## BIOGRAPHICAL SKETCH

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NAME: Kim, Yong-Mi

eRA COMMONS USER NAME (credential, e.g., agency login): YONGMIKIM

POSITION TITLE: Associate Professor of Pediatrics and Pathology

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

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Heinrich-Heine-University, Düsseldorf, Germany | M.D., PhD | 04/1998 | Medicine |
| Heinrich-Heine-University, Düsseldorf, Germany | Resident | 08/1999 | Pediatrics |
| Massachusetts General Hospital, Boston | Postdoctoral | 08/2002 | Immunology |
| Harvard School of Public Health, Boston | MPH | 07/2003 | Clinical Effectiveness |
| Dana Farber Cancer Institute, Boston | Postdoctoral | 08/2004 | Hematology |

### A. Personal Statement

As a postdoctoral fellow, I carried out research in Graft-versus-Host and Graft-versus-Leukemia effects and on leukemogenesis of acute myeloid. In addition, I have gained experience in murine and human leukemia models used to understand drug resistance of leukemia. My career was disrupted due to family obligations (08/04-08/06). Upon return, I have a demonstrated record of accomplished and productive research projects in an area of high relevance for drug resistance of leukemia. My lab works on the microenvironment of drug resistance of leukemia and is interested particularly in understanding the role of integrins a central adhesion molecules in drug resistance of leukemia. As a second focus my lab works on understanding survivin-associated apoptosis and wnt-regulated self-renewal of ALL. We have also developed a cell bank of primary ALL and AML and have developed expertise in preclinical drug evaluation using our xenograft model of ALL and AML. Recently, we have now included a xenograft model for CAR T cell relapse and included relapse ALL samples post-CAR T cell therapy. In summary, I have successfully administered the projects and collaborated with other researchers productively as reflected by our peer-reviewed publications.


1. Yu M, Gang EJ, PR Parameswaran, Stoddart S, Fei F, Schmidhuber S, Park E, Hsieh YT, Muschen M, Yang AS, Groffen J, Heisterkamp N[§], **Kim YM**[§]. (2011). AMD3100 sensitizes acute lymphoblastic leukemia cells to chemotherapy in vivo. *Blood Cancer*, J 1: e14; doi:10.1038/bcj.2011.13.
2. Duy C, Hurtz C, Shojaee S, Cerchietti L, Geng H, Swaminathan S, Klemm L, Kweon SM, Nahar R, Braig M, Park E, **Kim YM**, Hofmann WK, Herzog S, Jumaa H, Koeffler HP, Yu JJ, Heisterkamp N, Wu H, Ye BH, Melnick A & Müschen M. (2011). BCL6 enables leukemia cells to cope with inhibition of oncogenic tyrosine kinases. *Nature,* 473(7347), 384-388.
3. Behan JW, Ehsan Ehsanipour E, Xia Sheng X, Pramanik R, Hsieh YT*, **Kim YM,** Wang XC, Mittelman SD. (2013). Activation of Adipose Tissue Macrophages in Obese Mice does not Require Lymphocytes. *Obesity*, 21(7):1380-8.


### B. Positions and Honors

**Positions and Employment**

1997-1999 Intern and Resident, Heinrich-Heine-University, Childrens' Hospital, Düsseldorf, Germany
1999-2002 Fellow, Transplantation Biology Research Center, Massachusetts General Hospital, Boston, MA
2003-2004 Fellow, Harvard University, Dana Farber Cancer Institute, Boston, MA

2006-2014 Assistant Professor, Division of Hematology-Oncology, Departments of Pediatrics, and Pathology, Children's Hospital Los Angeles and University of Southern California, Keck School of Medicine, Los Angeles, CA

2014- Associate Professor (with tenure), Division of Hematology-Oncology, Departments of Pediatrics, and Pathology, Children's Hospital Los Angeles and University of Southern California, Keck School of Medicine, Los Angeles, CA

**Other Experience and Professional Memberships**

2007- Member, American Association for Cancer Research

2007- Member, American Society of Hematology

**Honors**

2007 Research Career Development Award (RCDA) of the Saban Research Institute

2011 St. Baldricks Scholar Award

2012 Hyundai Hope on Wheels Scholar Award

**C. Contribution to Science**

1. **We have identified integrin alpha4 as a central molecule in adhesion-mediated drug resistance.** Cell-adhesion mediated drug resistance is known to contribute to relapse of leukemia. It remains unkown which adhesion molecules are important for CAM-DR and how this knowledge can be translated to clinical trials. The adhesion protein integrin alpha4 (alpha4) regulates engraftment of normal hematopoietic progenitors in the bone marrow and engraftment of ALL cells. Formal studies of the role of alpha4 as a potential therapeutic target in ALL have not been performed. We evaluated interference with integrin alpha4-mediated stromal adhesion as a new acute lymphoblastic leukemia treatment. Integrin alpha4-blockade using Natalizumab in combination with chemotherapy sensitizes pre-B acute lymphoblastic leukemia to chemotherapy.

   **a)** Hsieh YT, Gang EJ, Geng HM, Park E, Huantes S, Chudziak D, Dauber K, Schaefer P, Scharman C, Shimada H, Shojaee S, Parameswaran R, Klemm L, Loh M, Kang ES, Koo HH, Hofmann WK, Andrade J, Crooks GM, Willman CL, Müschen M, Papayannopoulou T, Heisterkamp N, Bönig H, **Kim YM.** (2013). Integrin alpha4 blockade eradicates drug resistant pre-B acute lymphoblastic leukemia. *Blood*, 7;121(10):1814-8.

   **b)** Hsieh YT, Gang EJ, Shishido S, Kim HN, Pham J, Khazal S, Osborne A, Esguerra ZA, Kwon E, Jang J, Bonig H, Biediger RJ, Vanderslice P, **Kim YM**. (2014). Effects of the small-molecule inhibitor of integrin α4, TBC3486, on pre-B-ALL cells. *Leukemia* 28: 2101-2104.

   **c)** Shishido S., Bönig H, **Kim YM**. (2014). Role of Integrin Alpha4 in Drug Resistance of Leukemia. *Frontiers of Oncology,* 4:99

2. **We have determined the critical role of BIRC5/survivin in drug resistance of ALL**. Relapse of drug-resistant acute lymphoblastic leukemia (ALL) has been associated with increased expression of survivin/BIRC5, an inhibitor of apoptosis protein, suggesting a survival advantage for ALL cells. Our findings show the importance of survivin expression in drug resistance and demonstrate that survivin inhibition may represent a powerful approach to overcome drug resistance and prevent relapse in patients with ALL.

   **a)** Park E, Gang EJ, Hsieh YT, Schaefer P, Chae S, Klemm L, Huantes S, Loh M, Conway EM, Kang ES, Koo HH, Hofmann WK, Heisterkamp N, Pelus L, Keerthivasan G, Crispino J, Kahn M, Müschen M and **Kim, YM**. (2011). Targeting Survivin Overcomes Drug Resistance in Acute Lymphoblastic Leukemia. *Blood*, 118(8), 2191-9.

3. **We have shown that Wnt/catenin signaling plays a role in self-renewal and drug resistance in ALL. Deregulated** Wnt signaling is evident in chronic and acute myeloid leukemia, however little is known about acute lymphoblastic leukemia. ICG-001 is a novel small molecule modulator of Wnt/catenin signaling. We have demonstrated that selective disruption of the CBP/ catenin interactions using ICG-001 downregulates indirectly survivin and sensitizes ALL cells to chemotherapy.

a) **Kim YM**, Ma H, Oehler VG, Gang EJ, Nguyen C, Masiello D, Liu H, Zhao Y, Radich J, Kahn M (2011). The Gamma Catenin/CBP Complex Maintains Survivin Transcription in β-catenin Deficient/Depleted Cancer Cells. *Curr Cancer Drug Targets*, 11(2), 213-225.
b) Gang EJ, Hsieh YT, Pham J, Zhao Yi, Nguyen Cu, Huantes S, Park E, Naing K, Klemm L, Swaminathan S, Conway EM, Pelus L, Crispino J, Mullighan C, MacMillan M, Müschen M, Kahn M, **Kim YM**. (2014) Small molecule inhibition of CBP/catenin interactions eliminates drug resistant clones in acute lymphoblastic leukemia. *Oncogene*, 33(17):2169-78.
c) Ring A, **Kim YM**, Michael Kahn. (2014). Wnt Signaling and Stem cells. Review. *Stem Cell Reviews and Report,*10(4):512-25

**Complete List of Published Work in MyBibliography:**

https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/47458981/?sort=date&direction=ascending

## D. Research Support

### Ongoing Research Support

R01 CA172896-06 (Kim, PI) 07/01/2013 – 08/30/23
National Institutes of Health/NCI
Title: Understanding the niche of minimal residual disease leukemia cells
Role: PI

R01 CA201444-01A1 (Mittelman, PI; Kim, Co-I)
National Institutes of Health/NCI 07/15/16 - 06/30/21
Adipocytes are important players in the acute lymphoblastic leukemia microenvironment
Investigate role of adipocytes in bone marrow in ALL outcome
Role: Co-I

Pediatric Cancer Research Foundation
(Kim, PI; Heisterkamp, Abdel-Azim: Co-PI) 7/1/2015 – 12/31/2018
Evaluation of the PI3Kδ Inhibitor, idelalisib, in Childhood Acute Lymphoblastic Leukemia
Role: PI

Leukemia & Lymphoma Society 10/1/2016 - 9/30/2019
Translational Research Award
Overcoming drug resistance in leukemia using a novel integrin alpha4 inhibitor, AVA-4746
Role: PI

Alexis Lemonade Foundation
(Kim, PI) 09/1/2018 – 08/30/2020
Innovation Award
Physical properties of drug resistant leukemia cells
Role: PI

Margaret Early Foundation 01/01/2019 – 12/30/2019
(Stallcup, PI)
Epigenetic inhibitors to enhance glucocorticoid sensitivity in leukemia
Role: Co-PI

### Completed Research Support

V-Foundation (Heisterkamp, PI; Kim, Co-PI) 11/01/2012 – 09/30/2015
Title: Improving treatment outcome in leukemia by disruption of bone marrow leukemia interactions relevant to minimal residual disease

Role: Co-PI

Gilead (Kim, PI) 07/01/2015 – 06/30/16
Preclinical Evaluation of Idelalisib in ALL
Role: PI

Scholar Award 210074 (Kim, PI) 7/1/2011 – 06/30/2016
St. Baldricks' Foundation
Title: Role of CD49d in Chemoresistant Leukemia
Role: PI

Alexis Lemonade Foundation
(Kim, PI; Heisterkamp, Abdel-Azim: Co-PI) 07/1/2015 – 06/30/2018
REACH Award
Evaluation of the PI3Kδ Inhibitor, idelalisib, in Childhood Acute Lymphoblastic Leukemia;
Role: PI

St. Baldrick's Foundation 07/1/2016 - 6/30/2018
Research Award
Targeting integrin alpha 4 in ALL
Role: PI