

Division of Pediatric Surgery, St Jude Children's Research Hospital

The Division of Pediatric surgery at St Jude offers clinical and translational investigation and treatment of pediatric solid tumors, neuroblastoma in particular. The basic science laboratory is focused on the development of two newly emerging strategies for the treatment of neuroblastoma (and other tumor types)--immunotherapy and antiangiogenic therapy. Gene-therapy approaches are central to each of these strategies.

Angiogenesis appears to be required for the neoplastic growth of tumor cells, making it a potential target for anti-cancer strategies. Long-term expression of an angiogenesis inhibitor is likely to be required for the successful treatment of cancer. Therefore, gene therapy-mediated delivery of these agents is an alternative way to provide long-term expression of these therapeutic proteins. Vectors expressing a number of different angiogenesis inhibitors are currently being designed and tested in vitro and in vivo in murine models of neuroblastoma.

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Recent Publications:

1. Benjamin R, Khwaja A, Singh N, McIntosh J, Meager A, Wadhwa M, Streck CJ, Ng CY, Davidoff AM and Nathwani AC. Continuous delivery of human type I interferons (α/β) has significant activity against acute myeloid leukemia cells in vitro and in a xenograft model. *Blood*, 109 (3): 1244-47, February 2007.
2. Dickson PV, Hamner JB, Streck CJ, Ng CY, McCarville MB, Calabrese C, Gilbertson RJ, Stewart CF, Wilson CM, Gaber MW, Pfeffer LM, Skapek SX, Nathwani AC and Davidoff AM. Continuous delivery of interferon-beta promotes sustained maturation of intratumoral vasculature. *Mol Cancer Res*, 5(6):531-42, June 2007.
3. Dickson PV, Sims TL, Streck CJ, McCarville MB, Santana VM, McGregor LM, Furman WL, Davidoff AM. Avoiding misdiagnosing Neuroblastoma as Wilms Tumor. *J Ped Surg*, 43(6): 1159-63, June 2008.
4. Dickson PV, Nathwani AC, Davidoff AM. Delivery of antiangiogenic agents for cancer gene therapy. *Technol Cancer Res Treat*. 2005 Aug;4(4):331-41.
5. Dickson PV, Davidoff AM. Malignant neoplasms of the head and neck. *Semin Pediatr Surg*. 2006 May;15(2):92-8.
6. Dickson PV, Hamner JB, Cauthen LA, Ng CY, McCarville MB, Davidoff AM. Efficacy of zoledronate against neuroblastoma. *Surgery*. 2006 Aug;140(2):227-35.
7. Dickson PV, Hamner JB, Burger RA, Garcia E, Ouma AA, Kim SU, Ng CY, Gray JT, Aboody KS, Danks MK, Davidoff AM. Intravascular administration of tumor tropic neural progenitor cells permits targeted delivery of interferon-beta and restricts

- tumor growth in a murine model of disseminated neuroblastoma. *J Pediatr Surg.* 2007 Jan;42(1):48-53.
8. Dickson PV, Hagedorn NL, Hamner JB, Fraga CH, Ng CY, Stewart CF, Davidoff AM. Interferon beta-mediated vessel stabilization improves delivery and efficacy of systemically administered topotecan in a murine neuroblastoma model. *J Pediatr Surg.* 2007 Jan;42(1):160-5; discussion 165.
 9. Calbrese C, Poppleton H, Kocak M, Fuller C, Hamner B, Oh EY, Gaber MW, Finklestein D, Allen M, Frank A, Bayazitov IE, Zakharenko SS, Gajjar A, Davidoff A, Gilbertson RJ. A perivascular niche for brain tumor stem cells. *Cancer Cell.* 2007 Jan;11(1):69-82.
 10. Dickson PV, Hamner JB, Sims TL, Fraga CH, Ng CY, Rajasekeran S, Hagedorn NL, McCarville MB, Stewart CF, Davidoff AM. Bevacizumab-induced transient remodeling of the vasculature in neuroblastoma xenografts results in improved delivery and efficacy of systemically administered chemotherapy. *Clin Cancer Res.* 2007 Jul 1;13(13):3942-50.
 11. Dickson PV, Hamner B, Ng CY, Hall MM, Zhou J, Hargrove PW, McCarville MB, Davidoff AM. In vivo bioluminescence imaging for early detection and monitoring of disease progression in a murine model of neuroblastoma. *J Pediatr Surg.* 2007 Jul;42(7):1172-9.
 12. Hamner JB, Dickson PV, Sims TL, Zhou J, Spence Y, Ng CY, Davidoff AM. Bortezomib inhibits angiogenesis and reduces tumor burden in a murine model of neuroblastoma. *Surgery.* 2007 Aug;142(2):185-191.
 13. Hamner JB, Sims TL, Curshaw A, Dickson PV, Rosati S, McGee M, Ng CY, Davidoff AM. The efficacy of combination therapy using adeno-associated virus--interferon beta and trichostatin A in vitro and in a murine model of neuroblastoma. *J Pediatr Surg.* 2008 Jan;43(1):177-82
 14. Dickson PV, Sims TL, Streck CJ, McCarville MB, Santana VM, McGregor LM, Furman WL, Davidoff AM. Avoiding misdiagnosing neuroblastoma as Wilms tumor. *J Pediatr Surg.* 2008 Jun;43(6):1159-63.
 15. Sims TL, Williams RF, Ng CY, Rosati SF, Spence YH, Davidoff AM. Bevacizumab suppresses neuroblastoma progression in the setting of minimal disease. *Surgery.* Accepted.

Recent Presentations:

1. Dickson PV, Sims TL, Streck CJ, McCarville MB, Santana VM, McGregor LM, Furman WL, Davidoff AM. Avoiding misdiagnosing neuroblastoma as wilms tumor. American Academy of Pediatrics, National Conference and Exhibition, Section on Surgery, San Francisco, CA, Oct 26-28, 2007
2. Hamner JB, Dickson PV, Sims TL, Zhou J, Spence Y, Ng CY, Davidoff AM. Bortezomib Inhibits Angiogenesis and Reduces Tumor Burden in a Murine Model of Neuroblastoma. February 2007, 2nd Annual Academic Surgical Congress. Phoenix, AZ.
3. Hamner JB, Sims TL, Cutshaw A, Dickson PV, Rosati S, McGee M, Ng CY, Davidoff AM. The Combination of Interferon-Beta and Trichostatin A Inhibits Tumor Growth In Vivo and in a Murine Model of Neuroblastoma. May 2007, American Pediatric Surgical Association 38th Annual Meeting. Orlando, FL.

4. Sims TL, Hamner JB, Bush RA, Ng CY, Spence YH, Kim SU, Aboody KS, Danks MK, Davidoff AM. Neural progenitor cell-mediated delivery of osteoprotegerin limits disease progression in a pre-clinical model of neuroblastoma bone metastasis. American Pediatric Surgical Association 39th Annual Meeting (APSA), Phoenix, AZ, May 29-31, 2008, oral presentation
5. Sims TL, Hamner JB, Bush RA, Williams RF, Zhou J, Kim SU, Aboody KS, Danks MK, Davidoff AM. Neural progenitor cell-mediated delivery of interferon- β improves neuroblastoma response to cyclophosphamide. Cancer Forum, Society of Surgical Oncology's 61st Annual Cancer Symposium (SSO), Chicago, IL, March 13-16, 2008, oral presentation
6. Sims TL, Williams RF, Ng CY, Rosati SF, Spence YH, Davidoff AM. Bevacizumab suppresses neuroblastoma progression in the setting of minimal disease. 3rd Annual Academic Surgical Congress (SUS/AAS). Huntington Beach, CA. February 13-15, 2008, oral presentation.
7. Sims TL, McGee M, Hamner JB, Ng CY, Junfang Z, McCarville B, Gaber MW, Davidoff AM. Continuous interferon-beta sensitizes rhabdomyosarcoma xenografts to ionizing radiation. Surgical Forum, American College of Surgeons 93rd Annual Clinical Congress (ACS), New Orleans, LA. October 2007, oral presentation.