BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Nan Yang	Assistant Professor
eRA COMMONS USER NAME (credential, e.g., agency login) YANG.NAN	

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
Sichuan University, P.R.China	B.S.	7/2003	Biology
Fudan University, P.R.China	Ph.D.	7/2010	Genetics
University of California, San Francisco	Visiting student	7/2010	Neurology and Developmental biology
Stanford University	Postdoctoral scholar	2017	Stem Cell and Neural development
Icahn School of Medicine at Mount Sinai	Assistant Professor		Stem Cell and Neural development

A. Personal Statement

Research in my laboratory is focused on the understanding of the molecular programs that control the development of distinct cell types in the brain, facilitated by the development of approaches using stem cells to advance our knowledge of the fundamental processes underlying human neural development. We are using a combination of the *in vitro* stem cell models and *in vivo* embryological studies to decipher the *cis*-regulatory elements and *trans*-factors underlying developmental plasticity, commitment and differentiation in the central nervous system (CNS). We apply our knowledge in neural development and develop transcription factor mediated approaches to program the differentiation of human pluripotent stem cells into distinct cell types in the brain, including subclasses of interneurons for the establishment of human cell models for neuropsychiatric and neurological disorders. In addition, we derive induced pluripotent stem (iPS) cells from human fibroblasts and perform gene targeting in human iPS cells. These approaches allow us to study the phenotypic consequences of disease-causing mutations in human neurons and other neural lineages as well as the development of novel therapeutic gene targeting and cell transplantation-based strategies for numerous monogenetic diseases.

B. Positions and Honors:

Employment

2010-2017 Postdoctoral fellow, Dr. Marius Wernig, Department of Pathology and Institute for Stem Cell Biology and Regenerative Medicine, Stanford University School of Medicine

2017- Assistant Professor, Department of Neuroscience, Black Family Stem Cell Institute, Icahn School of Medicine at Mount Sinai

Honors

2001 Outstanding Student Award and Scholarship for Sichuan University
2002 Prize Fellowship for Sichuan University
2004 Fudan University Scholar
2013 ISSCR 11th Annual Meeting Travel Award
2013 The Sammy Kuo Prizes in Neuroscience, Stanford University
2011-2014 The Walter V. and Idun Berry Postdoctoral Fellowship, Stanford University
2015 Siebel Scholarship, Siebel Stem Cell Institute
2015- The NARSAD Young Investigator Award

C. Contributions to Science

Direct lineage conversion. A significant focus of my early and current research involves the discovery of induced neuronal cells (iN cells). Trans-differentiation across different germ layers could be achieved when functional neurons (induced neuronal cells, iNs) are induced from human fibroblasts by exogenous expression of four transcription factors Ascl1, Brn2, Myt1l and Neurod1. Given the potential to obtain cells for transplantation-based therapy through trans-differentiation, I worked closely with Dr. Ben Barres's team to generate oligodendrocyte progenitor cells (*OPCs*) through lineage reprogramming and found that the combination of Sox10, Olig2 and Zfp536 was sufficient to induce OPC-like cells from rodent fibroblasts. These studies have demonstrated the potential for changing the fates of cells on demand for research and therapeutic purposes. Intriguingly, the transcription factors that drive changes of cell fate are inevitably those crucial for cell lineage determination during development. Thus, lineage-reprogramming studies provide a unique way to identify and study the transcriptional regulatory hierarchy for cell fate control. The series of studies sparked a lot of renewed interest in direct lineage reprogramming as it suggested that in principle any cell could be converted into any other cell lineage if just the correct combination of transcription factors or reprogramming factors were known. There are many examples of somatic lineage conversions for different cell types such as conversion of fibroblasts to liver, heart or blood cells.

Yang N, Zuchero JB, Ahlenius H, Marro S, Ng YH, Vierbuchen T, et al. *Generation of oligodendroglial cells by direct lineage conversion*. Nat. Biotechnol. 2013 May;31(5):434–9. PMCID: 3677690

Marro S, Pang ZP, **Yang N**, Tsai M-C, Qu K, Chang HY, et al. *Direct lineage conversion of terminally differentiated hepatocytes to functional neurons*. Cell Stem Cell. 2011 Oct 4;9(4):374–82. PMCID: 3218088

Pang ZP*, **Yang N***, Vierbuchen T*, Ostermeier A, Fuentes DR, Yang TQ, et al. *Induction of human neuronal cells by defined transcription factors*. Nature. 2011 Aug 11;476(7359):220–3. PMCID: 3159048 (* equal contribution)

Establishing an in vitro cellular model for studying human neural system. Encouraged by the success in transcription factor-mediated lineage conversion, I applied the "iN factors" to direct human embryonic stem (*ES*) cell differentiation and detected rapid generation of neuronal cells. This observation led to the development of a robust method to obtain excitatory neurons from human pluripotent stem cells (i.e. ES cells and induced pluripotent stem cells (iPS cells)), which is now broadly used by research groups worldwide. Recently, I found that transient expression of Ascl1 and Dlx2 could direct the differentiation of human pluripotent stem cell into GABAergic neurons. Strikingly, in contrast to previous studies that derive progenitor cells from human ES cells and mature the resulting cells into functional neuronal subtypes that develop advanced physiological properties over a period of 30 weeks, these iN cells acquired an unprecedented degree of *in vitro* synaptic maturation within 5 weeks. These studies provide the foundation for studying the transcriptional mechanisms that regulate GABAergic neuron cell fate determination and take the initial steps toward studying inhibitory synaptic transmission *in vitro*.

In addition, to further realize the potential of iPS cells in disease modeling, I have spent a lot of effort on gene targeting in human pluripotent stem cells initially with the goal to repair disease-causing mutations for purposes in regenerative medicine. We now also use gene targeting to engineer human ES/iPS cell lines to study gene function or specific disease associated mutations. We believe that genetic engineering to generate conditional alleles in human pluripotent stem cells combined with efficient induction of defined cell populations allows for comprehensive analyses of the phenotypic consequences caused by specific mutations and provides a powerful toolkit for studying gene function in human cells. We have worked on several genes by now and have two manuscripts under review on this topic.

Zhang Y, Pak C, Han Y, Ahlenius H, Zhang Z, Chanda S, et al. *Rapid single-step induction of functional neurons from human pluripotent stem cells.* Neuron. 2013 Jun 5;78(5):785–98. PMCID: 3751803

Pang ZP*, **Yang N***, Vierbuchen T*, Ostermeier A, Fuentes DR, Yang TQ, et al. *Induction of human neuronal cells by defined transcription factors*. Nature. 2011 Aug 11;476(7359):220–3. PMCID: 3159048 (* equal contribution)

Various additional publications, not listed in one of the sections above, can be found on PubMed https://www.ncbi.nlm.nih.gov/pubmed/?term=nan+yang+and+wernig%2C+or+nan+yang+and+su+guo%2C+or+nan+yang+and+daming+ren

D. Research Support

NARSAD Young Investigator Grant 01/2015-
Interrogating synaptic transmission in human neurons
The study proposes to generate human inhibitory neurons from pluripotent stem cells. Inhibitory neurons are affected in many psychiatric illnesses, including ASD. To date, studies of brain processes have relied on animal models, imaging or human postmortem tissues. This new approach will be used to explore cellular characteristics associated with neuropsychiatric disorders, and the cells generated may also be useful for screening of new medications.
Role: PI