

Autophagy, Inflammation, and Metabolism (AIM) Center of Biomedical Research Excellence: supporting the next generation of autophagy researchers and fostering international collaborations

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ABSTRACT

Recently, NIH has funded a center for autophagy research named the Autophagy, Inflammation, and Metabolism (AIM) Center of Biomedical Research Excellence, located at the University of New Mexico Health Science Center (UNM HSC), with aspirations to promote autophagy research locally, nationally, and internationally. The center has 3 major missions: (i) to support junior faculty in their endeavors to develop investigations in this area and obtain independent funding; (ii) to develop and provide technological platforms to advance autophagy research with emphasis on cellular approaches for high quality reproducible research; and (iii) to foster international collaborations through the formation of an International Council of Affiliate Members and through hosting national and international workshops and symposia. Scientifically, the AIM center is focused on autophagy and its intersections with other processes, with emphasis on both fundamental discoveries and applied translational research.

Introduction

The purpose of this article is to inform the international autophagy research community about the establishment of a new center for autophagy research that we think will be a useful resource to the scientific community interested in fundamental and disease-related research on autophagy. The National Institutes of Health (NIH) Centers of Biomedical Research Excellence (CoBRE) program, of which the Autophagy, Inflammation, and Metabolism Center (AIM) is a part of and is funded by, has the mission to develop research capacity through several mechanisms housed within thematic centers focused on a multidisciplinary theme, such as autophagy, with cross-cutting implications for both fundamental science and translational research. The AIM center's specific mission is to provide a national and international hub for advancement of autophagy research. This includes autophagy and its connections with other fundamental processes, often in disease contexts but also from the perspective of basic science. The initial and evolving processes for achieving these goals are multi-pronged as described below.

Enabling junior investigators whose research is focused on autophagy as the central theme of the center

The research-building mechanism that will have the most significance and financial impact through the AIM center is to provide multi-year funding support to junior faculty. This funding of individual projects is at a level equivalent to a typical NIH R01 project, or independent group leader funding, enabling junior investigators (usually starting Assistant Professors on a tenure track, referred to as mentored Principal Investigators, or "mPIs") to develop their program sufficiently to be able to compete for their own independent R01-level funding. This is done in a mentored and collaborative environment, further bolstered by high-end shared equipment core facilities, accessible initially without added cost to both

mPIs and other AIM's members. The mPIs are appointed for a specific number of years (typically 3), after which they graduate. Upon graduation, former mPIs remain tightly associated with the center, maintaining their membership status, and transfer their experience to other active and new mPIs in the center. They retain the same space, which is usually provided by their home departments at the outset. An mPI's graduation in turn triggers formal searches for new junior investigators, who are identified via local and external competitive searches and selection processes. Upon their selection, new mPIs are given their funding and access to facilities through the center and are integrated into the center's activities.

Building a broader community of scholars with interests focused on the central theme of autophagy research

In addition to supporting junior investigators, the center provides an intellectual thematic hub for investigators at multiple stages of their career. This includes the scientific leadership of the center and other more senior investigators who play mentoring roles. These scientists are full members of the center along with the mPIs. Associate members join the center through the simple process of presenting their science in a seminar (physically given on the premises or remotely through teleconferencing), providing a brief synopsis (half a page) of their project and relatedness to the focal theme(s) of the AIM center, and their biosketch/cv. Upon receiving a formal vote by the scientific leadership (AIM's executive committee), associate members are installed and obtain privileges to access scientific cores and join ongoing formal collaborative initiatives. Whereas the use of AIM technological platforms housed in scientific cores, such as high-content microscopy quantification of autophagy processes, may be most accessible locally, fixed and processed samples can be shipped from distant sites thus providing global access to the facility.

External Advisory Board

The AIM center has a national External Advisory Board (EAB), with the present members being distinguished US scientists: Dr. Beth Levine, UT Southwestern, Dallas, Chairperson of the EAB and a leading autophagy researcher; Dr. Vishva Dixit, Vice-President of Genentech and international authority on inflammation, Dr. Randal Kaufman, the director of the Degenerative Diseases Program, Neuroscience and Aging Center at Sanford Burnham Prebys Medical Discovery Institute, La Jolla; and Dr. Philipp Scherer, director of the Touchstone Diabetes Center at UT Southwestern, Dallas. The role of the EAB is to provide advice to the center director, assess the function of the AIM center annually and participate in selection and appointments of new mPIs. The composition of the EAB is designed to ensure the fulfillment of the goals and broad scientific impact of the AIM center.

International Council of Affiliate members: global cooperation in autophagy research

The International Council of Affiliate Members (ICAM) is a key component of AIM, reaching out to the broader community of autophagy scholars across the globe. The role of ICAM is to participate in AIM activities, to foster international

collaborations, and to engage in the exchange of ideas and technologies of relevance for autophagy research. The ICAM members provide their input through tele- and video-conferencing and participate in person in the symposia and workshops organized at the AIM center. The ICAM is composed of internationally renowned leaders in autophagy research or international authorities in other fields of key interest to the AIM center. The members come from nearly all continents including Africa, Asia, Australia, Europe, North America; and South America (Figure 1). The founding members of the ICAM are: Eric H. Baehrecke (USA), Christian Behrends (Germany), Francesco Cecconi (Italy, Denmark), Patrice Codogno (France), Guang-Chao Chen (Taiwan), Zvulun Elazar (Israel), Eeva-Liisa Eskelinen (Finland) Bernard Fourie (South Africa), Devrim Gozuacik (Turkey), Wanjin Hong (Singapore), Gokhan Hotamisligi (USA), Marja Jäättelä (Denmark), Terje Johansen (Norway), Eun-Kyeong Jo (South Korea), Gábor Juhász (Hungary), Daniel Klionsky (USA), Nicholas Ktistakis (UK), Adi Kimchi (Israel), Guido Kroemer (France, Sweden), Noboru Mizushima (Japan), Christian Münz (Switzerland), Kevin Ryan (UK), Fulvio Reggiori (The Netherlands), David Rubinsztein (UK), Kate Schroder (Australia), Anne Simonsen (Norway), Sharon Tooze (UK), Maria I. Vaccaro (Argentina), Tamotsu Yoshimori (Japan), Li Yu (China), and Hong Zhang (China). It is anticipated that a subset of ICAM members will participate in person at the annual AIM meetings and/or workshops. The first such event is planned in 2019, in connection with the Keystone Symposium on autophagy taking place in Santa Fe, near the AIM center location. It is also expected that over time, the productive interactions might grow, at least in some cases, into inter-institutional cooperative agreements.

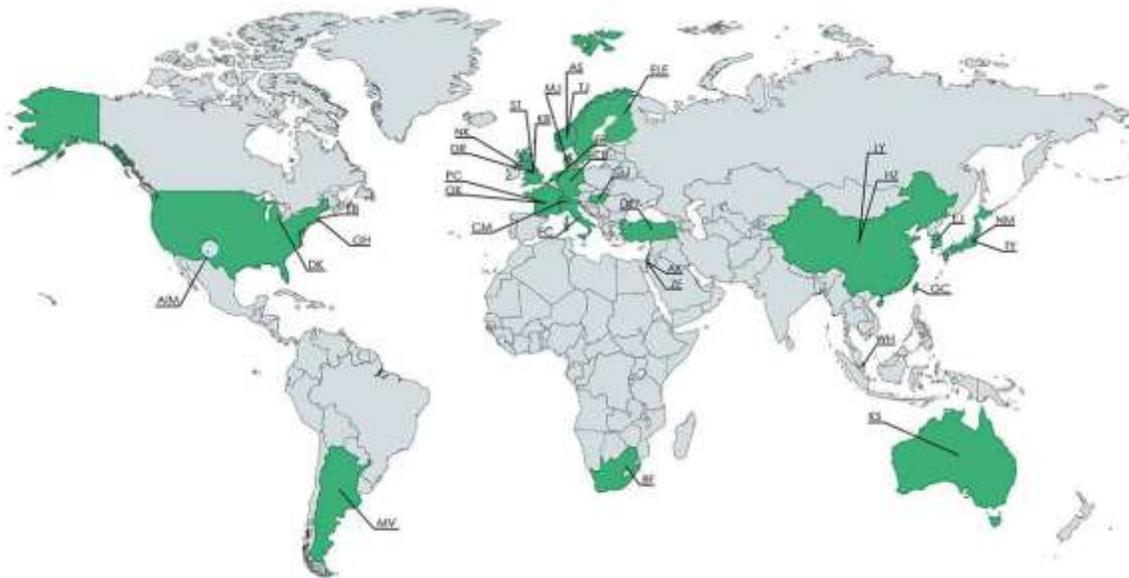


Figure 1. Global distribution of AIM’s International Council of Affiliate members (ICAM). Initials, affiliate members; full names are given in the text.

Core facilities

The AIM center has 3 core facilities: (i) Administrative core; (ii) Autophagy scientific core (ASC); and (iii) Inflammation and metabolism core (IMC).

The administrative core is composed of the leadership (Director and executive committee) from the ranks of scientists in different departments and schools at the UNM HSC. This ensures a broad local base of participants, which is an important aspect for the success of the AIM center. The center leadership is assisted by an internal advisory board, and by the EAB. The administrative core also provides mentoring infrastructure and evaluates progress of junior (mentored) PIs as well as the function and contributions of mentoring faculty. A centerpiece for mentoring is an individualized development plan for each mPI, customized to the needs of each junior faculty member. The mPIs select a small subset from the list of offered core competencies. This list is supplemented by unique, custom developed training in consultations with their mentors. This combination allows a high degree of personalization to enhance mPIs' careers and funding success. It is also expected that these junior investigators will gain access to broad international expertise and collaborations via interactions with the ICAM members.

The two technological cores, ASC and IMC, provide instrumentation designed not to duplicate but complement the existing conventional facilities, e.g. flow cytometry, genomics, confocal microscopy, electron microscopy, animal, and high-throughput drug screening facilities, etc., available at UNM HSC. The ASC focuses on high content microscopy for adherent cells (Cellomics) and for cells in suspension (Amnis), to quantitatively analyze in a highly rigorous manner (and thus promote reproducibility in research) autophagic profiles as well as other subcellular structures and changes. The IMC focuses on inflammatory (e.g. Amnis in its flow cytometry mode) and metabolic measurements (e.g. Seahorse, etc.). The AIM center has a development program to update and acquire new instruments over time. The instrumentation is covered by service contracts and appropriate user charges will be implemented in support of extended service contracts in the out years. The cores are supervised by core directors and daily operations (user scheduling, user training, and equipment maintenance) are carried out by the core technical director with users following clearly defined and web-accessible standard operating procedures. Importantly, the principal model for access to core instrumentation by AIM members, associate members, and affiliated members is not based on charges during the first several years, but rather by establishing a membership user base, with any charges being implemented in the out years as described above or for external non-member users from the outset. Because fixed specimens (e.g. cells in 96 well plates), can be shipped, AIM is prepared to provide service not just locally but also nationally and internationally via collaborative agreements.

Modes of growing the base and promoting autophagy research

The AIM center has pilot programs and announces Requests for Applications (RFA) that are offered at least twice a year. These can be themed or investigator

initiated, depending on the RFA, but are focused on autophagy and its intersections with other areas. The pilots stimulate autophagy research locally. Another process is hiring faculty through a national/international search for tenure-track Assistant Professors. These are usually triggered upon graduation of an mPI, when she or he acquires independent R01 or equivalent funding. The corresponding funds, in the amount (depending on circumstances) close to an R01-level funding, are then transferred to newly appointed mPIs. Mentors and mentees are also encouraged to collaborate and publish together, which further expands autophagy research to include more senior investigators. Finally, international collaborations fostered through ICAM are expected to provide a home to and a role for ICAM affiliate members and intend to integrate the AIM center within the international community of autophagy scholars.

Events, meetings, symposia and workshops

The AIM center has bi-weekly Tuesday AIM seminars (TAIMs). TAIMs are envisioned to be somewhat different than a conventional seminar series. First, formal presentations are 30 min, whereas the second half of an hour-long TAIM's meeting is reserved for informal discussions and mingling. The presentations at TAIMs are a mix of work in progress with raw data, a venue for presentation by potential associate members, summary of technical advances and equipment capabilities organized by cores' leadership, journal clubs, and a venue for progress presentations given by the mPIs.

Every year, the AIM center plans an annual symposium, where AIM members and invited speakers present their work and seminars, whereas trainees present posters or give short platform talks. Some of the annual meetings will be formatted as workshops and will include both practical and theoretical components and will drawing on the pool of speakers from the ICAM and other sources.

Dissemination of information

Events at, and news from, AIM that are of general interest to the international autophagy community are disseminated through the AIM center via its web site (<https://www.autophagy.center>), Twitter (www.twitter.com/AIM_autophagy) and Facebook (www.facebook.com/aimautophagy). Blog capabilities for active discussions are under development.

Present and evolving research at the AIM center

The research programs at the AIM center include mPIs funded projects centered on autophagy, but also addressing inflammation or metabolism as well as their interconnections. The more senior personnel have a diverse portfolio of research funded independently of the AIM center. Through collaborative efforts, it is expected that the majority of senior investigators will find synergy with the central theme of the center. Once mPIs "graduate" they remain as AIM members, and their role as contributors to the AIM center community of scholars is expected to remain permanent. Continued participation by former mPIs in AIM research activities, collaborations, and events and group activities will ensure continuing

connection with AIM and support from AIM will depend on maintaining such relationships and collegiality. New recruits at the level of Assistant Professors on tenure track will be brought into the system and their work will infuse the AIM center with evolving new directions that they will bring with them. This mechanism avoids stagnation and should ensure a dynamic research portfolio keeping up with the most recent research trends and technologies.

Future of the AIM center

The AIM center had a grand opening event in March 2018, with Randy Schekman delivering the keynote lecture, followed by a reception. Renovations of the floor on which AIM is located are underway. Two mPIs have already graduated, i.e. obtained their independent R01 grants, and faculty searches for new mPIs are underway. As noted above, the AIM symposium planned for 2019 will be associated with the autophagy Keystone Symposia meeting in Santa Fe. In other years, a subset of ICAM affiliate members will be invited for workshops or symposia. In some instances, there will be practical courses and demonstrations of new technologies. The AIM center is expected to contribute to the scientific progress in the area of autophagy, both fundamental and applied/translational, and enhance output and funding in the areas of autophagy, inflammation, and metabolism, through publications and funding, enabling junior investigators to achieve significant independent funding, and continuing replenishment of faculty ranks. It will strive to become a hub for national and international research in autophagy, enabling independent careers of junior faculty in a supportive, inviting and cooperative environment for which the international autophagy community has always been famous. Given that the mechanism of funding provides options for 3 phases each of 5 years in duration, the impact of the AIM center on the local, national and international scene may provide constant service and an intellectual gathering place over the next 15 years.

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