BIOGRAPHICAL SKETCH

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NAME: Bergmann, Dominique

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POSITION TITLE: Investigator

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)	END DATE MM/YYYY	FIELD OF STUDY
Carnegie Institution for Science, Plant Biology, Washington, DC	postdoc	2004	Plant Biology
University of Colorado Boulder, Molecular, Cellular and Developmental Biology, Boulder, CO	PhD	2000	Molecular, Cellular and Developmental Biology
University of California Berkeley, MCB, Berkeley, CA	B.A.	1993	MCB

A. Personal Statement

The overall goal of my research program is to understand how stem cell-like populations are created and maintained in the context of an intact and environmental responsive tissue. We use the Arabidopsis stomatal lineage for these studies as this epidermal cell lineage distills many of the features common to all tissue development: stomatal precursor cells are chosen from an initially equivalent field, they undergo asymmetric and self-renewing divisions, they communicate among themselves to establish pattern and they terminally differentiate into stable, physiologically important cell types. My training in cell and developmental biology of both plants and animals has allowed me to identify questions of broad interest that are best answered in a plant system. As a postdoctoral fellow I pioneered the use of transcriptional profiling to identify stomatal regulators and established roles for MAPK signaling in stomatal development. My group at Stanford identified the first gene absolutely required for stomatal development and three ‘master regulator” basic helix-loop-helix (bHLH) transcription factors that sequentially control stomatal development and connect this process to the molecules and logic that regulate muscle and neural development. In the past 20 years, we have developed the stomatal lineage into a conceptual and technical framework for the study of cell fate, stem-cell self-renewal, and cell polarity.

We developed ChIP-seq, RNA-seq, and BioID protocols on rare and transiently expressed transcription factors, which enabled us to uncover the broad influence of transcription factors on stomatal initiation, progression, and differentiation. Several iterations of transcriptional profiling of individual stomatal lineage cell types, and later individual cells, allowed us to determine how cells are reprogrammed upon entry into the stomatal lineage and identify the changes in gene expression as they transit out of this stage and into committed precursors and finally, terminally differentiated fates. As a complement to these genome-scale studies, detailed analysis of the interaction between the Arabidopsis Retinoblastoma homologue, RBR, and the stomatal differentiation bHLH, FAMA, revealed how RBR is recruited to promoters of early stomatal lineage genes to repress their expression. A feature of plant development—that cells are locked in place—allowed us to visualize how lack of RBR leads to reprogramming of terminally differentiated cells in vivo. To capture gene expression dynamics during this reprogramming, as well as during normal development, we designed and fabricated custom time-lapse chambers and imaging protocols to enable us to follow epidermal development at high spatial resolution in intact plants.

Since 2005, I have been the PI on NIH, NSF, DOE, and university-funded research, and since 2011, I

have been an investigator of the Howard Hughes Medical Institute (HHMI). Through these projects, my lab has grown in several directions and I have established collaborative interactions with ecophysiologists, computational biologists and imaging experts to allow us to approach biological questions from an integrative standpoint. The collaborations are also essential for interdisciplinary training of students and postdocs. I have a strong commitment to mentoring junior scientists, having trained >30 postdocs and 20 PhD students. I endeavor to create a supportive and inclusive research environment; more than half of my group are women, and among PhD students, 5 are members of groups historically excluded from science. I have learned to be aware of my biases through culturally appropriate mentor training, and also try to actively encourage young scientists through participation in programs to demystify the path to and through graduate education. In addition to individual and group discussion of experimental results and interpretations, each member of the group is mentored about identifying critical questions, career opportunities and project management through 1-on-1 biweekly research progress and yearly IDP meetings, as well as weekly meetings with our lab group, and biweekly meetings with a campus-wide community of plant and cell biologists. In our discussions I stress the importance of scientific rigor, accuracy, documentation, and honesty, and model the practice of these behaviors in my roles as a journal editor and conference organizer. I also teach in our University's graduate course on scientific rigor. I encourage trainees to consider their work in the context of a diverse society and how we might best be inclusive within our group. We work to make our science accessible to the public, in particular to people often excluded from seeing scientific information and practice. Lab alumni are involved in many aspects of science, and I am supportive of their journeys to many destinations: some in academic positions (U. Michigan, TAMU, NUS Singapore, Academica Sinica, NIAB, U. Bern, U. Louvain, U. Buenos Aires, UC Berkeley, UCSD), others in biomedical or plant biotech, in data science, or in policy (AAAS and CST fellows now working in international or metropolitan policy groups).

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2011 -	Investigator, Howard Hughes Medical Institute - Stanford University, Stanford, CA
2005 -	Professor, Stanford University, Biology, Stanford, CA

Honors

2010 - 2015	Presidential Early Career Award in Science and Engineering , NIH (NIGMS)
2009 - 2014	CAREER Award, NSF
2024	Member (International Associate), EMBO
2020	Shirley R. and Leonard W. Ely Professor of Humanities and Sciences (endowed chair), Stanford University
2017	Member, National Academy of Sciences
2010	Charles Albert Shull Award , American Society for Plant Biology

C. Contribution to Science

1. When I began my laboratory in 2005, I sought to identify the genes responsible for the remarkable suite of cell behaviors in the stomatal lineage. At the time, a small number of negative regulators, primarily signaling elements, had been identified. Not a single gene required to make stomata, however, was known. Using genetic screens in sensitized backgrounds and whole-genome transcriptional profiling, my lab found these missing regulators. We showed that a trio of closely related bHLH transcription factors, SPEECHLESS (SPCH), MUTE, and FAMA, act as master controllers of the asymmetric divisions that generate stomatal lineage stem-cells, the self-renewing divisions that amplify the lineage and the differentiation of stomata, respectively, and each is expressed in a domain correlated with its function. SPCH is in self-renewing meristemoids and MUTE is in committed GMCs, with an intriguing overlap during transitions. Recently, we investigated in a genome-wide scale how SPCH initiates the stomatal lineage and participates in cross-regulation with

hormone and environmental signals, modeled how distinct SPCH, MUTE and FAMA functions evolved over time, and exploited a physical link between FAMA and the retinoblastoma homolog RBR to reveal how terminal differentiation is maintained. Understanding how bHLHs act in diverse tissues and in diverse organisms with a variety of interesting co-factors is a prelude to understanding the core set of events that proteins in this family are well suited to control and may further illuminate common organizational and regulatory principles underlying all of development.

a. Davies K, Bergmann D. Functional specialization of stomatal bHLHs through modification of DNA-binding and phosphoregulation potential. Proceedings of the National Academy of Sciences. 2014 October 10; 111(43):15585-15590. Available from: https://pnas.org/doi/full/10.1073/pnas.1411766111 DOI: 10.1073/pnas.1411766111
b. Lau On Sun, Davies Kelli A, Chang Jessica, Adrian Jessika, Rowe Matthew H, Ballenger Catherine E, Bergmann Dominique C. Direct roles of SPEECHLESS in the specification of stomatal self-renewing cells. Science. 2014; 345(6204):1605--1609.
c. MacAlister CA, Ohashi-Ito K, Bergmann DC. Transcription factor control of asymmetric cell divisions that establish the stomatal lineage. Nature. 2007 Feb 1;445(7127):537-40. PubMed PMID: 17183265.
d. Matos J, Lau O, Hachez C, Cruz-Ramírez A, Scheres B, Bergmann D. Irreversible fate commitment in the Arabidopsis stomatal lineage requires a FAMA and RETINOBLASTOMA-RELATED module. eLife. 2014 October 10; 3:-. Available from: https://elifesciences.org/articles/03271 DOI: 10.7554/eLife.03271

2. The stomatal bHLHs are important individual regulators of cell and tissue behavior, but we also wish to understand the whole genome transcriptional, translational, and epigenetic changes that take place as cells transit through phases of acquiring, maintaining, and leaving self-renewing fates. We generated a “developmental map” by isolating RNA from fluorescence-activated cell sorted populations representing individual and overlapping stomatal lineage cell types. This was followed by true single-cell atlases. Computational analysis of transcriptional patterns of the stomatal lineage in comparison to other developing tissues revealed a number of conserved processes, each of which was associated with different members of large gene families. Hypotheses about specific genes or regulatory relationships generated by our models and large datasets are being tested using cell-type specific genetic manipulation systems. For example, we used these datasets to identify a role for the hormone cytokinin in stomatal development and identified signaling components used to provide cell-type-specific outcomes to broad inputs. As more cell-type-specific RNA-seq datasets are generated (by us and the community), an investment in computational resources to define cell-type signatures, especially amidst noisy gene expression, will be invaluable.

a. Liu A, Mair A, Matos J, Vollbrecht M, Xu S, Bergmann D. bHLH transcription factors cooperate with chromatin remodelers to regulate cell fate decisions during Arabidopsis stomatal development. PLOS Biology. 2024; 22(8):e3002770-. Available from: https://dx.plos.org/10.1371/journal.pbio.3002770 DOI: 10.1371/journal.pbio.3002770
b. Gong Y, Dale R, Fung H, Amador G, Smit M, Bergmann D. A cell size threshold triggers commitment to stomatal fate in *Arabidopsis*. Science Advances. 2023 September 22; 9(38):-. Available from: https://www.science.org/doi/10.1126/sciadv.adf3497 DOI: 10.1126/sciadv.adf3497
c. Lopez-Anido CB, Vatén A, Smoot NK, Sharma N, Guo V, Gong Y, Anleu Gil MX, Weimer AK, Bergmann DC. Single-cell resolution of lineage trajectories in the Arabidopsis stomatal lineage and developing leaf. Dev Cell. 2021 Apr 5;56(7):1043-1055.e4. PubMed Central PMCID: PMC8054824.
d. Adrian J, Chang J, Ballenger CE, Bargmann BO, Alassimone J, Davies KA, Lau OS, Matos JL, Hachez C, Lanctot A, Vatén A, Birnbaum KD, Bergmann DC. Transcriptome dynamics of the stomatal lineage: birth, amplification, and termination of a self-renewing population. Dev Cell. 2015 Apr 6;33(1):107-18. PubMed Central PMCID: PMC4390738.

3. Polarity is a phenotype of mature cells and of the asymmetric cell divisions leading to their creation. Defects in polarity lead can to failure in self-renewal, or conversely, to cancerous overgrowth in human cells. All organisms must generate polarities in connection with stem cell-like divisions, and at the level of transcriptional regulation, there are common behaviors. However, we know virtually nothing about how plant cells divide in a physically asymmetric manner. Structural constraints imposed by plant cell walls combined with the absence of recognizable homologues of animal or fungal cell polarity genes require plants to utilize new molecules and mechanisms to create cellular asymmetries. Our identification of BASL, a gene required for physical and fate asymmetries, was the first glimpse of an elusive plant polarity module. BASL protein is polarly localized and inherited unequally by the daughters of an asymmetric division. Genetic and physical interaction screens as well as transcriptional profiles of asymmetrically dividing cells have yielded additional proteins required for the orientation of division and distribution of materials during asymmetric cell divisions. Interestingly, all of these proteins are novel, plant specific, and lack domains of predicted function. While these attributes make their biochemical activity difficult to discern, genetic, transgenic, and imaging resources make it possible to establish functional relationships among the different polarity factors. One exciting use of these “unknown” proteins is as test cases for theoretical models of cell polarity. By testing the behaviors of the plant proteins, we have been able to show that despite different molecular details, many regulatory relationships are conserved across multicellular organisms.

    a. Bringmann M, Bergmann D. Tissue-wide Mechanical Forces Influence the Polarity of Stomatal Stem Cells in Arabidopsis. Current Biology. 2017 March; 27(6):877-883. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0960982217300945 DOI: 10.1016/j.cub.2017.01.059
    b. Dong J, MacAlister C, Bergmann D. BASL Controls Asymmetric Cell Division in Arabidopsis. Cell. 2009 June; 137(7):1320-1330. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0092867409004437 DOI: 10.1016/j.cell.2009.04.018
    c. Muroyama A, Gong Y, Hartman K, Bergmann D. Cortical polarity ensures its own asymmetric inheritance in the stomatal lineage to pattern the leaf surface. Science. 2023 July 07; 381(6653):54-59. Available from: https://www.science.org/doi/10.1126/science.add6162 DOI: 10.1126/science.add6162
    d. Wallner ES, Dolan L, Bergmann DC. Arabidopsis stomatal lineage cells establish bipolarity and segregate differential signaling capacity to regulate stem cell potential. Dev Cell. 2023 Sep 25;58(18):1643-1656.e5. PubMed PMID: 37607546.

4. Stomata provide a framework to study the fundamental processes of plants at different organizational levels, from molecules and cells to whole plants and ecosystems. In collaboration with ecophysiologists we have used tools derived from our molecular-scale studies to improve organismal-scale models for photosynthetic activity and provide the first experimental evidence that evolutionarily conserved stomatal patterns are essential for efficient photosynthesis. Such collaborations confirm the utility of Arabidopsis as a model for important plant processes, but it is equally important to acquire detailed mechanistic information about plants with different stomatal development and physiology. We identified conserved gene function broadly among plants. We have made inroads into Solanum species (like tomato, potato, peppers) and the grasses because they are major sources of human nutrition. In particular grasses feature unique improvements to stomatal development and biomechanics. Using a relative of wheat, Brachypodium, our lab has created tools for effective genetics, functional genomics, and live-cell imaging to uncover the key regulators of stomata in these group of plants so vital for human nutrition.

    a. Dow Graham J, Berry Joseph A, Bergmann Dominique C. The physiological importance of developmental mechanisms that enforce proper stomatal spacing in A rabidopsis thaliana. New Phytologist. 2014; 201(4):1205--1217.
    b. Nir I, Budrys A, Smoot NK, Erberich J, Bergmann DC. Targeting editing of tomato SPEECHLESS cis-regulatory regions generates plants with altered stomatal density in response to changing

climate conditions. bioRxiv. 2023 Nov 2; PubMed Central PMCID: PMC10635072.

c. Raissig MT, Abrash E, Bettadapur A, Vogel JP, Bergmann DC. Grasses use an alternatively wired bHLH transcription factor network to establish stomatal identity. Proc Natl Acad Sci U S A. 2016 Jul 19;113(29):8326-31. PubMed Central PMCID: PMC4961163.

d. Raissig MT, Matos JL, Anleu Gil MX, Kornfeld A, Bettadapur A, Abrash E, Allison HR, Badgley G, Vogel JP, Berry JA, Bergmann DC. Mobile MUTE specifies subsidiary cells to build physiologically improved grass stomata. Science. 2017 Mar 17;355(6330):1215-1218. PubMed PMID: 28302860.

5. Stomata and their self-renewing precursors are present in a well-patterned tissue and this tissue is responsive to environmental inputs. We have uncovered signaling components required for cells within this lineage to communicate among themselves and shown how broadly expressed kinases gain specificity by targeting cell-type restricted targets. Plants, like animals, produce a large number of secreted peptide ligands, many of which could engage common receptors. There must, therefore, be mechanisms to prevent inappropriate cross-talk. The stomatal lineage has become an excellent model for deciphering signaling specificity. We have contributed to this field by structure/function analysis of MAPK signaling, identifying peptide signals, and providing conceptual models for how spatially restricted co-receptors discriminate between signals appropriate for the stomatal lineage and those for internal tissues.

   a. Abrash Emily B, Davies Kelli A, Bergmann Dominique C. Generation of signaling specificity in Arabidopsis by spatially restricted buffering of ligand--receptor interactions. The Plant Cell. 2011; 23(8):2864--2879.

   b. Bergmann DC, Lukowitz W, Somerville CR. Stomatal development and pattern controlled by a MAPKK kinase. Science. 2004 Jun 4;304(5676):1494-7. PubMed PMID: 15178800.

   c. Lampard GR, Macalister CA, Bergmann DC. Arabidopsis stomatal initiation is controlled by MAPK-mediated regulation of the bHLH SPEECHLESS. Science. 2008 Nov 14;322(5904):1113-6. PubMed PMID: 19008449.

   d. Wengier Diego L, Lampard Gregory R, Bergmann Dominique C. Dissection of MAPK signaling specificity through protein engineering in a developmental context. BMC plant biology. 2018; 18(1):60.