Autophagy, Inflammation, and Metabolism (AIM) Center in its second year

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ABSTRACT

The NIH-funded center for autophagy research named Autophagy, Inflammation, and Metabolism (AIM) Center of Biomedical Research Excellence, located at the University of New Mexico Health Science Center is now completing its second year as a working center with a mission to promote autophagy research locally, nationally, and internationally. The center has thus far supported a cadre of 6 junior faculty (mentored PIs; mPIs) at a near-R01 level of funding. Two mPIs have graduated by obtaining their independent R01 funding and 3 of the remaining 4 have won significant funding from NIH in the form of R21 and R56 awards. The first year and a half of setting up the center has been punctuated by completion of renovations and acquisition and upgrades for equipment supporting autophagy, inflammation and metabolism studies. The scientific cores usage, and the growth of new studies is promoted through pilot grants and several types of enablement initiatives. The intent to cultivate AIM as a scholarly hub for autophagy and related studies is manifested in its Vibrant Campus Initiative, and the Tuesday AIM Seminar series, as well as by hosting a major scientific event, the 2019 AIM symposium, with nearly one third of the faculty from the International Council of Affiliate Members being present and leading sessions, giving talks, and conducting workshop activities. These and other events are often videostreamed for a worldwide scientific audience, and information about events at AIM and elsewhere are disseminated on Twitter and can be followed on the AIM web site. AIM intends to invigorate research on overlapping areas between autophagy, inflammation and metabolism with a number of new initiatives to promote metabolomic research. With the turnover of mPIs as they obtain their independent funding, new junior faculty are recruited and appointed as mPIs. All these activities are in keeping with AIM's intention to enable the next generation of autophagy researchers and help anchor, disseminate, and convey the depth and excitement of the autophagy field.

KEYWORDS: Autophagy, inflammation, metabolism

Introduction

In 2017, the National Institutes of Health (NIH) funded a new center for autophagy research, named Autophagy Inflammation and Metabolism (AIM) Center of Biomedical Research Excellence (CoBRE) through its research capacity building program. The mission of the CoBRE program is to develop research infrastructure through several mechanisms housed within thematic centers, each focused on a multidisciplinary theme. Autophagy, and its intersections with inflammatory and metabolic processes is an ideal multidisciplinary theme with cross-cutting implications for both fundamental science and translational research. The AIM center's specific intent is to provide a regional, national and international hub for the advancement of autophagy research. This includes autophagy as a standalone process and its intersections with other processes, often in a disease context. AIM encourages fundamental discoveries while cultivating connections with translationally oriented programs and research centers. The intent of this article is to report to the autophagy scientific community the progress made within the nearly 2 years of the existence of the AIM center, and to invite and welcome participation of all those interested.

AIM community of scholars starts with investment in junior faculty

The centerpiece of AIM, supported by the majority of funds coming to the AIM center through the CoBRE P20 mechanism, are the mentored faculty, also referred to as mentored principal investigators (mPIs). So far, 6 mPIs and their projects have been funded by AIM (Fig. 1A) at a near-R01 level through this mechanism. One mPI obtained an independent R01 and graduated. This PI has been recruited to Penn State, but remains connected to AIM, as evidenced by continued interactions and acknowledgement of the P20 grant in publications. After this mPI's graduation, AIM issued a Request for Applications (RFA) to appoint a new mPI, following standard operating procedures (SOPs) codifying admissions, progress assessment and graduation policies by AIM. This was a competitive process with several qualified applicants applying. Applications for mPIs include a 12-page R01 style research proposal plus a specific aims page, along with the biosketches for the candidate mPI and his/her mentor plus letters of support, usually from the chair of the home or hiring department. After external review that follows the NIH style assessment (but without going to an NIH study section for peer review), scores are tallied and the top candidate is approved by AIM's Executive Committee (EC), External Advisory Board, and NIH program administrators.

Another mPI from the original cohort graduated upon receiving her R01 funding. In this case, the mPI stayed at the institution and has been appointed to the EC to bring the perspective of an mPI who recently graduated as well as becoming a co-director of one of the scientific cores – Inflammation and Metabolism Core (ICM) – due to extensive experience with metabolism studies and the AIM leadership's intent to boost metabolism research at the center. Following the SOPs, AIM has appointed a second new mPI. The current "quartet" of mPIs study autophagy in antiviral immunity, aging, neurological/psychiatric disorders,

and T cell biology. Three of the 4 current mPIs have obtained new NIH funding consisting of 2 R21 awards and 1 R56 award. Future mPIs may also be recruited externally as new hires to UNM in collaboration with individual departments

A

mPI	Obtained funding	Status	Present role
Project 1 mPI (completed)	R01	mPI Graduated	Affiliate member
Project 2 mPI (completed)	R01	mPI Graduated	EC member IMC core co-director
Project 3 mPI	R21	In progress	Y2 mPI
Project 4 mPI	R21	In progress	Y2 mPI
Project 5 mPI		In progress	Y1 mPI
Project 6 mPI	RS6	In progress	Y1 mPI

B

Pilot or Enablement Grants	Number awarded
AIM	5(Y1) 3(Y2)
CTSA-AIM	1(Y2)
AIM-CIDI	2(Y2)
Mentor-engagement MEG	3(Y1) 4(Y2)
Enabling Pre-pilots	3(Y2)

C

Membership type	How	Function	Access	Institution
Founding Members & administration	PD, aPD, EC Admin staff	Governance Operations Admin and Reports	All AIM functions and facilities	UNM HSC
Mentored PI (mPI) & mentors	mPIs Selected	Large (R01-style) research projects + MEGs	Funds 150k/y 2-3y AIM cores Mentoring MEGs	UNM HSC
Associate members	Biosketch, TAIMS ½ p Research description	Scholarly and research community	AIM cores AIM community of scholars	UNM HSC
International Council of Affiliate Members	Appointment	Distinguished International scholars	Annual AIM symposium Collaborations	The World
Advisory committees	Appointment	EAB, IAB	Advisory and approval	National Regional

Figure 1. Summary of AIM progress, pilot and enablement programs, and membership. (**A**) Table of mentored PI's status: graduations, new appointments, and NIH grants received. (**B**) A sampling of pilot grant programs and enablement funds provided by the AIM center. (**C**) AIM membership, levels, and functions.

Mentoring junior faculty

AIM provides mentoring to mPIs in several ways. Each mPI is matched with a seasoned R01-funded senior faculty member who acts as a mentor. Mentors' salaries are in part supported by AIM corresponding to a time commitment of approximately 3 h per week. As one of mentoring enrichment programs, AIM provides small Mentor Engagement Grants (MEGs) to mentors. The purpose of MEGs is to increase interest within the mentor's laboratory in the work by the mentee and enhance the quality of scientific interactions and output of each mentor-mentee teem. Mentors are also members of the Mentoring Assessment Committee (MAC), which includes the Mentoring Director, departmental chairs of junior faculty, and additional invited experienced faculty. MAC assesses each mPI's progress in a formal way twice a year, with memoranda summarizing status and recommendations. Among monitored general criteria are progress in publications, grant applications and attendance of or presentations at conferences. Each mPI develops and adheres to an individual development plan (IDP). IDPs are custom tailored to each mPI through initial questionnaires and are meant to identify systematic needs for any existing training gaps or special interests. AIM leadership is cognizant of the potential to over-mentor, and AIM's mentoring team and EC carefully monitor and balance mentoring activities.

Vibrant campus initiative

The AIM center has a portfolio of evolving scholarly initiatives including AIM Symposia, Tuesday AIM Seminars (TAIMS), Visiting Scholars Program (present visiting scholars are from Norway and Brazil), various enablement activities such as the above mentioned MEGs, and disseminating information via the AIM web site (https://www.autophagy.center/) on international scientific output in the field of autophagy research. TAIMS meetings commonly include 2 talks of 20 min maximum each, fashioned after Keystone Symposia or Gordon Research Conference plenary presentations, followed by brief receptions in the newly renovated AIM conference room. These sessions are designed to showcase research activities as well as to promote informal interactions.

The 2019 AIM symposium

At the top of the initiatives promoting autophagy science and vibrant scholarly environment for all AIM members and their trainees are the annual AIM scientific symposia. After the success of the 2018 AIM symposium, the more ambitious 2019 AIM symposium (Fig. 2; https://www.autophagy.center/node/369) took place at the AIM center in Albuquerque, New Mexico, USA immediately following the 2019 Keystone Symposium in Santa Fe, the nearby state capital of New Mexico. The symposium was organized by Dr. Vojo Deretic (The AIM Center, USA), Dr. Leon Murphy (Casma Therapeutics, USA), and Dr. Li Yu (Tsinghua University, China).

The first session of the 2019 AIM symposium was chaired by Dr. Tamotsu Yoshimori, Osaka University, Osaka, Japan. It consisted of plenary talks on fundamentals of autophagy: Dr Sharon Tooze, The Francis Crick Institute, London, UK, spoke on "Initiation of autophagy by ATG9 vesicles and PI4P"; Dr

Fulvio Reggiori, University Medical Center Groningen, Netherlands spoke on "Supplying lipids to the forming autophagosome"; Dr Zvulun Elazar, Weizmann Institute of Science, Israel, spoke on “Relationship between fatty acid, lipid synthesis and Autophagy".

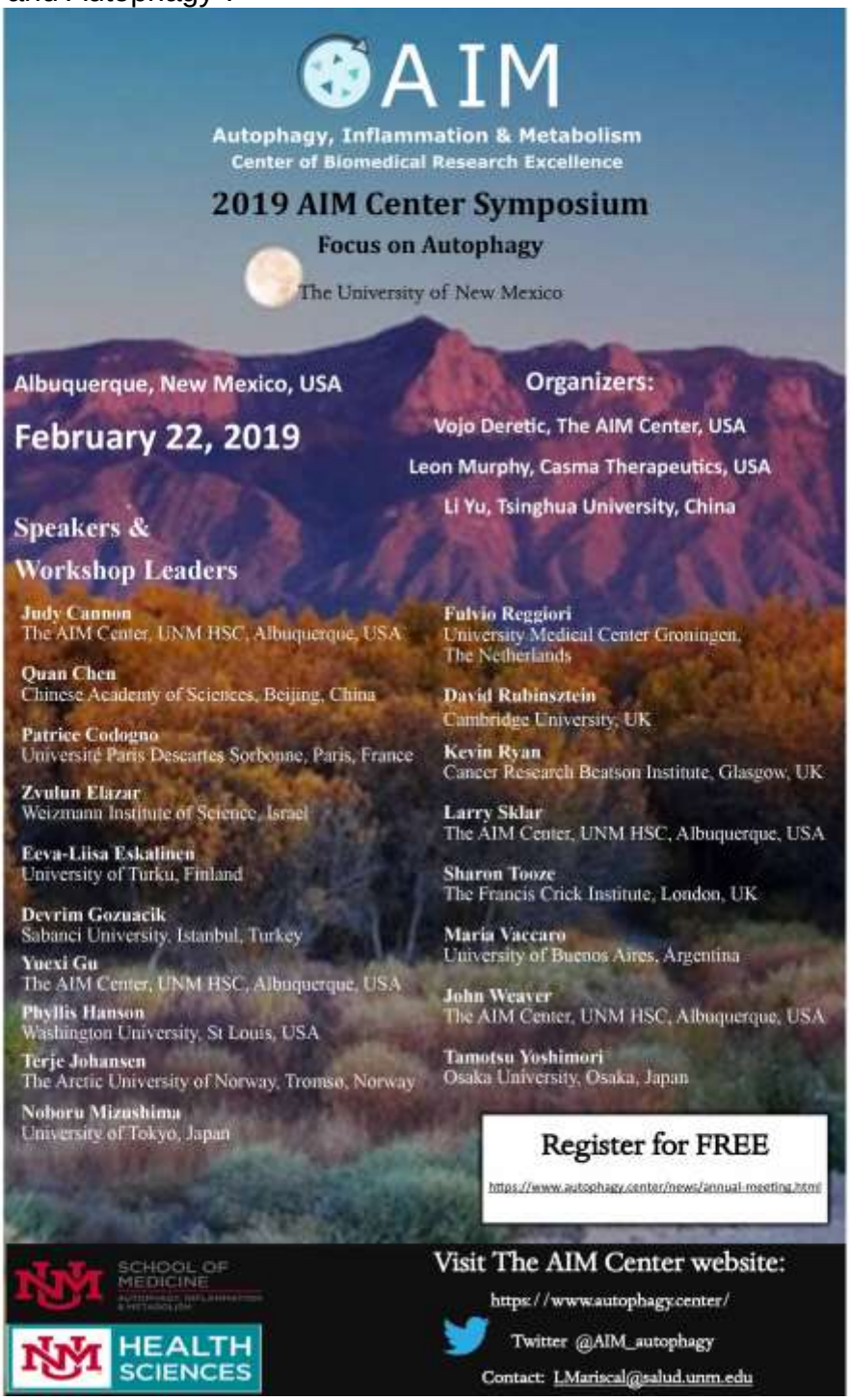

Figure 2. The 2019 AIM symposium scientific program and poster.

The second session was chaired by Dr. Noboru Mizushima, University of Tokyo, Japan. It was on “Autophagy Intersections with other Pathways”, with plenary talks by Dr. Patrice Codogno, Université Paris Descartes Sorbonne, Paris, France
who spoke on “Autophagy: a protective response to shear stress"; Dr. Gábor Juhász, Institute of Genetics, Biological Research Centre, Hungarian Academy of Sciences spoke on the "Intersections and different regulation of autophagy and crinophagy"; Dr. Thierry Galli, Institute of Psychiatry and Neurosciences of Paris, INSERM spoke on the "Role of VAMP7-dependent unconventional secretion in neurite growth"; and Dr. Phyllis Hanson, University of Michigan, Ann Arbor Michigan, USA spoke on "ESCRTs in endolysosomal membrane repair".

The third session on Autophagy in Models for Basic Science and Disease was chaired by Dr. Terje Johansen, The Arctic University of Norway, Tromsø, Norway. The plenary talks were by Dr. David Rubinsztein, Cambridge University, UK whose talk was entitled "Contact inhibition compromises autophagy"; Dr. Devrim Gozuacik, Sabanci University, Istanbul, Turkey, who spoke on "Novel regulators of autophagy"; and Dr. Quan Chen, Chinese Academy of Sciences, Beijing, China, who spoke on "Molecular regulation of selective mitophagy and its role in inflammasome activation and hepatocarcinogenesis".

In addition to the plenary talks, there was a workshop session covering a plethora of autophagy research topics and technical approaches, presented by some of the best experts in the world. This included: Dr. Christian Behrends, Ludwig Maximilian University of Munich, München, Germany who covered “Proteomics and autophagy network regulation”; Dr. Eeva-Liisa Eskelinen, University of Turku, Finland who covered “EM/autophagasome, autophagosomal ultrastructure”; Dr. Terje Johansen, who covered “Selective autophagy”; Dr. Noboru Mizushima who covered “Autophagy initiation and maturation”; Dr. Michael Ragusa, Dartmouth University, New Hampshire, USA, who covered “Structural biology of autophagy systems”; Dr. Kevin Ryan, Cancer Research, Beatson Institute, Glasgow, UK, who covered “Autophagy and cancer”; Dr. Maria Vaccaro, University of Buenos Aires, Argentina, who covered “Membrane proteins and autophagy”; and Dr. Tamotsu Yoshimori, Osaka University, Osaka, Japan who covered “Autophagy in diseases”. Finally, AIM capabilities and core facilities were covered by Drs. Judy Cannon, Yuexi Gu, Larry Sklar, and John Weaver of the AIM center.
The symposium finished with a reception where local and international attendees could interact with the speakers and workshop leaders.

Plans for third year

The plans for AIM in year 3 remain as originally proposed, with several enhancements and special points of emphasis. The AIM center is planning ahead on positioning itself for long-term success, which includes a renewal after the completion of phase I (first 5 years) and application for continuation/transition into phase II.

One of the goals for AIM is to promote is metabolism research. AIM includes 2 separate scientific cores: Autophagy core (AC) and Inflammation and Metabolism Core (IMC). Whereas AC has been developed in the first 2 years of the AIM center's becoming established, the AIM leadership has intentions to enhance IMC operations and promote metabolomics studies by providing a pipeline and workflow as well as financial support for outsourced metabolomics analyses. Several small but adequate grants sufficient to support pilot studies by AIM members will be provided to carry out initial metabolomics studies and spur metabolism research. This complements the Seahorse capabilities of the existing AIM instruments in the IMC facility.

Whereas the AIM center is doing well, the AIM leadership, with the concurrence of the External Advisory Board, has identified several areas of emphasis where opportunities for improvement exist, including increasing total publication output, which includes not just mPIs but also senior faculty, hosting technological workshops and open-house events, external searches for recruitment of faculty, career stage-adjusted mPI graduations, etc. AIM intends to graduate one more mPI and recruit new junior faculty into the AIM center within the next year. Additional plans include interactions with other IDeA programs and CoBRE centers. AIM also invites and appoints new members, at various levels following defined admission criteria and procedures. The membership brings benefits and access as shown in Fig. 1C. The essence of being an AIM member has been described at length in a previous editorial on AIM [1].

Acknowledgments
We thank ICAM members and 2019 AIM symposium organizers, speakers, workshop leaders, and attendees, and thank all our colleagues that we could not mention here but who are expected to play a role in a number of ways. The AIM center is supported by NIH grant P20GM121176.

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