

Project Title: Rapid Preclinical Development of a Targeted Therapy Combination for DIPG

Section 1: Contact Information signature pages follow

a. Primary Investigator: **Charles Keller MD**, Associate Professor; Leader, Pediatric Cancer Biology Program; and **Kellie J. Nazemi MD** (Co-Primary Investigator), Director, Pediatric Neuro-Oncology, Doernbecher Children's Hospital; Dept. of Pediatrics; **Nathan Selden** and **Daniel Guillaume** (Co-Investigators), Division of Pediatric Neurosurgery, Dept. of Neurosurgery; Oregon Health & Science University, 3181 S.w. Sam Jackson Park Rd, MC-L321, Portland, OR 97239, Tel: (503)494-1210, keller@ohsu.edu

Co-Primary Investigator: **Oren Becher MD**, Assistant Professor, Pediatric Neuro-Oncology, Department of Pediatrics, Preston Robert Tisch Brain Tumor Center, LSRC B359A, Duke University Medical Center, Tel: (919)681-0172, oren.becher@duke.edu

Co-Primary Investigator: **Michelle Monje MD, PhD**, Instructor, Department of Neurology, Stanford University, Lucile Packard Children's Hospital at Stanford, 750 Welch Road, Suite 317, Palo Alto CA 94304, Tel: (650)736-0885, mmonje@stanford.edu

Co-Primary Investigators: **Maryam Fouladi MD, MSc**, Medical Director of Neuro-oncology; Professor of Clinical Pediatrics, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, Cincinnati, OH 45229, Tel: (513)803-0721, Maryam.Fouladi@cchmc.org

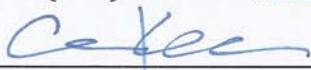
Co-Primary Investigator: **Cynthia Hawkins, MD, PhD, FRCPC**, Neuropathologist, Dept of Paediatric Laboratory Medicine, Associate Professor, University of Toronto; Scientist, Labatt Brain Tumour Research Centre, Hospital for Sick Children, 555 University Avenue, Toronto, ON, M5G 1X8, Tel: (416)813-5938, cynthia.hawkins@sickkids.ca

Co-Primary Investigator: **Xiao-Nan Li MD, PhD**, Associate Professor, Laboratory of Molecular Neurooncology, Texas Children's Cancer Center, Baylor College of Medicine, Tel: (832)824-4580, xiaonan@bcm.edu

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Oregon Health & Science University Contact Information

Primary Investigator: **Charles Keller MD**, Associate Professor; Leader, Pediatric Cancer Biology Program, 3181 SW Sam Jackson Park Rd, MC-L321, Portland, OR 97239, Tel: (503)494-1210, keller@ohsu.edu

signature: 

Other Investigators: **Kellie J. Nazemi MD** (Co-Primary Investigator), Director, Pediatric Neuro-Oncology, Doernbecher Children's Hospital; Dept. of Pediatrics; **Nathan Selden** and **Daniel Guillaume** (Co-Investigators), Division of Pediatric Neurosurgery, Dept. of Neurosurgery; Oregon Health & Science University, 3181 S.w. Sam Jackson Park Rd, MC-L321, Portland, OR 97239, Tel: (503)494-1210, keller@ohsu.edu

(Dr. Keller signing on behalf of all investigators)

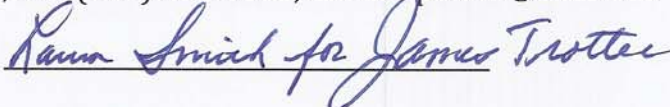
Individual with institutional authority to sign on behalf of the institution for application & award correspondence:

Jesse Null, Grants & Contracts Manager, Oregon Health & Science University, Research Grants & Contracts; 3181 SW Sam Jackson Park Road, L106RGC, Portland, OR 97239-3098, Tel: (503)494-7784, Email: orserv@ohsu.edu

signature: 

Individual with institutional authority to sign on behalf of the institution for financial reports and receiving checks:

James Trotter, Director, Sponsored Projects Administration, Oregon Health & Science University; 0690 SW Bancroft, L106SPA; Portland, OR 97239, Tel: (503) 494-0355, Email: spaweb@ohsu.edu

signature: 

Participating institution contact information is on the following 6 pages.



Research
Development &
Administration

Research Grants &
Contracts

Mail code L106
3181 S.W. Sam Jackson
Park Road
Portland, OR 97239-3098
tel 503 494-7784
fax 503 494-7787
www.ohsu.edu/research

**STATEMENT OF INTENT
TO ENTER INTO A CONSORTIUM AGREEMENT**

Title of Application: Rapid Preclinical Development of a Targeted
Therapy Combination for DIPG

Applicant Institution: Oregon Health & Science University

OHSU Principal Investigator: Dr. Charles Keller

Cooperating Institution: Duke University

Co-Investigator: Dr. Oren Becher
Assistant Professor
Department of Pediatrics and Pathology
LSRC B359A, 450 Research Drive
Durham, NC 27710
Duke University Medical Center
Ph (919) 681-0172, oren.becher@duke.edu

Oren Becher 6.14.11

Total Project Costs: \$100,000 (\$8,000 to Dr. Becher's laboratory)

Proposed Project Period: 08/01/11-07/31/12

The appropriate programmatic and administrative personnel of each institution involved in this grant application are aware of the appropriate grant policy and are prepared to establish the necessary inter-institutional agreement consistent with that policy.

Duke University

Laurie A Henry

Laurie Henry
Dir, Office of Research Admin
2200 West Main Street
Suite 820 Erwin Square Plaza



Research
Development &
Administration

**Research Grants &
Contracts**

Mail code L106
3181 S.W. Sam Jackson
Park Road
Portland, OR 97239-3098
tel 503 494-7784
fax 503 494-7787
www.ohsu.edu/research

Durham, NC 27705
(919) 684-5175
gcmal@mc.duke.edu

6/13/11
Date



Stanford University - Sponsored Projects Office

Research Management Group
301 Ravenswood Avenue
Menlo Park, CA 94025-3434
Phone (650) 736-0143 • Fax (650) 498-5876

**STATEMENT OF INTENT TO ESTABLISH A CONSORTIUM AGREEMENT
WITH Oregon Health & Science University**

Application Title: Rapid Preclinical Development of a Targeted Therapy Combination for DIPG

Sponsor: The Cure Starts Now Foundation

Proposed Project Period: 09/01/2011 – 08/31/2012

Proposed Subrecipient (Consortium) Amount: \$ 24,000

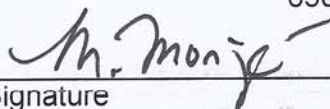
	Year 1	Sum for Project Period
Direct Costs	\$ 24,000	\$ 24,000
Facilities and Administrative Costs	\$ 0	\$ 0
Total Costs	\$ 24,000	\$ 24,000

Facilities and Administrative Cost Rate Applied: 0%
Congressional District: CA-014

In the event this grant application is funded, the appropriate programmatic and administrative personnel of each institution involved in this grant application are aware of the sponsor's consortium grant policy and are prepared to establish the necessary inter-institutional agreement consistent with that policy.

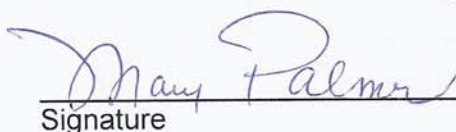
Sub-Recipient Organization: Stanford University

Principal Investigator: Michelle Monje-Deisseroth
Instructor, Department of Neurology and Neurological Sciences
750 Welch Road, Suite 317, Stanford, California, 94304
650-736-0885 mmonje@stanford.edu


Signature

7/7/11
Date

Authorized Representative: Mary Palmer
Research Process Manager, Research Management Group
301 Ravenswood Avenue, Menlo Park, CA 94025-3434
650-725-3199 mpalmer@stanford.edu


Signature

7/13/11
Date

Payment information on next page.

Stanford University - Sponsored Projects Office

Research Management Group
301 Ravenswood Avenue
Menlo Park, CA 94025-3434
Phone (650) 736-0143 • Fax (650) 498-5876

Payment Information:

1. Check made payable to: **Stanford University**
2. Address to which check should be sent:

First Class Mail Domestic or Foreign:

Attention (Name & Title):	Stanford University Lockbox
Address1	P.O. Box 44253
City, State Zip	San Francisco, CA 94144-4253

Federal Express:

Attention (Name & Title):	Wells Fargo Lockbox
Address1	Stanford University
Address2	Lockbox 44253
Address3	3440 Walnut Ave, Bldg A, 2nd Floor
City, State Zip	Fremont, CA 94538

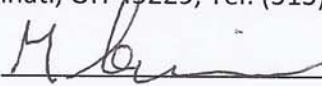
3. EIN (Employer Identification Number): **94-1156365**
4. Fiscal office representative to be copied on email correspondence related to Expenditure Reports:

Name:	Ada Kahsai
Title:	Research Accountant
Department:	Office of Sponsored Research
	340 Panama Street
	Stanford, California, 94305
Email address:	alkahasai@stanford.edu
Phone:	650-721-1398

Erin Eggerman Romer, Research Process Manager, Stanford University - Research Management Group, 301 Ravenswood Drive, Menlo Park, CA 94025-3434, Tel: (650) 725-8693, Email: eromer@stanford.edu


signature: *see willing letter*

Co-Primary Investigators: **Maryam Fouladi MD, MSc**, Medical Director of Neuro-oncology; Professor of Clinical Pediatrics, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, Cincinnati, OH 45229, Tel: (513)803-0721, Maryam.Fouladi@cchmc.org

signature:  6/24/11

Individual with institutional authority to sign on behalf of the institution:

Tana Housh, Manager Sponsored Programs, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, OH 45229 Tel: (513)636-1363, Fax: (513)636-1392, sponsoredprograms@cchmc.org,

signature:  6/24/11

Co-Primary Investigator: **Cynthia Hawkins, MD, PhD, FRCPC**, Neuropathologist, Dept of Paediatric Laboratory Medicine, Associate Professor, University of Toronto; Scientist, Labatt Brain Tumour Research Centre, Hospital for Sick Children, 555 University Avenue, Toronto, ON, M5G 1X8, Tel: (416)813-5938, cynthia.hawkins@sickkids.ca

signature: _____

Individual with institutional authority to sign on behalf of the institution:

Dr. Janet Rossant, Director, Research Institute, The Hospital for Sick Children 555 University Avenue, Toronto, Ontario, Canada, M5G 1X8
Phone: (416) 813-6577, Fax: (416) 813-5085
E-mail: janet.rossant@sickkids.ca

signature: *see willing letter*

Co-Primary Investigator: **Xiao-Nan Li MD, PhD**, Associate Professor, Laboratory of Molecular Neurooncology, Texas Children's Cancer Center, Baylor College of Medicine, Tel: (832)824-4580, xiaonan@bcm.edu

signature: _____

Individual with institutional authority to sign on behalf of the institution:

< Name and title >, < Address (for correspondence and for sending checks) >, Tel: < more goes here >, Email: < more goes here >

STATEMENT OF INTENT
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Title of Application: Rapid Preclinical Development of a
Targeted Therapy Combination for DIPG

Applicant Institution: Oregon Health & Science University

OHSU Principal Investigator: Dr. Charles Keller

Cooperating Institution: The Hospital for Sick Children

Co-Investigator: Dr. Cynthia Hawkins, Neuropathologist
Division of Pathology
The Hospital for Sick Children
555 University Avenue
Toronto, Ontario
Canada M5G 1X8
Phone: 416-813-5938
Email: Cynthia.hawkins@sickkids.ca

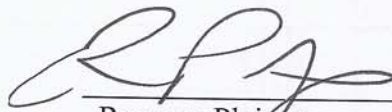
Signature: 

Total Project Costs: 16,000

Proposed Project Period: 08/01/11-07/31/12

The appropriate programmatic and administrative personnel of each Institution involved in this grant application are aware of the appropriate Grant policy and are prepared to establish the necessary inter-institutional Agreement consistent with that policy

Oregon Health and Science University The Hospital for Sick Children



Ramune Pleinys
Director, Research Operations
555 University Avenue
Toronto, ON
Canada M5G 1X8
Phone: 416-813-5997
Email: ramune.pleinys@sickkids.ca

June 9, 2011

Section 1

Primary Investigator: Xiaonan Li, Associate Professor of Pediatrics

Address: One Baylor Plaza, BCM 320
Houston, TX 77030-3411

Phone number: 832-824-4588

Email: xxli@txch.org

Signature:



Individual with institutional authority: Helen Shepherd, Executive Director for the Office of Research

Name of institution: Baylor College of Medicine

Address: Baylor College of Medicine
One Baylor Plaza, BCM 310
Houston, TX 77030-3411

Phone number of individual: 713-798-1297

Email of individual: spo@bcm.edu

Signature:



Rapid Preclinical Development of a Targeted Therapy Combination for DIPG

Section 2: Executive Summary

Patients with diffuse intrinsic pontine gliomas (DIPGs) have a uniformly dismal prognosis with a median survival of 9 months and long-term survival of less than 1%. Radiotherapy provides only temporary improvement of symptoms. No chemotherapy has ever proven effective. Novel therapies are desperately needed in this vulnerable population. Little was known about the biology of these tumors until recently. The availability of autopsy and some biopsy materials from children with DIPGs has finally led to a new understanding of the biology of these tumors. We are now identifying potentially important biological pathways in DIPGs that are readily targetable with currently available molecularly-targeted agents. In addition, we have successfully grown human DIPG tumors from autopsy materials in the petri dish and have developed mouse models of DIPGs – a key resource to functionally testing potential therapies. Since the number of children with this unfortunate disease is limited, and the number of available targeted agents is quite large, **we hypothesize that we can identify a promising combination of molecularly-targeted agents using a functional drug screening approach.** We propose first to **test the potentially effective molecularly-targeted drugs in the laboratory from DIPG tumors grown in the petri dish (Aim 1), and in mouse models of DIPG, whose biological characteristics we will first delineate (Aim 2).** We will then test the two or three most effective drugs in these models in combination. **The ultimate goal is to move the most effective single agent or combination therapy forward to early phase clinical trials in the next 18-24 months.** This is the first time that a group of basic and translational scientists and physicians from throughout North America have come together as a consortium to focus on DIPGs and to focus on a bench-to-bedside approach to rationally target therapy for children with DIPGs.