



The University of Wisconsin - Madison

CMP

Cellular and Molecular Pathology

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Program of the Thesis Defense Seminar for the
Degree of Doctor of Philosophy
in Cellular and Molecular Pathology

**“Induced Pluripotent Stem
Cell Model of Chronic Myeloid
Leukemia Revealed Olfactomedin 4
as a Novel Therapeutic Target in
Primitive Leukemia Cells”**

Monday, September 16, 2013
3 pm | 7170 WIMR

Research conducted in the lab of
Igor Slukvin, MD, PhD
Department of Pathology & Laboratory Medicine



Kran Suknuntha's Thesis Abstract

“Induced Pluripotent Stem Cell Model of Chronic Myeloid Leukemia Revealed Olfactomedin 4 as a Novel Therapeutic Target in Primitive Leukemia Cells”

Kran Suknuntha
Under the supervision of
Professor Igor Slukvin, MD, PhD
at the University of Wisconsin-Madison

The definitive cure of leukemia requires identification of novel therapeutic targets to eradicate leukemia stem cells (LSCs). However, rarity of LSCs within the pool of malignant cells remains a major limiting factor for their study in humans. Here we show that lin-CD34⁺CD45⁺ cells with LSC features can be generated de novo from reprogrammed primary chronic myeloid leukemia (CML) cells. Similar to somatic LSCs, induced lin-CD34⁺CD45⁺ (iCD34⁺) cells were resistant to tyrosine kinase inhibitor (TKI) imatinib, but became sensitive after maturation. Molecular profiling of CML and normal iCD34⁺ cells treated and not treated with imatinib identified olfactomedin 4 (OLFM4) as the one of the top-ranked genes induced by TKI. The knockdown of OLFM4 by siRNA inhibited growth of iCD34⁺ cells and primary somatic LSCs, and increased their responses to imatinib. This is the first study to show that induced pluripotent stem cell can be used to produce LSC-like cells and identify their novel drug targets.

Publications

Hu K, Yu J, **Suknuntha K**, Tian S, Montgomery K, Choi KD, et al. Efficient generation of transgene-free induced pluripotent stem cells from normal and neoplastic bone marrow and cord blood mononuclear cells. *Blood*. 2011 Apr 7;117(14):e109-19.

Togarrati PP, **Suknuntha K**. Generation of mature hematopoietic cells from human pluripotent stem cells. *Int J Hematol*. 2012 Jun;95(6):617-23.

Choi KD, Vodyanik MA, Togarrati PP, **Suknuntha K**, Kumar A, et al. Identification of the hemogenic endothelial progenitor and its direct precursor in human pluripotent stem cell differentiation cultures. *Cell Rep*. 2012 Sep 27;2(3):553-67.

Wei Xie, Matt Schultz, Ryan Lister, Zhonggang Hou, Nisha Rajagopal, Pradipta Ray, John W. Whitaker, Shulan Tian, R. David Hawkins, Danny Leung, Hongbo Yang, Tao Wang, Ah Young Lee, Scott A. Swanson, Jiuchun Zhang, Yun Zhu, Audrey Kim, Joseph Nery, Mark A. Urich, Samantha Kuan, Chia-an Yen, Sarit Klugman, Pengzhi Yu, **Kran Suknuntha**, Nicholas E. Propson, Huaming Chen, Lee E. Edsall, Ulrich Wagner, Yan Li, Zhen Ye, Ashwinikumar Kulkarni, Zhenyu Xuan, Wen-yu Chung, Neil C. Chi, Jessica Antosiewicz-Bourget, Igor Slukvin, Ron Stewart, Michael Q. Zhang, Wei Wang, James A. Thomson, Joseph R. Ecker, and Bing Ren. Epigenomic Analysis of Multi-lineage Differentiation of Human Embryonic Stem Cells. *Cell*. 2013 May 23;153(5):1134-48

Kran Suknuntha, Yuki Ishii, Kejin Hu, Jean YJ Wang, Scott Swanson, Ron Stewart, James Thomson, and Igor Slukvin. Induced Pluripotent Stem Cell Model of Chronic Myeloid Leukemia Revealed Olfactomedin 4 as a Novel Therapeutic Target in Primitive Leukemia Cells. In prep

Honor & Awards

Royal Thai Government Scholarships, 2009-present

Presentations

Poster Presentations:

Modeling CML Development and Drug Resistance Using iPSC Technology. American Society of Hematology, 2011, San Diego, CA

An induced pluripotent stem cell-based platform for in vitro study of chronic myeloid leukemia stem cell development and drug resistance. International Society for Stem Cell Research, 2013, Boston, MA

Oral Presentation:

T Generation of Leukemic stem cell-like cells from iPSCs derived from Chronic Myeloid Leukemia. Campus Stem Cell Lab Meeting, Wisconsin Institute of Discovery, 2013, Madison, WI

Induced Pluripotent Stem Cell Model of Chronic Myeloid Leukemia Revealed Olfactomedin 4 as a Novel Therapeutic Target in Leukemia Stem Cells. ISEH-The Society for Hematology and Stem Cells, 2013, Vienna, Austria



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