarding promising therapeutic options.*

Phillip Immesoete, M.D., sixth-year resident

- will complete his residency under the mentorship of Dr. Ehud Mendel, serving an internal fellowship in the spine laboratory. His specific duties will include organizing and presenting at the weekly spine conference, attending Dr. Mendel's clinic, and operating with Dr. Mendel, including emergency consultations and surgeries.

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OTHER AWARDS AND RECOGNITIONS, continued

Chris Karas, M.D., third-year resident

- elected to Alpha Omega Alpha Honor Medical Society, (AOA) January 2006. *AOA, the only national honor medical society in the world, comprises members at any stage in their medical career, from students in medical schools through faculty. The organization recognizes excellence in scholarship, research, and medical practice as well as exemplary standards of character and conduct in all aspects of the profession. The three Greek letters making up the group's name correspond to the initial letters of the essential words in the motto, "Worthy to serve the suffering."*

Balveen Kaur, Ph.D., assistant professor, Dardinger Laboratory for Neuro-oncology and Neurosciences

- received first grant award from the National Brain Tumor Foundation (NBTF) for the project, "Anti-angiogenic treatment for enhancement of oncolytic virus efficacy," award notification in June.
- Dr. Kaur's article, "Hypoxia and the hypoxia-inducible-factor pathway in glioma growth and angiogenesis," published with her colleagues at Emory in April 2005, was recognized as the most frequently read article in the journal, *Neuro-oncology*, May 2006.

Kazuhiko Kurozumi, M.D., Ph.D., postdoctoral researcher, Dardinger Laboratory for Neuro-oncology and Neurosciences

- received first-prize recognition in the therapeutic section for poster: **Kurozumi K, Cutter JL, Carson W, Yang M, Christoforidis G, Chiocca EA, Kaur B.** Anti-angiogenic treatment enhances anti-tumor effects of an oncolytic virus in an experimental rat glioma model, at The OSU Comprehensive Cancer Center's eighth annual meeting in February 2006.

John M. McGregor, M.D., assistant professor; director, Gamma Knife Radiosurgery; director, Blood-brain Barrier Disruption Program

- president, Ohio State Neurosurgical Society, 2004-2006
- Ohio representative, Northwest Quadrant, Council of State Neurosurgical Societies, 1999-present; member, Workforce Committee, 2001-present

Ehud Mendel, M.D., F.A.C.S., professor; director, OSU Spine Program and Spinal Fellowship Program

- appointed Justine Skestos Chair in Minimally Invasive Neurological Spinal Surgery through an endowment of \$1.5 million by George Skestos, September 2006
- recipient, \$150,000 spine fellowship donation from George Skestos, November 2006
- recipient, \$75,000 spine fellowship donation from SYNTHES Spine, November 2006
- invited to associate membership, OSU Center for Brain and Spinal Cord Research, November 2006
- appointed director, OSU Spinal Signature Program, November 2006
- appointed co-chair, Spine/Trauma Disease State Taskforce, OSU Neurosciences Signature Program
- appointed clinical co-director, OSU Spinal Biodynamics and Ergonomics Laboratory

Carole Ann Miller, M.D., professor; director, Residency Program

- recipient, 2006 Excellence in Teaching Award, The Ohio State University College of Medicine

Atom Sarkar, M.D., Ph.D., assistant professor; director, Functional Neurosurgery; director, Neurological Nanomedicine

- co-appointment as assistant professor, Department of Chemical & Biomolecular Engineering, November 2006

Joshua Shroll, B.S., American Brain Tumor Association (ABTA) summer fellow in the laboratory of Balveen Kaur, Dardinger Laboratory for Neuro-oncology and Neurosciences

- recipient, ABTA's Lucien J. Rubinstein Award, announced December 28, 2006.
Shroll's work was groundbreaking in that it led to the identification of a secreted protein that can be used as a potential biomarker for the ongoing oncolytic viral (OV) therapy of brain tumors. Although the exciting results are only preliminary experimental findings, no publication to date has shown the induction of a cellular-secreted protein upon OV infection and the impact of this induction on the propagation of the OV in tumors. Understanding the changes that occur in infected tumor cells and the tumor environment and the effect of such changes on the propagation of OV will elucidate why "cures" are not seen in clinical trials and will thus lead to better treatment strategies.



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