BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Wilber, Andrew Christopher	Assistant Professor
eRA COMMONS USER NAME (credential, e.g., agency login) A-WILBER	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Millikin University, Decatur, IL	B.S.	05/96	Biology and Chemistry
University of Minnesota, Minneapolis, MN	Ph.D.	08/06	Molecular Genetics
St. Jude Children's Research Hospital, Memphis, TN	Postdoctoral	12/07	Experimental Hematology

A. Personal Statement

My laboratory is divided into two areas:

Research Topic 1. Gene Therapy for Sever Hemoglobin Disorders and Developmental Erythropoiesis.

We are interested in the development of strategies to increase fetal hemoglobin production in children or adults with either sickle cell disease (SCD) or severe β-thalassemia (β-thal) following lentiviral vector-mediated gene transfer into the patient's own stem cells. Our published works focused on evaluating vectors designed to increase fetal hemoglobin production in cultured cells from normal donors and patients with β-thal major following delivery of (**i**) an exogenous γ-globin gene, (**ii**) an artificial transcriptional activator, GG1-VP64, designed to induce the endogenous γ-globin genes and (**iii**) shRNAs targeting the γ-globin gene repressor protein Bcl11A. Four patients with beta-thal have been studied in detail where data are emerging for three patients with SCD.

We are engaged in studies designed to understand the molecular aspects of developmental erythropoiesis and fetal (HbF) to adult (HbA) hemoglobin switching. For this, we utilize a two-phase culture model where late stage erythroblasts are derived directly from human CD34+ cells isolated from fetal liver, umbilical cord blood, or adult peripheral blood or bone marrow to identify differences in protein-DNA interactions at the β-globin locus and differences in the coding and non-coding RNA transcriptomes. We are very encouraged by our progress to define the specific constellation of molecular features that determine erythroid development and whether these cells will express HbF or HbA.

Research Topic 2. Trans-differentiation of Natural Killer Cells by Soluble Tumor-derived Factors.

Features of aggressive tumors include the ability to promote angiogenesis and evade immune surveillance. Natural killer (NK) cells have classically been associated with immune surveillance of tumors and are thought to destroy tumor cells via cytotoxicity. Similarities between embryo implantation and tumor growth/invasion have long been noted. Large influx of maternal NK cells into the decidua occurs during normal embryo implantation. Originally assumed to be cytotoxic, recent studies establish that these decidua-NK (dNK) cells have altered CD phenotypes, lose their cytotoxic capacities, elaborate pro-angiogenic factors (VEGF), and facilitate growth of the implant. Mechanisms driving these phenotypic and functional changes are not known but we propose that similar trans-differentiation of peripheral NK cells occurs in RCC.

Here, we are using clinical samples and a novel animal model to characterize the phenotype and pro-angiogenesis role of natural killer (NK) cells in renal cell carcinoma (RCC). We hypothesize that natural killer

(NK) cells, recruited to the site of renal cell carcinoma (RCC) and under the influence of prostaglandin E_2 (PGE_2) and/or TGFβ, trans-differentiate to display unique phenotypic markers (CD56+CD16-) and functional characteristics (loss of cytotoxicity, elaboration of pro-angiogenic VEGF) that are distinct from their peripheral counterparts (CD56+CD16+). Here our focus is RCC, but this concept could represent a paradigm shift in the generalized role of NK cells in tumor biology and metastasis and warrants study.

B. Positions, Experience and Honors

Positions and Employment

1996-1998 Research Assistant, Megan Health Inc., St. Louis, MO
1998-1999 Microbiologist I, Taylor Pharmaceuticals, Decatur, IL
2000-2002 Researcher II, Southern Illinois University School of Medicine, Springfield, IL
2007 Postdoctoral Fellow, St. Jude Children's Research Hospital, Memphis, TN
2008- Assistant Professor, Department of Medical Microbiology, Immunology and Cell Biology and Simmons Cancer Institute, Southern Illinois University School of Medicine, Springfield, IL

Other Experience and Professional Memberships

2008- Member, American Society of Gene and Cell Therapy
2008- Member, Infection Control and Safety Committee
2008-2012 Member, Springfield Committee on Research Involving Human Subjects
2009-2012 Chaiman, Springfield Committee on Research Involving Human Subjects, Exempt and Expedited Study Review Panel
2009- Director, Vector Production Core Facility for Somatic Cell Gene Transfer
2010- Chairman, Infection Control and Safety Committee
2010-2012 Vice-Chairman, Springfield Committee on Research Involving Human Subjects
2010- Academic Editor, PLoS One
2010- Reviewer: PLoS, BioMed Central, Stem Cells and Development, and Blood Journals
2011- Member, New Investigator Committee, American Society of Gene and Cell Therapy
2011- Member, American Society of Hematology
2011- Abstract Reviewer, American Society of Gene and Cell Therapy

Honors

2003-2005 University of Minnesota, NIGMS Training Grant in Biotechnology (T32 GM08347)
2005-2006 University of Minnesota Doctoral Dissertation Fellowship
2006 Student Travel Award, American Society of Gene Therapy 9th Annual Meeting
2006 Excellence in Research Award, American Society of Gene Therapy 9th Annual Meeting
2006 Student Travel Award, International Society of Experimental Hematology 35th Annual Meeting
2006 New Investigator Award, International Society of Experimental Hematology 35th Annual Meeting
2006 NIH/NCI 1st Annual National Graduate Student Research Festival
2007 St. Jude 2nd Annual Postdoctoral Fellows Retreat Best Oral Presentation
2013 Medical Innovator, Sangamon County Medical Society

C. Peer-reviewed Publications (from 2002-2013)

1. Volk-Draper L.D., Rajput S., Hall K.L., **Wilber A.**, & Ran S. (2012) Novel model for basaloid triple-negative breast cancer: behavior in vivo and response to therapy. Neoplasia, 14(10):926-942. PMID: 23097627

2. Liu Z., Yan R., Al-Salman A., Shen Y., Bu Y., Ma J., Luo D.X., Huang C., Jiang Y., **Wilber A.**, Mo Y.Y., Huang M., Zhao Y. & Cao D. (2012) Epidermal growth factor induces tumor marker AKR1B10 expression through activator protein-1 signaling in hepatocellular carcinoma cells. Biochemical Journal, 442(2):273-282. PMID: 22136414

3. Okuda H., Kobayashi A., Xia B., Watabe M., Pai S.K., Hirota S., Xing F., Liu W., Pandey P.R., Fukuda K., Modur V., Ghosh A., **Wilber A.** & Watabe K. (2012) Hyaluronan synthase HAS2 promotes tumor progression in bone by stimulating the interaction of breast cancer stem-like cells with macrophages and stromal cells. Cancer Research, 72(2):537-547. PubMed PMID: 22113945

4. Kobayashi A., Okuda H., Xing F., Pandey P.R., Watabe M., Hirota S., Pai S.K., Liu W., Fukuda K., Chambers C., **Wilber A.** & Watabe K. (2011) Bone morphogenetic protein 7 in dormancy and metastasis of prostate cancer stem-like cells in bone. Journal of Experimental Medicine, 208(13):2641-2655. PMID: 22124112

5. Groesch K.A., Torry R.J., **Wilber A.C.**, Abrams R., Bieniarz A., Guilbert L.J. & Torry D.S. (2011) Nitric oxide generation affects pro- and anti-angiogenic growth factor expression in primary human trophoblast. Placenta, 32(12):926-931. PMID: 21977042

6. **Wilber A.**, Ulloa Montoya F., Hammer L., Moriarity B.S., Geurts A.M., Largaespada D.A., Verfaillie C.M., McIvor R.S. & Lakshmipathy U. (2011) Efficient non-viral integration and stable gene expression in multipotent adult progenitor cells. Stem Cells International, 717069. PMID: 21977042.

7. **Wilber A.**, Nienhuis A.W. & Persons D.A. (2011) Transcriptional regulation of fetal to adult hemoglobin switching: new therapeutic opportunities. Blood, 117(15):3945-3953. PMID: 21321359

8. **Wilber A.**, Hargrove P.W., Kim Y.S., Riberdy J.M., Sankaran V.G., Papanikolaou E., Georgomanoli M., Anagnou N.P., Orkin S.H., Nienhuis A.W. & Persons D.A. (2011) Therapeutic Levels of fetal hemoglobin in erythroid progeny of β-thalassemic $CD34^+$ cells following lentiviral vector-mediated gene transfer. Blood, 117(10):2817-2826. PMID: 21156846

9. Halford W.P., Püschel R., Gershburg E., **Wilber A.**, Gershburg S. & Rakowski B. (2011) A live attenuated HSV-2 ICP0 virus elicits 10 to 100 times greater protection against genital herpes than a glycoprotein D subunit vaccine. Public Library of Science (PLoS) One, 6(3):e17748. PMID: 21412438

10. Pandey P.R., Okuda H., Watabe M., Pai S.K., Liu W., Kobayashi A., Xing F., Fukuda K., Hirota S., Sugai T., Wakabayashi G., Koeda K., Kashiwaba M., Suzuki K., Chiba T., Endo M., Fujioka T., Tanji S., Mo Y.Y., Cao D., **Wilber A.C.** & Watabe K. (2011) Resveratrol suppresses growth of cancer stem-like cells by inhibiting fatty acid synthase. Breast Cancer Research Treatment, 130(2):387-398. PMID: 21188630

11. Huang X., Haley K., Wong M., Guo H., Lu C., **Wilber A.** & Zhou X. (2010) Unexpectedly high copy number but low frequency of persistent expression of the *Sleeping Beauty* transposase following trans-delivery in primary human T cells. Human Gene Therapy, 21(11):1577-1590. PMID: 20528476

12. Multhaup M.M., Karlen A.D., Swanson D.L., **Wilber A.**, Somia N.V., Cowan M.J. & McIvor R.S. (2010) Cytotoxicity associated with Artemis over-expression after lentiviral vector mediated gene transfer. Human Gene Therapy. Human Gene Therapy, 21(7):865-875. PMID: 20163250

13. Rajput S. & **Wilber A**. Roles of inflammation in cancer initiation, progression, and metastasis. (2010) Frontiers in Bioscience (Scholar Edition), 2:176-183. PMID: 20036938

14. **Wilber A.**, Tschulena U., Hargrove P.W., Kim Y.S., Persons D.A., Barbas C.F. & Nienhuis, A.W. (2010) A zinc-finger transcriptional activator designed to interact with the γ-globin gene promoters enhances fetal hemoglobin production in primary human adult erythroblasts. Blood, 115(15):3033-3041. PMID: 20190190

15. Flister M.J., **Wilber A.**, Hall K.L., Iwata C., Miyazono K., Nisato R.E., Pepper M.S., Zawieja D.C. & Ran S. (2010) Inflammation induces lymphangiogenesis through upregulation of VEGFR-3 and NF-kappaB and Prox-1. Blood, 115(2):418-429. PMID: 19901262

16. Podetz-Petersen K.M., Bell J.B., Steele T.W., **Wilber A.**, Shier W.T., Belur L.R., McIvor R.S. & Hackett P.B. (2010) Gene expression in lung and liver after intravenous infusion of polyethyleneimine complexes of *Sleeping Beauty* transposons. Human Gene Therapy, 21(2):210-220. PMID: 19761403

17. Huang X., **Wilber A.**, McIvor R.S. & Zhou X. (2009) DNA transposons for modification of human primary T lymphocytes. Methods in Molecular Biology, 506:115-126. PMID: 18470650

18. Wangensteen K.J., **Wilber A.**, Keng V.W., Chen Y., Matise I., Wangensteen L., Steer C.J., McIvor R.S., Largaespada D.A., Wang X. & Ekker S.C. (2008) A facile method for somatic, lifelong manipulation of multiple genes in the mouse liver. Hepatology, 47(5):1714-1724. PMID: 18435462

19. Belur L.R, McIvor R.S. & **Wilber A**. (2008) Liver-directed gene therapy using the *Sleeping Beauty* transposon system. Methods in Molecular Biology, 434:267-276. PMID: 18470650

20. **Wilber A.**, Linehan J.L., Tian X., Woll P.S., Morris J.K., Belur L.R., McIvor R.S. & Kaufman D.S**.** (2007) Efficient and stable transgene expression in human embryonic stem cells using transposon-mediated gene transfer**.** Stem Cells, 25(11):2919-2927. PMID: 17673526

21. Wilber A., Wangensteen K.J., Chen Y., Zhou L., Frandsen J.L., Bell J., Chen Z.J., Ekker S.C., McIvor R.S. & Wang X. (2007) Messenger RNA as a source of transposase for *Sleeping Beauty* transposon-mediated correction of Hereditary Tyrosinemia type I. Molecular Therapy, 15(7):625-630. PMID: 17440442
22. Balciunas D., Wagensteen K.J., **Wilber A.**, Bell J.B., Geurts A.M., Sivasubbu S., Wang X., Hackett P.B., Largaespada D.A., McIvor R.S. & Ekker S.C. (2006) Harnessing an efficient large cargo-capacity transposon for vertebrate gene transfer applications. Public Library of Science (PLoS) Genetics, 2(11):e169. PMID: 17096595
23. Geurts A.M., **Wilber A.**, Carlson C.M., Lobitz P.D., Clark K.J., Hackett P.B., McIvor R.S. & Largaespada D.A. (2006) Conditional gene expression in the mouse using a *Sleeping Beauty* gene-trap transposon. BMC Biotechnology, 6:30-45. PMID: 16800892
24. Wilber A., Frandsen J.L., Geurts J.L., Largaespada D.A., Hackett P.B. & McIvor R.S. (2006) RNA as a source of transposase for *Sleeping Beauty*-mediated gene insertion and expression in somatic cells and tissues. Molecular Therapy, 13(3):625-630. PMID: 16368272
25. Huang X., **Wilber A.**, Bao L., Tuong D., Tolar J., Orchard P.J., Levine B.L., June C.H., McIvor R.S., Blazar, B.R. & Zhou X. (2006) Stable gene transfer and expression in human primary T-cells by the *Sleeping Beauty* transposon. Blood, 107(2):483-491. PMID: 16189271
26. Wilber A., Frandsen J.L., Wangensteen K.J., Ekker S.C., Wang X. & McIvor R.S. (2005) Dynamic gene expression following systemic delivery of plasmid DNA as determined by *in vivo* bioluminescent imaging. Human Gene Therapy, 16(11):1325-1332. PMID: 16259566
27. Osborn M.J., Panoskaltsis-Mortari A., McElmurry R.T., Bell S.K., Vignali D.A., Ryan M.D., **Wilber A.**, McIvor R.S., Tolar J. & Blazar B.R. (2005) A picornaviral 2A-like sequence-based tricistronic vector allowing for high-level therapeutic gene expression coupled to a dual-reporter system. Molecular Therapy, 12(3):569-574. PMID: 15964244
28. Wilber A., O'Connor T.P., Lu M.L., Karimi A. & Schneider M.C. (2003) DNase1l3 deficiency in lupus- prone MRL and NZB/W F1 mice. Clinical & Experimental Immunology, 134(1):46-52. PMID: 12974753
29. Wilber A., Lu M.L. & Schneider M.C. (2002) Deoxyribonuclease I-like-III is an inducible macrophage barrier to liposomal transfection. Molecular Therapy, 6(1):35-42. PMID: 12095301D.

D. Research Support

CURRENT SUPPORT (NO OVERLAP WITH CURRENT PROPOSAL)

Simmons Cancer Institute (Wilber, PI) 03/01/12-02/28/14 5% effort
Southern Illinois University School of Medicine $50,000/year
Title: Renal cell tumor-mediated trans-differentiation of natural killer cells
Goal: To determine the generalized role of non-cytotoxic NK cells in tumor biology and metastasis and provide evidence for the role of PGE_2 and/or TGFβ signaling pathways in this program.
Role: Principal Investigator

2010037 (Wilber, Co-PI) 06/01/10-05/30/13 20% effort
Doris Duke Charitable Foundation $59,220 direct/year
Title: Identification of Novel Factors and Mechanisms Influencing Expression of Fetal Hemoglobin.
Goal: To uncover novel factor and mechanisms that influence expression of fetal hemoglobin in developing erythroid cells.
Role: Co-Principal Investigator

2P01HL053749-16 (Sorrentino, PI) 09/01/10-08/30/15 20% effort
NIH/NHLBI $41,847 direct/year
Title: Project 1: Gene Therapy of Sickle Cell Disease through Enhancement of Fetal Hemoglobin
Goal: To examine transcription factors for their ability to induce gamma globin gene expression and enhance fetal hemoglobin production using lentiviral vector mediated transfer into enriched hematopoietic stem cells.
Role: Co-Investigator (Subcontract Only)

APPLIED/PENDING SUPPORT

R15 AREA (Wilber, PI) 12/01/12-11/30/15 15% effort
NIH/NCI $299,553 direct for 3yrs
Title: Renal cell tumor-mediated trans-differentiation of natural killer cells
Goal: To determine the role of non-cytotoxic NK cells in tumor biology and metastasis and provide evidence for the role of PGE_2 and/or TGFβ signaling pathways in this program.
Status: Initial Submission Reviewed May 24, 2012 (Impact Score=39); Resubmitted October 15, 2012
Role: Principal Investigator

COMPLETED SUPPORT

Doris Duke Charitable Foundation (Wilber, PI) 08/01/11-07/30/12
Collaborations in Sickle Cell Disease
Title: Identification of optimal vector design for gene addition in sickle cell disease
Goal: To directly compare the production levels and anti-sickling effect achieved using gamma- and modified beta-globin encoding lentiviral vectors in erythroblasts derived from transduced CD34+ cells from SCD patients.
Role: Principal Investigator

Concept Development Award (Wilber, PI) 12/05/10-12/04/12
Southern Illinois University School of Medicine
Title: A System for Controlling Gene Expression in Mammalian Systems
Goal: To harness the herpes simplex virus IE1 bi-directional promoter for the purpose of achieving co-ordinate and controlled levels of gene expression in mammalian cells and tissues.
Role: Principle Investigator (Inventor)

2P01HL053749 (Nienhuis, PI) 01/01/08-08/31/10
NIH/NHLBI
Title: Project 3: Gene Transfer into Hematopoietic Stem Cells
Goal: To examine transcription factors for their ability to induce gamma globin gene expression and enhance fetal hemoglobin production using lentiviral vector mediated transfer into enriched hematopoietic progenitor cells.
Role: Co-Investigator (Subcontract Only)