Sanford Burnham Prebys
MEDICAL DISCOVERY INSTITUTE

Sanford Consortium FOR REGENERATIVE MEDICINE

EVAN Y. SNYDER, M.D., PH.D., F.A.A.P.
Professor
Human Genetics Program; Aging, Immunity, & Tumor Microenvironment Program
Director, Center for Stem Cells & Regenerative Medicine
Director, Stem Cell Research Center & Core Facility
Co-Director, Stem Cell Training Program
Director, Richmond Family Laboratory for Research into Pediatric Brain Disorders
Physician, Sanford Children's Health Research Center
Sanford Burnham Prebys (SBP) Medical Discovery Institute
Faculty, Biomedical Sciences Graduate Program, *University of California, San Diego*
Scientific Steering Committee, *Sanford Consortium for Regenerative Medicine*

Office Phone: 858-646-3158; Mobile Phone: 617-686-5361
Fax: 858-246-1575; E-mail: esnyder@sbp.edu

Executive Administrator & Center Coordinator: Sinead King
Phone: 858-795-5006; E-mail: sking@sbp.edu

Re Application: INFR6.2-15372
(from Sanford Burnham Prebys Medical Discovery Institute [SBP]):
"*A Shared Resource Laboratory for Stem Cell High-Throughput Biology & Comprehensive Techniques Training*"

January 23, 2024

Dear Members of the CIRM Application Review Subcommittee of the ICOC and CIRM Program Directors,

This letter will *NOT* be a point-by-point rebuttal of the critiques of the Grants Working Group (GWG) for the above-cited application, or a plea for immediate funding. We did not score well, we believe, not because we do not have depth of talent, skill, personnel, resources, extensive experience, and a long track record of productivity and impact for accomplishing the innovative, cutting-edge program we proposed, but rather because we did a poor job in *demonstrating* that we *have* accomplished, and *continue* to accomplish, all that we put forward (e.g., **material appended to this letter**). Basically, we were criticized for being overly ambitious, that our aspirations were not feasible. We proposed to be the first academic CIRM Shared Resource Lab [SRL]) to bring cutting-edge ***high-throughput (HT) biology/drug discovery*** to California investigators and clinicians through the use of patient-derived hiPSCs (at academic prices), while also continuing our long-standing mission to reach out to, engage, and mentor less experienced stem cell investigators – in this case, to help them enter the drug discovery pipeline (which will likely define the goals of disease modeling for the next generation). HOWEVER, although we were essentially told that our "reach exceeded our grasp", *this program is precisely what we are already doing*, albeit without the valued support and structure that only CIRM can provide. (Our Stem Cell Core and HT facility are self-sustaining, but CIRM's imprimatur and statewide network means much more than that). Also, I fear we errantly viewed this RFA as a continuation of what we have done for the past 17 years, under the aegis of CIRM's first round of SRL funding, which cast a different net in a different era.

All we please request is simply an opportunity to expeditiously resubmit and be re-judged on a revised proposal (as was offered some applicants) which **(a)** addresses the concerns/questions voiced by the referees (all readily addressable); **(b)** clarifies points that were unclear; **(c)** constrains our scope and aspirations; and **(d)** better highlights what we actually do accomplish every day at SBP (e.g., please see the representative **Tables** & **Figures** appended to this letter which, because of space limitations, unfortunately did not make it into our original application); it is *not* true that there is, to quote a reviewer, "[a lack of] availability of necessary expertise"). We suspect that our request simply entails the ICOC designating us as *"Tier 2, Revision allowed"*. We *please* ask for this opportunity to revise and resubmit what we know will be a competitive application. We believe California and the field – and the many early-stage scientists we will train -- will benefit from according us this chance. Continuing our SRL's 2-decade mission is a passion of SBP.

To be a bit more granular, the **Tables** & **Figures** appended to this letter, which will be better fleshed out in a revised application, include: **(a)** Evidence of a long track-record of service to academic and non-profit researchers by generating hiPSCs at academic prices that typically contribute to high-tier publications **[Table 1]**; **(b)** A history of providing HT technology and drug discovery services to intramural and extramural academic as well as industry users **[Table 2]**; **(c)** A track record of generating and publishing (in peer-reviewed journals) novel protocols (and patents) **[Table 3]**; **(d)** a legacy of having trained scores of students in the fundamentals of stem cell biology, giving rise to a textbook/manual **[Fig. 1]** and widely disseminated protocols **[Fig. 2]** (both of which help guide the curriculum and syllabus of our proposed course). Since 2003, SBP has provided cutting-edge stem cell services (e.g., hESCs; defined media; cryopreservation; differentiation regimes for a range of lineages, including heart, vasculature, nervous system, cartilage, skin, lung; hiPSC-generation); and even an embryo bank.

The novel and impactful areas that SBP's SRL will offer fall into 3 broad categories:

1. **High Throughput (HT) Biology & Drug Discovery [Fig. 3]**

SBP, by virtue of its *Conrad Prebys Center for Chemical Genomics (CPCCG),* has long-standing strength and prominence in these fields (particularly when combined with stem cell biology). CPCCG ranks among the premier (some would say the most successful), HT/Drug Discovery entities in academia, *and the only one to show a commitment to being a CIRM SRL*. CPCCG is not only in the center of SBP's campus, but also at the heart of its mission (contrary to some critiques), and its influence extends throughout the Torrey Pines Mesa (which includes not only numerous academic institutions but a robust biotech/big pharma cluster). It is our desire to disseminate this cutting-edge technology widely throughout the State and make it broadly accessible to the stem cell community (including not only enabling users to use and learn such techniques, but also to incorporate the rigor, thought processes, and potential of HT biology into designing experiments and acquiring, managing, and interpreting the unique and powerful datasets that can be generated. We possess all the cutting-edge equipment and expertise to enable users and trainees to become positioned at the forefront of chemical and genetic screening, HT drug discovery, high-content imaging, assay development, functional analysis, pharmacology & medicinal chemistry (as further detailed on the CPCCG website: *https://sbpdiscovery.org/biomedical-research/centers/prebys-center/research-technology)*. Importantly, while CPCCG can provide service-for-a-fee to stem cell users, we also created a separate aligned structure focused on providing training in handling HT equipment and developing stem cell-based assays – expertise critical to HT Biology. It is also a space where adequately trained users may perform their own experiments, employing HT technologies to phenotype hiPSC-derived cardiac and neural lineages and perform focused screening of small molecule, siRNA, and arrayed CRISPR using multiple modalities, including high content imaging and multi-electrode arrays (MEA).

SBP's SRL will leverage the considerable infrastructure at CPCCG to access compounds, and for spotting compounds/siRNAs and CRISPR guides into plates. Furthermore, the results and assays generated through the SRL (e.g., targets and/or phenotypes identified through HT Biology experiments) will naturally synergize with CPCCG's or other drug discovery enterprises (e.g., medicinal chemistry through hit-to-lead and lead optimization, pre-clinical development, etc.), possibly constituting the first step in the development of a new drug discovery program at SBP or at the user's home Institute.

The integration of HT technologies with stem cells as reagents, models, and targets should catalyze the development of pertinent stem-cell based assays, the generation of extensive datasets from functional genomic and chemical screens, the discovery of novel drug targets, and the potential identification of approved drugs for repurposing.

Facilitating implementation of early drug discovery programs has the possibility of enabling California stem cell biologists to feed into pipelines of drug screening facilities or partnering with pharma, hence promoting intellectual property creation, and, more generally, stimulating innovation in the State.

2. Enabling clinicians with their clinical material, as well as less experienced stem cell biologists, to enter the HT biology/drug discovery pipeline [Fig. 3]

Although we will be offering services and training in HT Biology, we do not want to abandon our long-standing commitment to ensuring that a next generation of investigators can enter the pipeline (including at the beginning) to avail themselves, and even master, these cutting-edge offerings. As **Fig. 3** shows, users may enter the HT workflow at 3 points depending on their needs, goals, prior skills, and quality of materials. Sophisticated users may enter the pipeline with projects and samples that will immediately benefit from our ability to deeply phenotype hiPSC-derived cardiac and neural cells and/or perform focused screening. Less experienced users, or investigators/clinicians with patient samples but no stem cell resources and/or expertise, may enter the pipeline at the beginning where hiPSCs would be generated from somatic cells by the SRL [as per **Table 1**], differentiated into neural or cardiac cells, and then transitioned onto the *deep phenotyping* & *HT functions* of the SRL in consultation with SRL leaders. SBP, like most Mesa Institutes, has a close relationship with UCSD's health care system (as well as Scripps, Sharp, and Kaiser), enabling clinicians' ready access to its SRL.

3. Teaching "the basics" (including for enabling disease modeling) with a commitment to DEI [Fig. 1]

Not only our *Core Offerings*, but also our *Techniques Course* is directed to engaging the spectrum of stem cell investigators – from the novice who needs a *Basic Hands-On Techniques Course* to the sophisticated user who wishes to gain familiarity with cutting-edge HT Biology.

SBP has a long track record of extensive engagement in educational activities and outreach. In the early days of the stem cell field, it was designated one of the first 6 *NIH Exploratory Human Stem Cell Research Centers* in the country (5P20GM75059) and one of the first 5 *NIH hESC training courses*. It was among the first CIRM-funded SRLs (CL1-00511). From those courses and cores emerged the textbook, *Human Stem Cell Manual* (Loring & Peterson, Academic Press) **[Fig. 1]**. Dr. Suzanne Peterson, assisted by Dr. Jeanne Loring, both of whom have led many stem cell techniques courses in addition to editing this textbook (which will serve as the curriculum guide), will be course directors for our *Basic Techniques Course*. Our second course offering for more advanced users, *Introduction to HT Techniques*, (led by CPCCG and SBP faculty) was described above.

The SBP's SRL has always engaged extensively in outreach for its educational activities, for example, to regional colleges (which often serve under-represented communities) where stem cell facilities may not be as well-developed. We intend to use as much of our grant funds as possible (and certainly whenever revenue exceeds costs) for *Travel Awards* to draw in students from throughout California. SBP has a demonstrable commitment to DEI. SBP's SRL and its Techniques course will continue to be critical components in the education of the CIRM trainees SBP hosts at all levels of experience – BRIDGEs interns; EDUC4 grad students, post-docs, & clinical fellows; SPARK high-school students; and COMPASS undergrads. (SBP is the only San Diego institution with participation in all 4 of CIRM's training programs). Alumni of these programs may also serve as teaching assistants ("learning to mentor") and help in some Core offerings. These CIRM programs are designed to help benefit underserved and under-represented communities. After completion of the courses, enrollees will become members of *SBP's Stem Cell Alumni group* with access to an online discussion group and annual symposium that will connect classmates with instructors and with each other to address questions, share knowledge, follow-up on experiments, foster collaborations. In addition to CIRM programs, SBP will be serving as host for an NIH-funded course designed to engage students from communities under-represented in science and medicine.

In summary, our unique proposal brings HT equipment handling expertise together with human stem cell-based disease modeling expertise (e.g., application of HT biology technologies to hiPSC-based disease models, use of high content imaging assays to identify novel mechanism-of-action hits to inform druggable targets in a pathway and begin a drug discovery cascade, etc.) to create a new capacity for accelerating the pace of stem-cell based research focused on understanding disease-causing mechanisms and discovering the pharmacotherapeutics/molecules to thwart them. Our **goal** is making the interface between stem cell biology and HT biology a capability for all California investigators, not only to generate data that can be used in users' papers and grants, but also to bring that expertise back to their home institutions.

Given our long-standing experience with combining HT and stem cell-based disease modeling, we believe we are ideally and uniquely positioned to disseminate this expertise to the California stem cell community – much needed, but presently not available.

All we ask, please, is a chance to revise our proposal and better demonstrate our ability to serve that California stem cell community.

Thanks for your consideration.

Sincerely,

Evan Y. Snyder, M.D., Ph.D., F.A.A.P
Professor
Director, Center for Stem Cells and Regenerative Medicine

TABLE 1: PARTIAL LIST OF hiPSCS GENERATED BY THE SBP SCRC FOR REPRESENTATIVE USERS				
PI or Company	**# of Patient Samples**	**Sample Type**	**Disease Type**	**Ref.** (Where used)
Joseph Gleeson/UCSD	113	Skin FBs	Autism, epilepsy, CNS malformation	17
Alysson Muotri/UCSD	14	Skin FBs	Autism, Rett Syndrome; Schizophrenia	
Gene Yeo/UCSD	13	Skin FBs	ALS, Autism	
Kelly Frazer/Larry Goldstein/UCSD	6	Skin FBs	Parkinson; Alzheimer's, ALS	
Kang Zhang/UCSD	6	Skin/Eye FBs	Retinal diseases	
Gabriel Sternik/Salk	4	Skin FBs	Wilson's Disease	
Evan Snyder/SBP	4	Skin FBs/MSC	Bipolar Disorder; Krabbe disease	10,20-1,3
AJ Wilkinson/Salk	2	Skin FBs	Aging-related	
Biotime, Inc (Mountainview)	3	Skin FBs	Normal	21-4
Johnson & Johnson/Jansen	12	Lymphocytes	Bipolar Disorder	
Neural Stem Cell Institute (NY)	12	Skin FBs	Parkinson's Disease	
Brian Tobe/SBP	12	Lymphocyte	Bipolar Disorder	20,24-3,5
Hudson Freeze/SBP	8	Skin FBs	Congenital Disorders of Glycosylation	40-11
Radha Ayyagari/UCSD	8	Lymphocyte	Retinal diseases	
Jeff Neul/UCSD & Vanderbilt	2	Skin FBs	Rett Syndrome	
Lori Broderick/UCSD	2	Skin FBs	Hoffman syndrome	41-12
Michael Kruer (Sanford Health, ND)	6	PBMCs	Parkinson's Disease (PD)	
ReproCell (Company)	4	PBMCs	Confidential/proprietary	
Vertex (Company)	6	Skin FBs	Confidential/proprietary	
Martin Friedlander/Scripps	10	PBMCs	Eye Disease: Macular Degeneration	
Tariq Rana/SBMPI/UCSD	6	Skin FBs	Normal Donors	42-13
Paul Grossfeld/UCSD	2	Skin FBs	Cardiac Hypertrophy	
Jonathan Sebat/UCSD	2	Skin FBs	Psychiatric disorders	
Michel Ibrahim (Minia University)	2	Skin FBs	Normal	37,38-8.9
Al La Spada/UCSD/Duke	3	Lymphocytes	PD (LRRK2+LRRK2 KO; PARK1)	
Yanjun Kong (University of Shanghai)	4	Tumor cells	Thyroid cancer	25-6
Richard Song (UCSD, Dept. of Peds)	3	Umbilical cord	Normal	33-7
Vincent Chen (SBP)	3	Skin Fb	Cardiac arrhythmia	46-14

1. Katkov II, et al, DMSO-Free Programmed Cryopreservation of Fully Dissociated and Adherent Human Induced Pluripotent Stem Cells. Stem Cells Int. 2011;2011:981606.
2. Novarino G, et al, Mutations in BCKD-kinase lead to a potentially treatable form of autism with epilepsy, *Science* 338(6105):394-7 (2012) doi: 10.1126/science.1224631.
3. Tobe BTD, et al, Challenges of modeling complex neuropsychiatric disorders with human induced pluripotent stem cells (hiPSCs): From "disease-in-a-dish" to personalized drug discovery, Curr Opinion Pharmacol 11(5) 429-572 (2012).
4. Vaziri H, et al, , Spontaneous reversal of the developmental aging of normal human cells following transcriptional reprogramming, Regenerative Medicine doi:10.2217/rme.10.21 (2010).
5. Tobe BTD–[52 authors of an international team]–Snyder EY, Probing the lithium-response pathway in hiPSCs implicates the phosphoregulatory set-point for a cytoskeletal modulator in bipolar pathogenesis, PNAS 114:E4462-E4471 (2017).
6. Kong Y, Gimple RC, McVicar RN, Hodges AP, Yin J, Liu Y, Zhan W, Snyder EY. "Reprogram Enablement" as an assay for identifying early oncogenic pathways by their ability to allow neoplastic cells to reacquire an epiblast state. Stem Cell Reports. 2020 Sep 8;15(3):761-775. doi: 10.1016/j.stemcr.2020.07.016.
7. Song RS, Carroll JM, Acevedo L, Wu D, Liu Y, **Snyder EY,** Generation, expansion, & differentiation of human induced pluripotent stem cells (hiPSCs) derived from the umbilical cords of newborns, *Current Protocols in Stem Cell Biol* 2014 May 16;29:1C.16.1-1C.16.13. doi: 10.1002/9780470151808.sc01c16s29.
8. Lindquist JN, Cheresh DA, Snyder EY, Derivation of vasculature from embryonic stem cells, *Curr Protocols Stem Cell Biol* Mar; Chapter 1: Unit 1F.9 (2010).
9. Ibrahim MR, et al. Deriving keratinocyte progenitor cells and keratinocytes from human-induced pluripotent stem cells. *Curr Protoc Stem Cell Biol.* 2020;54(1):e119.
10. Ibrahim MR, Medhat W, El-Fakahany H, Abdel-Raouf H, Snyder EY, The developmental & molecular requirements for ensuring that human pluripotent stem cell-derived hair follicle bulge stem cells have acquired competence for hair follicle generation following transplantation, *Cell Transplantation* (2021) doi.org/10.1177/09636897211014820.
11. Ng B, et al, A mutation in SLC37A4 causes a dominantly inherited congenital disorder of glycosylation characterized by liver dysfunction. Am J Hum Genet. 108(6): 1040–1052 (2021)
12. Broderick L, et al, Disease-associated mutations in topoisomerase IIβ result in defective NK cells, J Allergy Clin Immunol 149(6):2171-2176 (2022)
13. Sakurai K, et al. Kinome-wide functional analysis highlights the role of cytoskeletal remodeling in somatic cell reprogramming. Cell Stem Cell 14(4):523-34.
14. Kim C, et al, Studying arrhythmogenic right ventricular dysplasia with patient-specific iPSCs. Nature. 2013 494(7435):105-10. doi: 10.1038/nature11799

TABLE 2: SAMPLE OF USERS OF SBP'S HIGH-THROUGHPUT DRUG DISCOVERY SERVICES*	
External faculty	
Al La Spada	Distinguished Professor and Jack W. Peltason Endowed Chair, Pathology & Laboratory Medicine, Neurology, Biological Chemistry, and Neurobiology & Behavior, Director, UCI Center for Neurotherapeutics
Christina Sigurdsen	Professor, Dept. of Pathology, UCSD
Alysson Muotri	Professor, Depts. Pediatrics/Cellular & Molecular Medicine, UCSD
Gene Yeo	Professor, Dept. Cellular and Molecular Medicine, UCSD
Joseph Gleeson	Professor, Depts. of Neurosciences and Pediatrics at UCSD, Investigator with the Howard Hughes Medical Institute
Internal (SBP) faculty	
Rolf Bodmer	Director, Center for Genetic Disorders and Aging Research and Professor of Development, Aging and Regeneration Program
Lorenzo Puri	Director and Professor, Development, Aging and Regeneration Program
Alessandra Sacco	Dean Graduate School of Biomedical Sciences, Director and Professor Development, Aging and Regeneration
Hudson Freeze	Director and William W. Ruch Distinguished Professor, Human Genetics Program; Director, Sanford Children's Health Research Center
Sanjeev Ranade	Asst. Professor, Development, Aging and Regeneration Program
Shengjie Feng	Asst. Professor, Development, Aging and Regeneration Program
Xiao Tian	Asst. Professor, Development, Aging and Regeneration Program
Pharma/Biotech	
BioMarin	San Rafael, CA
Janssen Pharmaceuticals	San Diego site
Epigen	San Diego
Regencor	San Francisco
Bloom Science	San Diego
* *Letter of support provided in application*	

TABLE 3: PUBLISHED PROTOCOLS ORIGINATED AT SBP's SHARED LAB RESOURCE

1. Katkov II, et al, DMSO-Free Programmed Cryopreservation of Fully Dissociated and Adherent Human Induced Pluripotent Stem Cells. Stem Cells Int. 2011;2011:981606.
2. Müller FJ, et al, Bioinformatic assay for pluripotency in human cells. Nat Methods 8(4):315-7 (2011).
3. Tobe BTD–[52 authors of an international team]–Snyder EY, Probing the lithium-response pathway in hiPSCs implicates the phosphoregulatory set-point for a cytoskeletal modulator in bipolar pathogenesis, PNAS 114:E4462-E4471 (2017).
4. Kong Y, Gimple RC, McVicar RN, Hodges AP, Yin J, Liu Y, Zhan W, Snyder EY. "Reprogram Enablement" as an assay for identifying early oncogenic pathways by their ability to allow neoplastic cells to reacquire an epiblast state. Stem Cell Reports. 2020 Sep 8;15(3):761-775. doi: 10.1016/j.stemcr.2020.07.016. Epub 2020 Aug 13. PMCID: PMC7486218.
5. Leibel SL, Winquist A, Tseu I, Wang J, Luo D, Shojaie S, Nathan N, Snyder EY, Post M. Reversal of surfactant protein B deficiency in patient specific human induced pluripotent stem cell derived lung organoids by gene therapy. *Sci Rep.* 2019 Sep 17;9(1):13450. doi: 10.1038/s41598-019-49696-8. PMCID: PMC6748939.
6. Leibel SL, McVicar RN, Winquist AM, Niles WD, Snyder EY. Generation of complete multi-cell type lung organoids from human embryonic and patient-specific induced pluripotent stem cells for infectious disease modeling and therapeutics validation. *Curr Protoc Stem Cell Biol.* 2020 Sep;54(1):e118. doi: 10.1002/cpsc.118. PMCID: PMC7361156.
7. Leibel SL, McVicar RN, Winquist AM, Snyder EY. Generation of 3D whole lung organoids from induced pluripotent stem cells for modeling lung developmental biology and disease. *J Vis Exp.* 2021 Apr 12;(170). doi: 10.3791/62456. PMID: 33900299.
8. Acevedo LM, Lindquist JN, Walsh BM, Sia P, Cimadamore F, Chen C, Denzel M, Ranscht B, Terskikh A, Snyder EY*, Cheresh DA* (2015). Human embryonic stem cells differentiation toward an autonomic neuronal cell fate depends on distinct cues from the co-patterning vascular cells. *Stem Cell Reports* 4:1075-88. doi: 10.1016/j.stemcr.2015.04.013. PMCID: PMC4471822.
9. Singec I, et al, Quantitative analysis of human pluripotency and neural specification by in-depth (phospho)proteomic profiling, *Stem Cell Reports* 7: 527–542 (2016)
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11. Liu Y, Wu D, Lao D, Peterson C, Elliott KAH, **Snyder EY**, Laser-assisted generation of human induced pluripotent stem cells, *Current Protocols in Stem Cell Biology* 31: 4A.1 – 4A.15 (2014).
12. Song RS, Carroll JM, Acevedo L, Wu D, Liu Y, **Snyder EY,** Generation, expansion, & differentiation of human induced pluripotent stem cells (hiPSCs) derived from the umbilical cords of newborns, *Current Protocols in Stem Cell Biol* 2014 May 16;29:1C.16.1-1C.16.13. doi: 10.1002/9780470151808.sc01c16s29.
13. Olee, T, Grogan SP, Lotz M, Colwell Jr CW, D'Lima D, **Snyder EY**, Repair of cartilage defects in arthritic tissue with differentiated human embryonic stem cells, Tissue Engineering 20(3-4):683-92 (2014). doi: 10.1089/ten PMID: 24028447
14. Sternberg H, Murai J, Erickson IE, Funk WD, Das S, Wang Q, **Snyder E**, Chapman KB, C. Vangsness T, West MD, A human embryonic stem cell-derived clonal progenitor cell line with chondrogenic potential and markers of craniofacial mesenchyme, Regenerative Medicine 7(4):481-501 (2012).
15. Lindquist JN, Cheresh DA, Snyder EY, Derivation of vasculature from embryonic stem cells, *Curr Protocols Stem Cell Biol* Mar; Chapter 1: Unit 1F.9 (2010).
16. Ibrahim MR, Medhat W, El-Fakahany H, Abdel-Raouf H, Snyder EY. Deriving keratinocyte progenitor cells and keratinocytes from human-induced pluripotent stem cells. *Curr Protoc Stem Cell Biol.* 2020;54(1):e119.
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19. Gonzalez R, Loring JF, Snyder EY, Preparation of autogenic human feeder cells for growth of human embryonic stem cells, *Current Protocols in Stem Cell Biology*, 1: 1C.5 (2008).
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21. Niles WL, Snyder EY, A tool for accurate stoichiometric composition of cryopreservative media for fetal- and induced pluripotent stem cell-derived human neural stem cells, *Current Protocols* 1, e123. (2021); doi: 10.1002/cpz1.123
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23. Curchoe CL, et al, Early acquisition of neural crest competence during hESCs neuralization *PLoS One* 5(11):e13890 (2010). doi: 10.1371/journal.pone.0013890

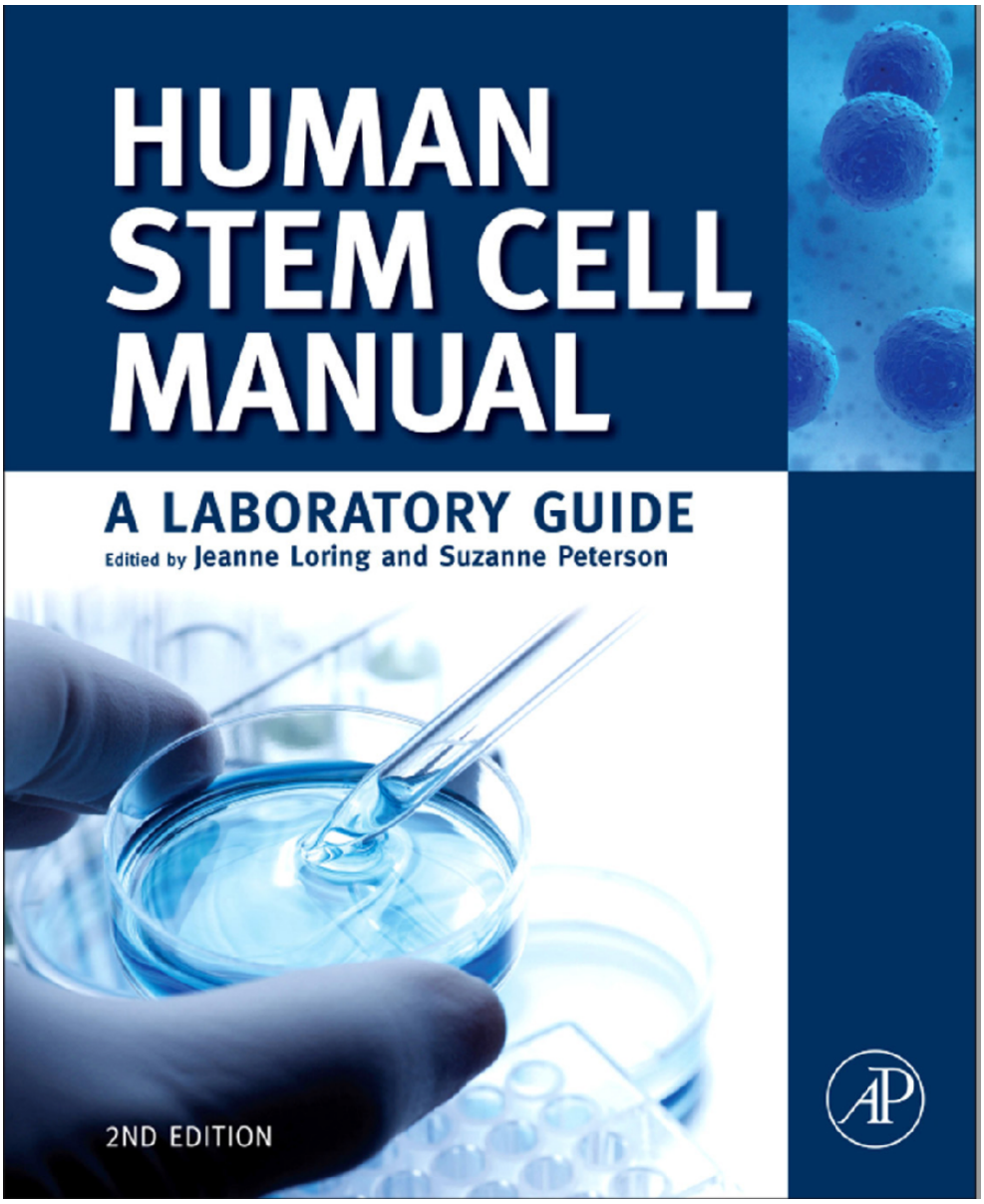
HUMAN
STEM CELL
MANUAL
A LABORATORY GUIDE
Editied by Jeanne Loring and Suzanne Peterson
2ND EDITION

FIGURE 1

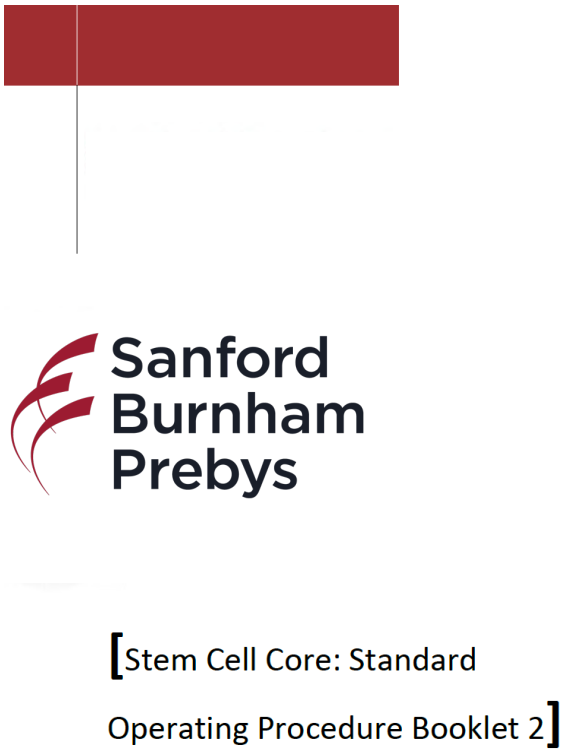

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FIGURE 2: Cover & first page of Table of Contents of Sanford Burnham Prebys (SBP) Stem Cell Core Standard Operating Procedure (SOP) manual. Many of these were published as peer-reviewed protocols **[Table 3]** and/or were published in the *Human Stem Cell Manual* **[Fig. 1]** which is used world-wide & will guide the curriculum/syllabus of SBP's proposed basic training course.

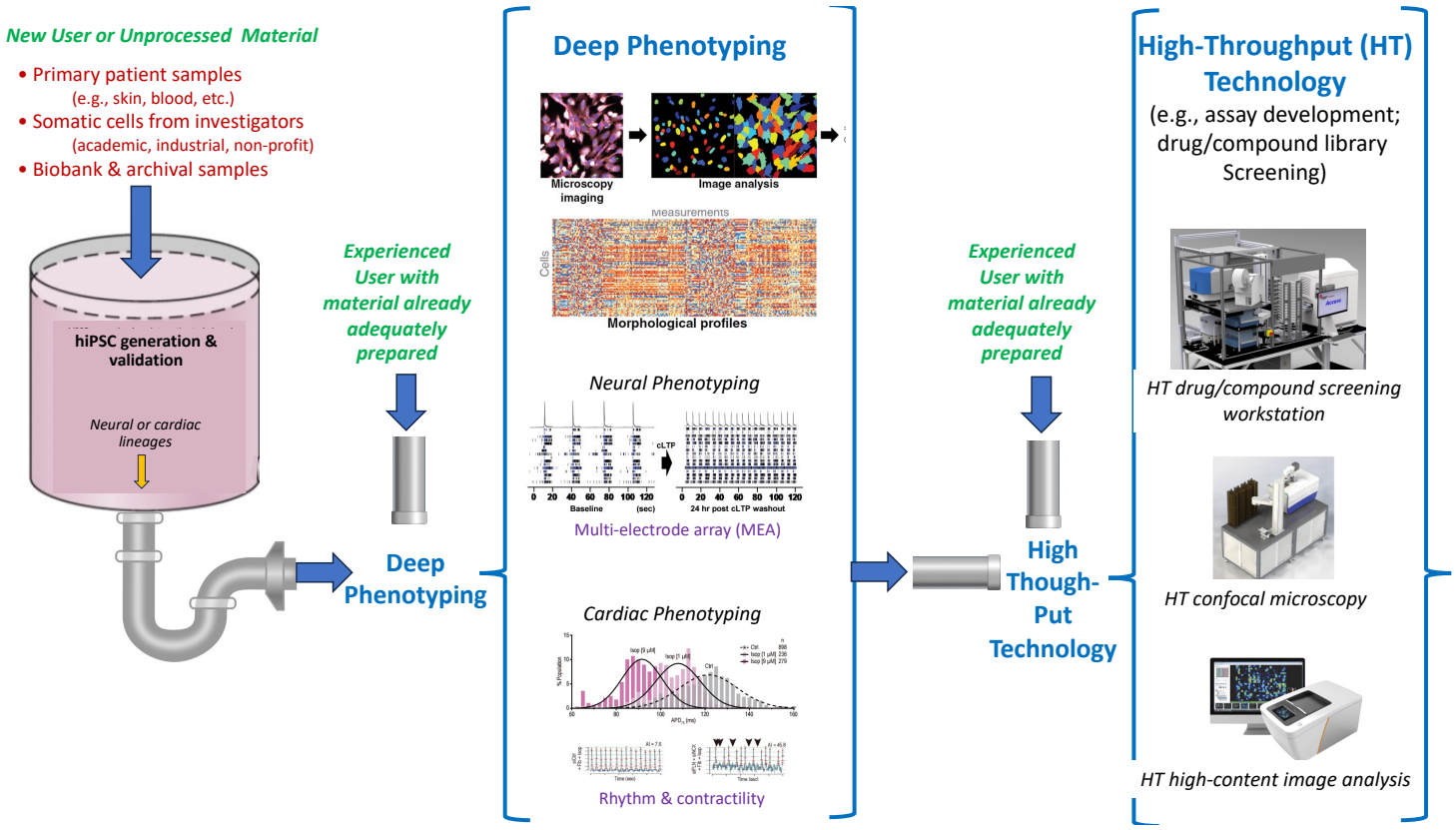

FIGURE 3: Workflow of SBP's Shared Lab Resource (SRL), capable of accommodating the needs of both unexperienced (first entrance point) & experienced users (later entrance points), allowing them to avail themselves of the cutting-edge potential of *high-throughput biology & drug discovery*. (Note a focus on neural & cardiac lineages & diseases.)