WALTERHOUSE, DAVID

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Children's Memorial Hospital

Children's Memorial Foundation

Children's Memorial Research Center

Pediatric Faculty Foundation

NORTHWESTERN UNIVERSITY

Faculty of Northwestern University's Feinberg School of Medicine

November 1, 2007

Richard M. Green, ND
Associate Professor
Chief, Division of Hepatology

Re: Cover letter explaining the reasons for your interest in becoming a mentor

Dear Dr. Green:

I am writing to express my interest in once again serving as a mentor for the Medical Student Summer Research Program (MSSRP). I have participated in this program for a number of years. I served as a mentor in this program in 2006, 1999, 1998, 1997, and 1992 and served on the Medical Student Research Committee from 1994 – 2002.

I am a member of the Developmental Biology Program at the Children's Memorial Research Center (CMRC) and the Division of Hematology/Oncology at Children's Memorial Hospital (CMH). Students conduct projects in my research laboratory at CMRC, the focus of which is to understand the function of the oncogene GLI1 in human cancers. In addition to running my laboratory, I serve as Program Director for the Pediatric Hematology/Oncology Fellowship Program, serve as the institutional Principal Investigator for the Children's Oncology Group (COG), and am study chair for an international Phase III rhabdomyosarcoma study conducted through COG. Therefore, I bring consider mentoring experience and a breadth of clinical and research experience that I feel can be valuable for medical students. Teaching has always been a priority for me and I have found this program to be particularly rewarding.

If you have questions please feel free to contact me at 773-755-6514 or at d-walterhouse@northwestern.edu.

Sincerely,

David O. Walterhouse

David O. Walterhouse
Associate Professor of Pediatrics
Northwestern University Feinberg School of Medicine

Medical Student Summer Research Program (MSSRP) and Research Thesis Program (RTP): David Walterhouse, MD (Fall 2007)

Roles for the GLI1 oncogene in human cancers

General Research Description: The Hedgehog signal transduction pathway plays a variety of important roles during vertebrate development, including patterning of the central nervous system, somites, and limbs, and epithelial-mesenchymal cell communication in the developing lung, gastrointestinal tract, hair follicle, prostate, and breast. At a cellular level, activation of the pathway that results from the interaction of the Hedgehog ligand with the Patched receptor, which in turn activates the GLI family of transcription factors (GLI1, GLI2, and GLI3) through a protein called Smoothened, drives cell proliferation in some situations and differentiation in others. It is now known that aberrant activation of the pathway occurs in a significant fraction of human cancers, including prostate carcinoma, small cell lung cancer, colon carcinoma, pancreatic carcinoma, medulloblastoma, rhabdomyosarcoma, and basal cell carcinoma. The precise roles that activation of the Hedgehog signal transduction pathway plays in these cancers have been incompletely characterized although appear to vary in different tumors. Roles in tumorigenesis have been suggested in medulloblastoma, rhabdomyosarcoma and basal cell carcinoma, while roles in tumor progression and metastasis have been suggested in prostate carcinoma. Therapeutic strategies to target components of the Hedgehog signal transduction pathway are beginning to be developed. Understanding how the pathway and in particular the GLI1 oncogene works, the effects of GLI1 activation in tumor cells, and developing strategies to inhibit the oncogenic activities of GLI1 represent the major efforts of the laboratory.

Description of potential MSSRP or RTP student projects:

Testing the function of polymorphic variants of the GLI1 oncogene in human keratinocytes: The laboratory identified two polymorphic sites in the GLI1 gene in the human population and showed that individuals with some haplotypes appear to be at increased risk for developing basal cell carcinoma compared with individuals with other haplotypes. This suggests the possibility of functional differences among the various forms of GLI1 that need to be explored, including environmental-gene interactions.

Testing desmoplastic medulloblastomas for p53 mutations: The laboratory has determined that the p53 tumor suppressor gene is a target of the oncogene GLI1 in the desmoplastic form of medulloblastoma (20% of all medulloblastomas). This creates an intriguing situation with co-expression of an oncogene and tumor suppressor. This led the laboratory to hypothesize that inactivating mutations in p53 may sometimes be found in this setting. Although p53 mutations are believed to occur in <10% of medulloblastomas, their frequency has not been specifically assessed in the desmoplastic form of the tumor.

Testing a possible role for the Hedgehog pathway in epithelial-mesenchymal cell communication in neuroblastoma: The laboratory has evidence that components of the Hedgehog signaling pathway are expressed in neuroblastoma cells in a pattern suggesting that the pathway is involved in the cross-talk between ectoderm-derived tumor neuroblasts and mesoderm-derived tumor Schwann cells. Experiments to prove that the Schwannian cells respond to the neuroblast-derived Hedgehog signal at a cellular and molecular level can now be conducted.

Trainees over the past 5 years (undergraduate, medical or graduate students; post-doctoral fellows): Walterhouse

Clinical Preceptor
Bethany Freeman, Northwestern University MD/PhD student, 2001 - 2003
Jackie Suen, 2nd year UIC Medical Student, 2005 – 2006

Laboratory Mentor
Laurie Eldridge, NU MD/PhD student, laboratory rotation 2002
Paul Kent, NU Pediatric Hematology/Oncology Fellow, Research advisor, 2000-2002
Jasmine Otkins, Cancer Center Cure program, 2002
Jennifer Cueto, Cancer Center Cure Program, 2003
Liset Banuelos, Cancer Center Cure Program, 2004
Olga Lakiza, Post-doctoral fellow, co-mentor, 2002 - 2006
Anastashia Magee, Cancer Center Cure program, 2005, 2006
Andrea Watson, NU Pediatric Hematology/Oncology Fellow, Research advisor, 2006 – 2008
Edward Chang, NU Medical Student Summer Research Program, 2006
Dara Davenport, Cancer Center Cure Program, 2007

Pediatric Hematology/Oncology Program Director
Andrew Campbell, 1999 – 2002
Joanna Weinstein, 2000 – 2003
Yasmin Gosiengfiao, 2001 - 2004
Laurie MacDonald, 2002 – 2003
Peter Zage 2002 - 2005
Jennifer Schneiderman, 2003 - 2006
Katie Ender, 2003 - 2006
Mike Burke, 2003 - 2006
Radhika Peddinti, 2004 – 2007
Amy Rosenfeld, 2004 – 2007
Andrea Watson, 2005 – present
Michelle Drillon, 2005 – present
Jennifer McNeer, 2006 – present
Steve Aller, 2006 – present
Rukhmi Bhat, 2006 – present
Jeff Andolina, 2007 – present
Rishi Lulla, 2007 – present
Colleen Morrison, 2007 - present

Research area (check all that apply): Walterhouse

X Basic Science
X Translational Science
Clinical Science