Center for Applied Biotechnology Studies

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Date the review was submitted: April 2018

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Dear Marie:

Thank you for the quick feedback, we appreciate your perspectives and considered your comments to guide the future of CABS.

Please, find the answers to your comments in the following paragraphs. Your comments are in blue and the responses in black.

To facilitate the reading, the original review is attached at the end of this document.

Advisory Committee Goals. The Advisory Committee met and developed six goals and an action plan. Five of the six goals require external funding or new physical space. The Committee prioritized one of these goals (a self-sustaining annual meeting) and accomplished it. It may be worth re-examining the remaining goals for alignment with the overall Center goals listed on p. 1 of the self-study and feasibility issues given the highly constrained

I totally agree with this statement and the immediate future plans align with it. We plan to call an in-person meeting of the Advisory Committee to evaluate CABS' past performance and formulate the future goals including re-examining the goals delineated in the past review cycle. After the experience of the past three years and the requirements for each of the goals, one possibility the committee will evaluate is to define two classes of goals: immediate future goals and long-term goals. This strategy could result in a more realistic list of objectives.

Future Vision. The level of activity reported in the self-study may be the optimal level. Alternatively, CABS may wish to partner with others broadly committed to biomedical research so as to pool any available resources and energies in a symbiotic fashion. Now seems an ideal time to consider whether or not the status quo is broad enough, or if we could find untapped potential to expand the vision.

In an informal way CABS has already started to explore these ideas. Although it did not happen, there were conversations to merge CABS*Con2* with a sister symposium by CCAM. We will continue this conversation to try to expand the symposium to an event organized by the two centers.

The scope of CABS seems to be broad enough at the moment; we accept as members practically any faculty that wishes to belong to the center as a full member or associate member depending on how close their research interests coincide with applied biotechnology. However, it is true that CABS should improve its communication with potential members and newer faculty who are not aware of the objectives of the center. The Advisory Committee should discuss how to reach out to faculty to make them feel more included in the center activities as well as enhance and improve communication. Likewise, the committee should discuss how to increase the cooperation with CCAM or other centers within CSUF.

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Mission and Goals

Mission

The mission of CABS is to provide research, educational and consulting opportunities and services to the local and state biotechnology/biomedical communities through its applied research programs and workforce-oriented curriculum.

Goals

1. To develop educational programs that will support workforce development in biocomputing, bioengineering and biopharmaceutics.

2. To create an environment where applied research by faculty and students is a primary objective.

3. To foster interactions with biotechnology/biomedical industry locally, regionally, and statewide.

CABS aligns with Goal 2 of the Strategic Plan 2013-2018 through enhancement of High Impact Practices that are best illustrated by incentivizing students to participate in research joining CABS faculty laboratories. Learning through research is an enriching experience that favors student persistence and graduation rates. Furthermore, the high diversity student population in our university results in a large number of students belonging to underrepresented minorities participating in research. A high percentage of these students decide to pursue research careers based on this experience.

CABS also aligns with Goal 3 by inviting all new faculty to join CABS and participate in its activities. Some of them became the most active CABS members.

CABS aligns with Goal 4 by stimulating all faculty to apply for federal and state funding. Furthermore, CABS seeks funds from private companies.

Activities

An advisory committee was formed. It consists of a tenured faculty (Dr. Math Cuajungco), an untenured faculty (Dr. Verónica Jimenez Ortiz), an external faculty with a leadership position (Dr. Chandra Srinivasan), and the CEO of a biotech company (Dr. Gary Fujii, Molecular Express, Inc.). The advisory committee met and produced a document that delineates directions and an action plan. The advisory committee identified goals that will be given priority through a Strategic Plan to be developed in the future in association with the Director and member of CABS. These goals are: 1) establishing a system to award minigrants in a yearly manner, 2) creating a Prep Room to serve the CABS laboratories, 3) identifying space for the Prep Room as well as other CABS activities such as location of common equipment or performance of experiments by visiting students or scientists, 4) identifying companies that can offer internships to students, 5) organizing an annual meeting to showcase CABS achievements and foster collaboration, 6) establishing a fund to give incentives (cash funds or release time) to faculty involved in infrastructure grant writing.

Of the goals listed in the previous paragraph in the past three years priority was given to establish a self-sustained annual meeting. As a consequence, an Organizing Committee was formed, and a conference named CABS*Con* took place for the first time in Fall 2016. Four speakers from diverse disciplines in academia and industry were invited, and there was a student poster presentation session. The attendance was about 100 between faculty and students, mainly local, but many from other campuses. Sixteen students presented posters. CABS*Con* was very successful allowing students to present work to an audience composed of peer students, faculty from CSUF and other campuses, and members of the Biotech industry. In Fall 2017 took place CABS*Con*2 with the same format but this time with an international speaker (Dr. Sonia Trigueros, Co-Director of the Nanotechnology Institute, University of Oxford) and 23 students presenters. In both opportunities, there were modest funds provided by a private company (Embi Tec) and the STEER program. We are seeking more external funds to ensure sustainability for this conference that will become better known as it is organized every year and attracts more attendants. CABS*Con* is increasing the visibility of the research that takes place at CSUF and promoting interactions between members of the industry and CABS faculty and students.

Another activity that fosters interactions with biotechnology/biomedical industry members is the creation of a seminar series. The CABS-sponsored seminars occur once a semester at the time the Biology seminars usually take place. Faculty and students have an opportunity to interact with the speaker before the seminar. Also, when possible, a group of faculty members with the appropriate research interests, takes the speaker to dinner for further discussions.

CABS faculty were also active in their individual research projects, seeking external funding and publishing scientific articles, preferably with students as co-authors.

It is worth mentioning that the Strategic Plan devised by the Advisory Committee is ambitious and it was designed with the purpose to develop one or two goals per three-year period. For the period 2015-2017, it was decided to focus on achievable goals that expand the connections between members of CABS, students, and the private sector through the organization of the seminar series and the CABS*Con* conferences.

Organizational Structure and Governance

The governance of CABS became formalized with the formation of the Advisory Committee in the previous review round. The Director and members of the Advisory Committee met informally in person or online.

Resources and Sustainability

CABS has limited funds in a CSUF Philanthropic Foundation account that have been used for organizing CABS*Con* and CABS*Con*2. Also, two biotech companies, Embi Tec and Molecular Resources, have contributed a total of $2,250 towards funding the conference. Although so far, the funds were sufficient for the organization of the conferences, we are exploring other avenues for seeking continuous funding that increase the resources and would make the operation sustainable. In addition, in the following period, the Advisory Committee will explore venues to seek funds towards achieving another of the goals originally listed in the Strategic Plan.

Highlights and Accomplishments

The accomplishments of CABS in the past three-year period are the individual scientific publications and funded research grants by individual members and the organization of the seminar series and the conferences CABS*Con* and CABS*Con*2.

CABS*Con* was showcased in the online and printed versions of The Orange County Register (see https://www.ocregister.com/2016/11/14/csuf-aims-to-strengthen-its-off-campus-biotechnology-presence/).

Although these accomplishments may seem too modest in comparison with the list of goals in the Strategic Plan, the Director and the Advisory Committee preferred to concentrate in achieving realistic goals rather than trying to pursue all of them, which would have been very hard to achieve. It must be considered that every CABS member has a busy agenda and CABS does not provide release time to pursue the goals of the Strategic Plan.

A list of publications and funded grant proposals by CABS members follows:

Publications** (CABS faculty member underlined)**:

Arivett, B. A., Fiester, S. E., Ream, D. C., Centron, D., Ramirez, M. S., Tolmasky, M. E., & Actis, L. A. (2015). Draft genome of the multidrug-resistant *Acinetobacter baumannii* strain A155 clinical isolate. *Genome Announc, 3*(2). doi:10.1128/genomeA.00212-15

Bradley, J. A., Daille, L. K., Trivedi, C. B., Bojanowski, C. L., Stamps, B. W., Stevenson, B. S., Nunn, H., Johnson, H., Loyd, S., Berelson, W., Corsetti, F., & Spear, J. R. (2017). Carbonate-rich dendrolitic cones: insights into a modern analog for incipient microbialite formation, Little Hot Creek, Long Valley Caldera, California. *NPJ Biofilms Microbiomes, 3*, 32. doi:10.1038/s41522-017-0041-2

Chiem, K., Fuentes, B. A., Lin, D. L., Tran, T., Jackson, A., Ramirez, M. S., & Tolmasky, M. E. (2015). Inhibition of aminoglycoside 6'-*N*-acetyltransferase type Ib-mediated amikacin resistance in *Klebsiella pneumoniae* by zinc and copper

pyrithione. *Antimicrob Agents Chemother, 59*(9), 5851-5853. doi:10.1128/AAC.01106-15

Chiem, K., Hue, F., Magallon, J., & Tolmasky, M. E. (2018). Inhibition of aminoglycoside 6'-*N*-acetyltransferase type Ib-mediated amikacin resistance by zinc complexed with clioquinol, an ionophore active against tumors and neurodegenerative diseases. *Int J Antimicrob Agents, 51*(2), 271-273. doi:10.1016/j.ijantimicag.2017.08.002

Chiem, K., Jani, S., Fuentes, B., Lin, D. L., Rasche, M. E., & Tolmasky, M. E. (2016). Identification of an inhibitor of the aminoglycoside 6'-*N*-acetyltransferase type Ib [AAC(6')-Ib] by glide molecular docking. *Medchemcomm, 7*(1), 184-189. doi:10.1039/C5MD00316D

Davies-Sala, C., Soler-Bistue, A., Bonomo, R. A., Zorreguieta, A., & Tolmasky, M. E. (2015). External guide sequence technology: a path to development of novel antimicrobial therapeutics. *Ann N Y Acad Sci, 1354*, 98-110. doi:10.1111/nyas.12755

Forsgren, K. L., Jamal, H., Barrios, A., & Paig-Tran, E. W. M. (2017). Reproductive morphology of oarfish (*Regalecus russellii*). *Anat Rec (Hoboken), 300*(9), 1695-1704. doi:10.1002/ar.23605

Hess, K., Oliverio, R., Nguyen, P., Le, D., Ellis, J., Kdeiss, B., Ord, S., Chalkia, D., & Nikolaidis, N. (2018). Concurrent action of purifying selection and gene conversion results in extreme conservation of the major stress-inducible Hsp70 genes in mammals. *Sci Rep, 8*(1), 5082. doi:10.1038/s41598-018-23508-x

Ishida, Y., McCallister, C., Nikolaidis, N., Tsangaras, K., Helgen, K. M., Greenwood, A. D., & Roca, A. L. (2015). Sequence variation of koala retrovirus transmembrane protein p15E among koalas from different geographic regions. *Virology, 475*, 28-36. doi:10.1016/j.virol.2014.10.036

Jackson, A., Jani, S., Sala, C. D., Soler-Bistue, A. J., Zorreguieta, A., & Tolmasky, M. E. (2016). Assessment of configurations and chemistries of bridged nucleic acids-containing oligomers as external guide sequences: a methodology for inhibition of expression of antibiotic resistance genes. *Biol Methods Protoc, 1*(1). doi:10.1093/biomethods/bpw001

Jani, S., Jackson, A., Davies-Sala, C., Chiem, K., Soler-Bistue, A., Zorreguieta, A., & Tolmasky, M. E. (2018). Assessment of external guide sequences' (EGS) efficiency as inducers of RNase P-mediated cleavage of mRNA target molecules. *Methods Mol Biol, 1737*, 89-98. doi:10.1007/978-1-4939-7634-8_6

Jimenez, V., & Docampo, R. (2015). TcPho91 is a contractile vacuole phosphate sodium symporter that regulates phosphate and polyphosphate metabolism in *Trypanosoma cruzi*. *Mol Microbiol, 97*(5), 911-925. doi:10.1111/mmi.13075

Lin, J., Nishino, K., Roberts, M. C., Tolmasky, M E., Aminov, R. I., & Zhang, L. (2015). Mechanisms of antibiotic resistance. *Front Microbiol, 6*, 34. doi:10.3389/fmicb.2015.00034

Lopez, C., Arivett, B. A., Actis, L. A., & Tolmasky, M. E. (2015). Inhibition of AAC(6')-Ib-mediated resistance to amikacin in *Acinetobacter baumannii* by an antisense peptide-conjugated 2',4'-bridged nucleic acid-NC-DNA hybrid oligomer. *Antimicrob Agents Chemother, 59*(9), 5798-5803. doi:10.1128/AAC.01304-15

McCallister, C., Kdeiss, B., & Nikolaidis, N. (2015). HspA1A, a 70-kDa heat shock protein, differentially interacts with anionic lipids. *Biochem Biophys Res Commun, 467*(4), 835-840. doi:10.1016/j.bbrc.2015.10.057

McCallister, C., Kdeiss, B., & Nikolaidis, N. (2016). Biochemical characterization of the interaction between HspA1A and phospholipids. *Cell Stress Chaperones, 21*(1), 41-53. doi:10.1007/s12192-015-0636-6

McCallister, C., Kdeiss, B., Oliverio, R., & Nikolaidis, N. (2016). Characterization of the binding between a 70-kDa heat shock protein, HspA1A, and phosphoinositides. *Biochem Biophys Res Commun, 472*(1), 270-275. doi:10.1016/j.bbrc.2016.02.103

McCallister, C., Siracusa, M. C., Shirazi, F., Chalkia, D., & Nikolaidis, N. (2015). Functional diversification and specialization of cytosolic 70-kDa heat shock proteins. *Sci Rep, 5*, 9363. doi:10.1038/srep09363

Monson, C., Forsgren, K., Goetz, G., Harding, L., Swanson, P., & Young, G. (2017). A teleost androgen promotes development of primary ovarian follicles in coho salmon and rapidly alters the ovarian transcriptome. *Biol Reprod, 97*(5), 731-745. doi:10.1093/biolre/iox124

Montana, S., Schramm, S. T., Traglia, G. M., Chiem, K., Parmeciano Di Noto, G., Almuzara, M., .Barberis, C., Vay, C., Quiroga, C., Tolmasky, M. E., Iriarte, A., & Ramirez, M. S. (2016). The genetic analysis of an *Acinetobacter johnsonii* clinical strain evidenced the presence of horizontal genetic transfer. *PLoS One, 11*(8), e0161528. doi:10.1371/journal.pone.0161528

Ramirez, M. S., & Tolmasky, M. E. (2017). Amikacin: uses, resistance, and prospects for inhibition. *Molecules, 22*(12). doi:10.3390/molecules22122267

Ramirez, M. S., Xie, G., Traglia, G. M., Johnson, S. L., Davenport, K. W., van Duin, D., Ramazani, A., Perez, F., Jacobs, M., Sherratt, D. J., Bonomo, R. A., Chain, P. S., & Tolmasky, M. E. (2016). Whole-genome comparative analysis of two carbapenem-resistant ST-258 *Klebsiella pneumoniae* strains isolated during a North-Eastern Ohio outbreak: differences within the high heterogeneity zones. *Genome Biol Evol, 8*(6), 2036-2043. doi:10.1093/gbe/evw135

Ruiz-Rodriguez, C. T., Brandt, J. R., Oliverio, R., Ishida, Y., Guedj, N., Garrett, E. F., Kahila Bar-Gal, G., Nikolaidis, N., Cardoso, F., & Roca, A. L. (2017). Polymorphisms of the toll-like receptor 2 of goats (*Capra hircus*) may be associated with somatic cell count in milk. *Anim Biotechnol, 28*(2), 112-119. doi:10.1080/10495398.2016.1232267

Stietz, M. S., Lopez, C., Osifo, O., Tolmasky, M. E., & Cardona, S. T. (2017). Evaluation of the electron transfer flavoprotein as an antibacterial target in *Burkholderia cenocepacia*. *Can J Microbiol, 63*(10), 857-863. doi:10.1139/cjm-2017-0350

Traglia, G. M., Dixon, C., Chiem, K., Almuzara, M., Barberis, C., Montana, S., Merino, C., Mussi, M., Tolmasky, M. E., Iriarte, A., Vay, C., & Ramirez, M. S. (2015). Draft genome sequence of *Empedobacter* (formerly *Wautersiella*) *falsenii* comb. nov. Wf282, a strain isolated from a cervical neck abscess. *Genome Announc, 3*(2). doi:10.1128/genomeA.00235-15

Tran, T., Chiem, K., Jani, S., Arivett, B. A., Lin, D. L., Lad, R., Jimenez, V., Farone, M., Debevec, G., Santos, R., Giulianotti, M., Pinilla, C., & Tolmasky, M. E. (2018). Identification of a small molecule inhibitor of the aminoglycoside 6'-*N*-

acetyltransferase type Ib [AAC(6')-Ib] using mixture-based combinatorial libraries. *Int J Antimicrob Agents*. doi:10.1016/j.ijantimicag.2018.01.019

Grants:

C. Brennan	1SC2AI133653-01	NIGMS NIH	2017-2020	$417,300
C. Brennan	New Inv Grant	CSUPERB	2015-2016	$ 15,000
M. Cuajungco	1R15NS101594-01	NINDS NIH	2017-2020	$382,074
M. Cuajungco	Res Devel Grant	CSUPERB	2015-2016	$ 15,000
V. Jimenez Ortiz	1R15AI122153-01	NIAID NIH	2016-2019	$404,813
V. Jimenez Ortiz	R00AI101167	NIAID NIH	2013-2016	$490,766
V. Jimenez Ortiz	16GRNT30280014	AHA	2016-2018	$153,993
V. Jimenez Ortiz	New Inv Grant	CSUPERB	2015-2016	$ 15,000
H. Johnson	Res Devel Grant	CSUPERB	2015-2016	$ 15,000
N. Nikolaidis	1SC3GM121226-01	NIGMS NIH	2017-2021	$417,300
M. Ramirez	1SC3GM125556-01	NIGMS NIH	2018-2022	$423,500
A. Orchard	New Inv Grant	CSUPERB	2015-2016	$ 15,000
M. Rasche	CHE-1508801	NSF-RUI	2015-2018	$200,000
M. Rasche/N.Salzameda/A. Orchard (Co-PIs) PI: P. Hudson				
	CHE-1726903	NSF-MRI	2017-2018	$488,159
M. Rasche	Curriculum Dev G	CSUPERB	2016-2017	$ 15,000
P. Shahrestani	New Inv Grant	CSUPERB	2016-2017	$ 15,000
M. Tolmasky	2R15AI047115-04	NIAID NIH	2013-2018	$397,987
M. Tolmasky	Joint Venture Prog	CSUPERB	2014-2015	$ 25,000

Planning and Strategic Outlook

The Director and the Advisory Committee members are aware that CABS has achieved important but limited goals. This was not to be an unexpected outcome because, despite the ambitious strategic planning and the goals included in it, it is clear that faculty volunteering overload time sustains CABS. There is no recurring budget to offer release time to increase the time dedicated by faculty to CABS or to enhance infrastructure. However, a group faculty in the Advisory Committee and the CABS Organizing Committee found the ways to achieve the goals identified as a priority for the past three-year period.

The Advising Committee will meet again in person in Spring or Fall 2018 to evaluate the goals and establish the priority(ies) for the next three years. Of course, we will continue the seminar series and the organization of the CABS*Con* annual conference attempting to expand its visibility and size. We will continue with the strategy of identifying priorities that are achievable. This strategy will permit us to continue building a vibrant biotechnology community at CSUF that will fulfill the CABS Mission and Goals.