

A legacy of enabling others

A tribute to my mentor, collaborator and
friend, Dr. Bill Skarnes

Bill builds tools that enable an entire field

- Pioneered gene trapping in mouse ES cells
- Nature, 2011: established a conditional knockout resource for genome-wide mouse gene function
- Carried the same philosophy into human iPSCs, shared reference lines, and disease modeling

nature

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Article | Published: 15 June 2011

A conditional knockout resource for the genome-wide study of mouse gene function

[William C. Skarnes](#) , [Barry Rosen](#), [Anthony P. West](#), [Manousos Koutsourakis](#), [Wendy Bushell](#), [Vivek Iyer](#), [Alejandro O. Mujica](#), [Mark Thomas](#), [Jennifer Harrow](#), [Tony Cox](#), [David Jackson](#), [Jessica Severin](#), [Patrick Biggs](#), [Jun Fu](#), [Michael Nefedov](#), [Pieter J. de Jong](#), [A. Francis Stewart](#) & [Allan Bradley](#).

[Nature](#) **474**, 337–342 (2011) | [Cite this article](#)

I first met the man behind that legacy at Sanger in 2015



Scientific Training
and Events

Our events

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Genetic Engineering of Mammalian Stem Cells

16–28 February 2015

Wellcome Genome Campus, Hinxton, UK



He looked intimidating, but the course was a lot of fun



Our paths crossed again in 2016

Science & Technology

Yale Stem Cell Center marking 10th anniversary Nov. 10-11

The Yale Stem Cell Center will celebrate its 10th anniversary Nov. 10-11 with two events illustrating its accomplishment and potential, to be held at the Mary S. Harkness Auditorium, 333 Cedar St.

Nov 7, 2016



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William Skarnes to lead cellular engineering at The Jackson Laboratory for Genomic Medicine

Article | June 6, 2016

I started my lab with Bill's KOLF2 iPSCs



We shared ideas and welcomed each other to our labs

PURDUE UNIVERSITY | MCMP SEMINARS

Bill Skarnes at Purdue

April 19, 2018 | 4:00 PM

Biallelic genome editing of human iPS cells for functional studies and disease modeling

Dr. Bill Skarnes

The Jackson Laboratory

Location: RHPH 164

Yang Yang at JAX

July 2022 | Invited research talk

The Jackson Laboratory for Genomic Medicine
Invited by Bill Skarnes



Five papers later, Bill became my closest collaborator

Received: 10 August 2020 | Revised: 22 December 2020 | Accepted: 22 December 2020
DOI: 10.1111/gbb.12725

ORIGINAL ARTICLE

Genes, Brain
and Behavior

Generation and basic characterization of a gene-trap knockout mouse model of *Scn2a* with a substantial reduction of voltage-gated sodium channel $\text{Na}_v1.2$ expression

Muriel Eaton^{1,2} | Jingliang Zhang^{1,2} | Zhixiong Ma^{1,2} | Anthony C. Park^{1,2} | Emma Lietzke^{1,2} | Chloé M. Romero^{1,2} | Yushuang Liu^{1,2} | Emily R. Coleman^{1,2} | Xiaoling Chen^{1,2} | Tiange Xiao^{1,2} | Zhefu Que^{1,2} | Shirong Lai^{1,2} | Jiaxiang Wu^{1,2} | Ji Hea Lee^{1,2} | Sophia Palant^{1,2} | Huynhvi P. Nguyen^{1,2} | Zhuo Huang³ | William C. Skarnes⁴ | Wendy A. Koss^{2,5} | Yang Yang^{1,2}

Cell Reports

CellPress
OPEN ACCESS

Report

Severe deficiency of the voltage-gated sodium channel $\text{Na}_v1.2$ elevates neuronal excitability in adult mice

Jingliang Zhang,^{1,2,10} Xiaoling Chen,^{1,2,3,10} Muriel Eaton,^{1,2} Jiaxiang Wu,^{1,2} Zhixiong Ma,^{1,2} Shirong Lai,^{1,2} Anthony Park,^{1,2} Talha S. Ahmad,^{1,2} Zhefu Que,^{1,2} Ji Hea Lee,^{1,2} Tiange Xiao,^{1,2} Yuansong Li,^{1,2} Yujia Wang,^{1,2} Maria I. Olivero-Acosta,^{1,2} James A. Schaber,⁴ Krishna Jayant,^{2,3} Chongli Yuan,⁸ Zhuo Huang,⁹ Nadia A. Lanman,^{7,8} William C. Skarnes,⁹ and Yang Yang^{1,2,11,*}

Neurobiology of Disease

Hyperexcitability and Pharmacological Responsiveness of Cortical Neurons Derived from Human iPSCs Carrying Epilepsy-Associated Sodium Channel Nav1.2-L1342P Genetic Variant

Zhefu Que,^{1,2,*} Maria I. Olivero-Acosta,^{1,2,*} Jingliang Zhang,^{1,2} Muriel Eaton,^{1,2} Anke M. Tukker,^{2,3} Xiaoling Chen,^{1,2} Jiaxiang Wu,^{1,2} Junkai Xie,² Tiange Xiao,^{1,2} Kyle Wettschurack,^{1,2} Layan Yunis,^{1,2} J. Marshall Shafer,^{1,2} James A. Schaber,⁴ Jean-Christophe Rochet,^{1,2} Aaron B. Bowman,^{2,3} Chongli Yuan,⁸ Zhuo Huang,⁶ Chang-Deng Hu,^{1,7} Darci J. Trader,¹ William C. Skarnes,⁸ and Yang Yang^{1,2}

Neurobiology of Disease

Human IPSC-Derived Microglia Sense and Dampen Hyperexcitability of Cortical Neurons Carrying the Epilepsy-Associated SCN2A-L1342P Mutation

Zhefu Que,^{1,2,*} Maria I. Olivero-Acosta,^{1,2,*} Morgan Robinson,^{1,2,3} Ian Chen,^{1,2} Jingliang Zhang,^{1,2} Kyle Wettschurack,^{1,2} Jiaxiang Wu,^{1,2} Tiange Xiao,^{1,2} Conrad Max Otterbacher,^{1,2} Vinayak Shankar,^{1,2} Hope Harlow,^{1,2} Seoyong Hong,^{1,2} Benjamin Zirkle,^{1,2} Muhan Wang,^{1,2} Ningren Cui,^{1,2} Purba Mandal,^{1,2} Xiaoling Chen,^{1,2} Brody Deming,^{1,2} Manasi Halurkar,^{1,2} Yuanrui Zhao,^{1,2} Jean-Christophe Rochet,^{1,2} Ranjie Xu,⁴ Amy L. Brewster,⁵ Long-jun Wu,⁶ Chongli Yuan,³ William C. Skarnes,⁷ and Yang Yang^{1,2}

SCIENCE ADVANCES | RESEARCH ARTICLE

NEUROSCIENCE

Human microglia in brain assembloids display region-specific diversity and respond to hyperexcitable neurons carrying *SCN2A* mutation

Jiaxiang Wu^{1,2,†}, Xiaoling Chen^{1,2,†}, Jingliang Zhang^{1,2,†}, Kyle Wettschurack^{1,2,†}, Morgan Robinson^{1,2,3}, Weihao Li⁴, Yuanrui Zhao^{1,2}, Ye-Eun Yoo^{1,2}, Brody A. Deming^{1,2}, Yue Shu^{1,2}, Akila D. Abeyaratna^{1,2}, Zhefu Que^{1,2}, Dongshu Du⁵, Matthew Tegtmeyer^{2,6}, Chongli Yuan³, William C. Skarnes⁷, Zhong-Yin Zhang¹, Jean-Christophe Rochet^{1,2}, Long-Jun Wu⁸, Yang Yang^{1,2,*}

Yes, this really hangs on our lab wall



*From molecular biology to mouse genetics or human iPSCs,
if you have questions, Bill has answers.*

Outside the lab, collaboration became friendship



Then we took the collaboration off-road

Wahweap Hoodoos

hike





OFF THE BEATEN PATH: yes

BEST SEASON: Spring fall

VEHICLE: hike only

DURATION: 9 miles round trip

AVERAGE TIME: full day

DIFFICULTY: easy to hard depending on weather

ELEVATION: 4042 feet

GETTING THERE:

- From Kanab, take HWY 89 east, approximately 55 miles to Big Water.
- Turn left on the Ethan Allen Road, between mile 7 and 6, across the highway from the Grand Staircase-Escalante Visitor Center.
- Follow Ethan Allen past several streets to a "T" in the road. Turn left at the "T" and bypass the old softball field on the left side of the gravel road. Follow this road past two fish hatcheries.
- Continue north past the corral which is 3 miles from HWY 89. 2-wheel drive vehicles, park on the right side of the road just before the creek.
- Start your hike here by hiking up Wahweap Creek.
- High clearance 4-wheel drive vehicles can continue past the corral, crossing Wahweap Creek, and then continue .3 miles. The trail begins in Wahweap Creek just below the 4WD parking.
- Hike north up Wahweap Creek.

DISCLAIMER:

"This map and directions are intended for general reference use only. Always check local road and weather conditions. Stay on designated roads. Dirt roads are impassable when wet. Please respect Private Property. Be prepared for a wilderness experience. Always bring extra water, food, sunscreen, and supplies. Cell phone service is non-existent." **BASE CAMP** in most areas! Do not remove artifacts or deface the 'rock art'. Leave no trace of your visit so others may enjoy."

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KANAB



We had an amazing adventure



At one point, I knew I had to keep going on my own



During our trip, we spotted the goats



But I realized I had been traveling with the *GOAT* all along
Greatest Of All Time



Thank you, Bill, for a remarkable journey together

