

**Stellungnahme zum
Leibniz-Institut für Altersforschung – Fritz-Lipmann-Institut e. V.
(FLI), Jena**

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Vorbemerkung

Die Einrichtungen der Forschung und der wissenschaftlichen Infrastruktur, die sich in der Leibniz-Gemeinschaft zusammengeschlossen haben, werden von Bund und Ländern wegen ihrer überregionalen Bedeutung und eines gesamtstaatlichen wissenschaftspolitischen Interesses gemeinsam gefördert. Turnusmäßig, spätestens alle sieben Jahre, überprüfen Bund und Länder, ob die Voraussetzungen für die gemeinsame Förderung einer Leibniz-Einrichtung noch erfüllt sind.¹

Die wesentliche Grundlage für die Überprüfung in der Gemeinsamen Wissenschaftskonferenz ist regelmäßig eine unabhängige Evaluierung durch den Senat der Leibniz-Gemeinschaft. Die Stellungnahmen des Senats bereitet der Senatsausschuss Evaluierung vor. Für die Bewertung einer Einrichtung setzt der Ausschuss Bewertungsgruppen mit unabhängigen, fachlich einschlägigen Sachverständigen ein.

Vor diesem Hintergrund besuchte eine Bewertungsgruppe am 13. und 14. Oktober 2016 das FLI in Jena. Ihr stand eine vom FLI erstellte Evaluierungsunterlage zur Verfügung. Die wesentlichen Aussagen dieser Unterlage sind in der Darstellung (Anlage A dieser Stellungnahme) zusammengefasst. Die Bewertungsgruppe erstellte im Anschluss an den Besuch den Bewertungsbericht (Anlage B). Das FLI nahm dazu Stellung (Anlage C). Der Senat der Leibniz-Gemeinschaft verabschiedete am 11. Juli 2017 auf dieser Grundlage die vorliegende Stellungnahme. Der Senat dankt den Mitgliedern der Bewertungsgruppe und des Senatsausschusses Evaluierung für ihre Arbeit.

1. Beurteilung und Empfehlungen

Das Leibniz-Institut für Alternsforschung – Fritz-Lipmann-Institut e. V. (FLI) in Jena betreibt biomedizinische Grundlagenforschung mit dem Ziel, die molekularen Mechanismen des menschlichen Alterns sowie alternsassoziierter Erkrankungen zu entschlüsseln. Die Arbeiten dienen dazu, Grundlagen für die Entwicklung neuer Therapien zu bieten und sind damit von großer gesellschaftlicher Relevanz.

Die Bewertungsgruppe bewertete vier der insgesamt fünf thematischen Teilbereiche des Instituts einmal als „sehr gut bis exzellent“ und dreimal als „sehr gut“. Es wurde festgehalten, dass die **wissenschaftlichen Leistungen** international in hohem Maße wettbewerbsfähig sind. So wurde etwa die Etablierung der kurzlebigen Fischart *Nothobranchius furzeri* als neues Wirbeltiermodell für die Alternsforschung maßgeblich durch Wissenschaftlerinnen und Wissenschaftler in der *subdivision 4: (epi)genetics and models of aging* vorangetrieben und bildet inzwischen die Grundlage für zahlreiche Folgeprojekte im Hause sowie mit Partnerinstitutionen im In- und Ausland.

Den fünften, vom Direktor des FLI geprägten Teilbereich (*subdivision 1: stem cell aging*) bewerteten die Sachverständigen als „exzellent“. Wesentliche Grundlagen, die diese hohe Bewertung begründeten, sind inzwischen jedoch entfallen.

¹ Ausführungsvereinbarung zum GWK-Abkommen über die gemeinsame Förderung der Mitgliedseinrichtungen der Wissenschaftsgemeinschaft Gottfried Wilhelm Leibniz e. V.

Am 15. Juni 2017 veröffentlichte das Präsidium der Leibniz-Gemeinschaft die Ergebnisse einer Überprüfung von Vorwürfen wissenschaftlichen Fehlverhaltens gegen den Direktor. Ein Untersuchungsausschuss, den das Präsidium im November 2016 eingesetzt hatte, stellte Verstöße gegen die Regeln guter wissenschaftlicher Praxis in Publikationen fest. „Zu all diesen Verstößen konnte es kommen, weil Herr Rudolph [der Direktor des FLI] über einen Zeitraum von mehr als 5 Jahren seine Aufsichtspflicht als Arbeitsgruppenleiter (und hauptverantwortlicher *senior author*) verletzt hat. [...] Da erst hierdurch die zahlreichen Mängel der durch den Untersuchungsausschuss betrachteten Publikationen, welche das Ausmaß gelegentlich vorkommender, versehentlicher Fehler deutlich übersteigen, möglich wurden, bewertet der Untersuchungsausschuss die Verletzung der Aufsichtspflicht als Arbeitsgruppenleiter und hauptverantwortlicher Autor durch Herrn Rudolph als grob fahrlässig.“ Das Präsidium der Leibniz-Gemeinschaft erteilte aufgrund der Untersuchungsergebnisse eine schriftliche Rüge „wegen grob fahrlässigen wissenschaftlichen Fehlverhaltens“. Es beschloss weitgehende Sanktionen gegen den Direktor des FLI, die sich auch auf das Institut insgesamt auswirken, z. B. den Ausschluss des FLI unter der Leitung von Herrn Rudolph vom Wettbewerbsverfahren der Leibniz-Gemeinschaft für drei Jahre. Das Leibniz-Präsidium erwartet zudem umgehend Veränderungen am FLI, um künftig die Einhaltung der Standards guter wissenschaftlicher Praxis zu gewährleisten.²

Das FLI gab in der Evaluierungsunterlage, auf deren Grundlage die Sachverständigen die Arbeiten bewerteten, 52 Originalbeiträge in Zeitschriften mit Begutachtungssystem als Leistungsnachweise der die *subdivision 1* tragenden Arbeitsgruppen an, daneben neun *reviews* (Erscheinungsjahre 2013-2016). Bei 36 der Originalbeiträge wird der Direktor als einer der Verfasser genannt, bei 10 dieser 36 Publikationen wird er allein oder gemeinsam mit einem anderen Verfasser als hauptverantwortlicher Autor ausgewiesen. Die Überprüfung der Vorwürfe bezog sich u. a. auf sechs dieser 10 Veröffentlichungen. Der Untersuchungsausschuss stellte in jeder dieser sechs Publikationen Verstöße gegen die Regeln guter wissenschaftlicher Praxis fest.

Bei der Bewertung der *subdivision 1* hoben die Sachverständigen die Arbeiten des Direktors besonders hervor. In diesem Teilbereich arbeiten aber – wie der Senat nachdrücklich hervorhebt – auch viele Wissenschaftlerinnen und Wissenschaftler mit, die von den Untersuchungen zu wissenschaftlichem Fehlverhalten nicht betroffen sind und deren Leistungen insofern auch nicht in Frage zu stellen sind.

Für die wissenschaftlichen Arbeiten aller *subdivisions* werden wichtige **Forschungsinfrastrukturen** am FLI vorgehalten. Dazu gehören auch die Einrichtungen für die Züchtung und Haltung von Versuchstieren, überwiegend Mäuse und Fische. Die räumlichen Kapazitäten für die Maushaltung wurden 2013 annähernd verdoppelt.

² Vgl. „Stellungnahme der Leibniz-Gemeinschaft zum Bericht des Untersuchungsausschusses zur Überprüfung von Vorwürfen wissenschaftlichen Fehlverhaltens“ vom 13. Juni 2017, veröffentlicht am 15. Juni 2017 auf der Website der Leibniz-Gemeinschaft. – Dem Senatsausschuss Evaluierung lag über die publizierte Stellungnahme des Präsidiums hinaus gemäß Beschluss des Präsidiums der vollständige Bericht des Untersuchungsausschusses zur vertraulichen Kenntnisnahme vor.

Allerdings führten grundlegende Vorwürfe zu Fehlverhalten beim Umgang mit Tierversuchen zur Rücknahme von zahlreichen Tierversuchsgenehmigungen sowie zu weiteren behördlichen und staatsanwaltlichen Ermittlungen, die im Mai 2016 begannen und noch andauern. In Reaktion auf die staatlichen Untersuchungen und eine vom Institut selbst bereits im März 2016 in die Wege geleitete externe Beurteilung der Tierversuchseinrichtungen wurden die Organisation und die Leitung der Tierhäuser grundlegend neu geordnet. Dies führte bereits zur Wieder- und Neugenehmigung von Tierversuchsvorhaben durch die zuständige Behörde.

Die neuen Regelungen und Maßnahmen werden auch von der Bewertungsgruppe und vom Senat als geeignet angesehen, um Fehlentwicklungen in Tierzucht und -haltung zu vermeiden. Es wird aber nach Abschluss aller laufenden Ermittlungen zu prüfen sein, ob weitere Änderungen erforderlich sind. Es ist eine zentrale und laufende Aufgabe für Leitung, Beirat und Aufsichtsgremium, die Beachtung und Umsetzung der Regelungen und Maßnahmen sicherzustellen. Die Sachverständigen äußern sich positiv zur Förderung des wissenschaftlichen Nachwuchses. Es wird allerdings auf die Verantwortung des Instituts in Bezug auf die Promovierenden verwiesen, deren Arbeitsprogramm angesichts von zurückgezogenen Tierversuchsgenehmigungen geändert werden muss.

Die geschilderten, auf jeweils unterschiedliche Weise äußerst kritischen Sachverhalte sind vor dem folgenden Hintergrund zu beurteilen:

Das heutige FLI war 2001 vom Wissenschaftsrat als leistungsschwach beurteilt worden. Es wurde eine vollständige Neuausrichtung und Neustrukturierung gefordert. In den Jahren 2003 bis 2012 leitete ein erfahrener und engagierter Wissenschaftler das FLI. Der Senat stellte bei der letzten Evaluierung 2008 fest, dass unter seiner Leitung eine „beeindruckende Aufbauleistung“ stattgefunden habe. Er verantwortete die konzeptionelle Fokussierung auf die molekulare Alternsforschung, die sich auch in einem neuen Institutsnamen niederschlug, schuf neue Strukturen z. B. in der Nachwuchsförderung und erreichte eine bemerkenswerte Dynamik und Internationalisierung des Instituts. Erhebliche bauliche Erweiterungen im Jahr 2013 im Bereich der Tierhaltung (s. o.) und unmittelbar für die Forschung wurden in seiner Amtszeit vorbereitet.

Wie die Bewertungsgruppe nun feststellt, entwickelte der seit 2012 amtierende Direktor das FLI auf diesen ausgezeichneten Grundlagen weiter. Strategische Schwerpunkte setzte er vor dem Hintergrund seiner eigenen Vorarbeiten bei den Themen Stammzellaltern und Organerhalt. Für die nächsten Jahre war eine Stärkung der Translation in die klinische Praxis vorgesehen. Außerdem soll ein neuer Bereich „Mikrobiota und Altern“ mit zusätzlichen Mitteln der institutionellen Förderung geschaffen werden. Die Sachverständigen bewerteten diese, vor allem zur Stärkung der Arbeiten in der *subdivision 4* geplante Erweiterung als thematisch innovativ und förderungswürdig.

Der Senat würdigt, dass am FLI auch in den Jahren seit der letzten Evaluierung 2008 vielfältige positive Leistungen erbracht wurden. Er sieht das Institut derzeit jedoch in einer gravierenden und grundlegenden Krise. Das nachgewiesene Fehlverhalten erschüttert die wissenschaftliche Integrität des Direktors und führt zu einem grundlegenden Autoritätsverlust. Das Aufsichtsgremium muss Wege finden, um die Führungskrise am FLI schnellstmöglich zu überwinden. Die Aufgabe einer neuen und unbelasteten

Führung wird es sein, im Anschluss an unverzüglich erforderliche Maßnahmen zur Sicherung der Regeln guter wissenschaftlicher Praxis die wissenschaftlichen und organisatorischen Strukturen des Instituts angemessen zu reformieren. Eine Ausweitung der institutionellen Förderung für einen neuen Bereich „Mikrobiota und Altern“ zu beantragen wird vor dem Hintergrund der positiven Bewertung durch die Sachverständigen eine Möglichkeit sein.

Die Verantwortlichen müssen die Krise des FLI zügig überwinden, damit es seine vollständige wissenschaftliche Leistungsfähigkeit zurückerhält. Das FLI widmet sich mit seinen Arbeiten zu wesentlichen Fragen der lebenswissenschaftlichen Altersforschung einem Thema von hoher gesellschaftlicher Relevanz. In der intensiven Bündelung und in der Form können sie an einer Hochschule nicht erfüllt werden. Eine Eingliederung in eine Hochschule wird daher nicht empfohlen. Die Förderung des FLI als Einrichtung von überregionaler Bedeutung und gesamtstaatlichem wissenschaftspolitischem Interesse ist weiterhin gerechtfertigt. Der Senat möchte in drei Jahren erneut zum FLI Stellung nehmen.

2. Zur Stellungnahme des FLI

Der Senat hat die Stellungnahme des FLI zum Bewertungsbericht zur Kenntnis genommen.

3. Förderempfehlung

Der Senat der Leibniz-Gemeinschaft empfiehlt Bund und Ländern, das FLI als Einrichtung der Forschung und der wissenschaftlichen Infrastruktur auf der Grundlage der Ausführungsvereinbarung WGL weiter zu fördern.

Ferner empfiehlt der Senat, die nächste Überprüfung der Fördervoraussetzung bereits nach drei Jahren (2020) vorzusehen.

Annex A: Status report

Leibniz Institute on Aging – Fritz Lipmann Institute e. V., Jena (FLI)

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1. Structure, tasks and institutional environment

Development and funding

In the aftermath of the German reunification, two research institutes emerged from the former GDR-based Central Institute for Microbiology and Experimental Therapy: the Hans Knöll Institute for Natural Product Research – and the Institute for Molecular Biotechnology (IMB) which became a member of the Leibniz Association in 1997. In 2004, the institute shifted its focus to biomedical research on human aging, and, consequently, assumed a new name: Leibniz Institute for Age Research – Fritz Lipmann Institute (FLI). In 2015, after refocusing again, the institute's name was adjusted to Leibniz Institute *on Aging* – Fritz Lipmann Institute (FLI).

FLI was last evaluated in 2008. Based on the recommendations of the Leibniz Senate and a joint statement by the responsible departments at federal and *Länder* (state) level, the Joint Science Conference confirmed that FLI meets the requirements for joint funding.

Responsible department at *Länder* level: Thuringian Ministry of Economy, Science and the Digital Society

Responsible department at federal level: Federal Ministry of Education and Research

Legal form and organization

FLI has the legal status of a registered association (e. V.). Its relevant executive bodies are the Members Assembly, the Board of Trustees, the Board of Directors, The Assembly of Research Group Leaders, the Institute Council and the Scientific Advisory Board.

The Members Assembly is composed of representatives of the University of Applied Sciences Jena, the Friedrich Schiller University Jena, the city of Jena and the Thuringian Ministry of Economy, Science and the Digital Society. It approves the budget and actions of the Board of Trustees and the Board of Directors.

FLI's Board of Trustees has up to nine members with voting power. It consists of representatives of the responsible departments at *Länder* and federal level, of Friedrich Schiller University Jena and from Science and Economy. Non-voting members are the chairperson of the Scientific Advisory Board as well as his or her deputy. The Board of Trustees supervises the management of the FLI. It is responsible for defining the general research focus and for deciding on the mid-term financial and investment planning of the institute.

FLI's Scientific Advisory Board (SAB) is composed of six to twelve external scientists and representatives of industry. Members are appointed for four years and can be reappointed once. The SAB advises both the Board of Trustees and the Scientific Director on scientific and technical issues. It is also responsible for the evaluation of FLI's scientific results (see Chapter 7).

The Board of Directors consists of the Scientific Director and the Administrative Director. It represents and leads the institute and manages the allocation of human and financial resources according to the guidelines provided by the Board of Trustees.

The Assembly of Research Group Leaders meets with the Board of Directors at least once every quarter to exchange and agree, among other things, on research and development programs, research collaborations and institutional issues.

In agreement with the Assembly of Research Group Leaders the Scientific Director nominates up to four senior group leaders for two-year terms in the Institute Council. Additional members are one representative elected by the junior group leaders and the Head of Core. The Institute Council meets regularly (at least on a monthly basis) in order to advise the Board of Directors on important scientific decisions.

Mission and tasks

According to its statutes, FLI's mission is to promote research and science in the field of aging. The institute's main objective is to unravel basic mechanisms that lead to impairments in stem cell function and organ maintenance during aging. It aims at providing a foundation for the development of future therapies that extend the health span – the proportion of life that can be spent in preferably optimal health.

Research structure

FLI's organizational structure is characterized by a flat hierarchy with senior (tenured) and junior (tenure track) research groups being the relevant organizational units (cf. Appendix 1: Organizational Chart). Apart from a majority of in-house groups the institute also features cooperation groups with other institutions (part-time employment at FLI) as well as associated groups.

Each research group (for details see Chapter 3) works primarily in one out of five interconnected thematic Subdivisions (but also contributes to others) from two major Program Areas:

Program Area I: Stem Cell Aging and Organ Maintenance

1. Stem Cell Aging
2. Organ Maintenance in Aging

Program Area II: Accumulation of Molecular Damages and (Epi)Genetics of Aging

3. Molecular Damages in Aging
4. (Epi)Genetics and Models of Aging

One Subdivision is currently being developed and is supposed to connect and contribute to both program areas:

5. Systems Biology of Aging

Scientific services and infrastructures provided to all research groups are organized in the section

6. Facilities and Services

National and international scientific environment

FLI names the following important institutions in Germany that also work on aging but have largely complementary foci:

- Max-Planck Institute on the Biology of Aging, Cologne
- Cologne excellence cluster on aging-associated diseases (CECAD)
- German Center for Neurodegenerative Diseases (DZNE), Bonn
- Max-Planck Institute for demographic research, Rostock
- Leibniz Research Institute for Environmental Medicine (IUF), Düsseldorf
- Medical Faculty, Ulm University

Additionally, age-related research on individual diseases is conducted at different institutions throughout Germany. This encompasses, for example, research on diabetes at the German Institute of Human Nutrition (DIFE), the German Diabetes Center (DDZ) and the Helmholtz Center Munich (HMGU) as well as research on cardiovascular diseases at the Max Planck Institute for Heart and Lung Research, the Max Delbrück Center for Molecular Medicine and the Universities of Giessen and Frankfurt.

On the European level, FLI highlights the following institutions:

- Institute for Research on Cancer and Aging, Nice (France)
- Newcastle University (GB)
- European Research Institute for the Biology of Ageing (ERIBA), Groningen (Netherlands)

Here, FLI sees the largest overlap in scientific research areas with the ERIBA, which is a collaboration partner of the institute.

Finally, on the intercontinental level, according to FLI, the Buck Institute on Aging, Novato, California (USA) and the Institute of Aging at Hangzhou Normal University (China) have a similar research focus; both institutes are collaboration partners of FLI. Also, scientifically closely related are, amongst others, groups at Harvard Stem Cell Institute, Baylor College of Medicine, University of California and Stanford University.

National interest and justification for funding as a non-university institution

According to the institute, increasing the health span will be the most important contribution that aging research can make to modern societies characterized by high average life expectancies, which often come at the cost of a phase of morbidity in the last decade of a person's life. FLI points out that in 2004, it was the first national institute in Germany to devote its research to aging. Since then, the importance of this subject has led to the establishment of several other institutes focusing on aging research (see above). According to the institute, however, it has developed a unique research focus on impairments in stem cell function and organ maintenance, concentrating on the molecular, genetic, and epigenetic causes leading to these deficiencies.

The institute illustrates that research teams at FLI are international and interdisciplinary, cooperating in the areas of genetics, epigenetics, molecular damages, comparative and functional genomics, and computational biology. According to FLI, results are based on the long-term development of new models and methodologies in the framework of strategic, goal-oriented research programs on aging, which is hardly possible within the usual capacities of a university. An example illustrating this fact is the newly developed model for aging research, the short-lived African killifish, *Nothobranchius furzeri*. The FLI started the development of this new model of aging research in 2006 and reported on the aging characteristics of this model system since then including last year's publication on the genome assembly of *N. furzeri*, which is now available to the scientific community.

2. General concept and profile

Development of the institution since the last evaluation

After the introduction of aging as the new research focus in 2004, FLI first took a rather broad scientific perspective ranging from comparative genomics, structural biology, endocrinology, development and neurobiology to cancer. Following a central recommendation of the last evaluation, starting in 2012, the new director focused the institute's aging-related work on aging-associated impairments in stem cell function and organ maintenance in order to establish a profile complementary to upcoming other aging research institutions. FLI points out that all group leaders are involved in shaping the scientific focus of the institute via the Assembly of Group Leaders and the Institute Council (cf. Chapter 1). In May 2013, a new research building was completed, doubling the institute's research space.

Since the last evaluation, in order to implement the new research focus, seven out of currently thirteen research groups at FLI were newly recruited. These changes were accompanied by the career development of former Junior Group Leaders at FLI, which moved into group leader positions in other institutions. Specifically, 4/6 former Junior Group Leaders (including one fellow) moved into Group Leader positions in Germany and international institutions. Changes at senior group leader level were as follows:

- Three senior research groups were closed down due to retirement.
- One senior group leader accepted a university position elsewhere.
- One senior group was discontinued because of the new research focus.
- One senior group leader passed away prematurely; his group is currently led by a provisional head until the end of 2016.

According to the new focus, FLI organized its research in the before-mentioned two program areas and five thematic Subdivisions (see Chapters 1 and 3). FLI has also restructured its scientific services and infrastructures into independent "Core Facilities" and "Core Service" units (see Chapter 3 and 4.6.).

Results

According to the institute, despite this intense restructuring process performance measures remained stable and even showed an upward trend. In the period 2013-2015, FLI published a total of 310 articles in peer-reviewed journals (see Appendix 2). This amounts to an annual average of 1.4 peer-reviewed publications per full-time equivalent in “research and scientific services” (excluding doctoral candidates), as compared to 1.0 in the period 2005-2007. The institute states that the annual cumulative impact factor of all publications has approximately doubled from 401 to 802 since the last evaluation in 2008; 34 % of all FLI publications in 2013-2015 appeared in journals with an impact factor of seven or higher. FLI scientists were asked to write reviews or comments for journals like *Cell*, *Nature Cell Biology*, *Trends in Genetics* or *Cell Stem Cell*. In the period 2013-2015, 48 % of FLI publications appeared under open access policy.

One of the lighthouse projects of the last few years was the establishment of the short-lived fish *Nothobranchius furzeri* as a new vertebrate aging model. Related research from FLI scientists led to the initial characterization of various aging markers, provided first proof-of-principle experiments demonstrating lifespan extension, supplied the genome sequence and paved way to genetic manipulation. According to the institute, the project also triggered an increasing number of scientific collaborations and led to FLI organizing and hosting the *Nothobranchius* symposium in June 2016. As another lighthouse project, the institute highlights the JenAge systems biology program funded by the Federal Ministry of Science and Education (BMBF, 2009-2014). This collaborative initiative attempted to combine computational science with genetics and biological sciences on aging of multiple species. The aim was to identify genetic networks that could preserve organ maintenance during aging. It resulted in 28 FLI-authored publications and led to the establishment of the new research Subdivision “Systems Biology of Aging” (cf. below and Chapters 3 and 4.5.) and the acquisition of an advanced grant of the European Research Council (“StemCellGerontoGenes”, 2013-2018).

Scientific services (cf. Chapter 3) are provided by FLI’s Core Facilities and Core Services to collaborating external partners (10-20 % of users).

Scientific consultancy activities involve participation in panel discussions, support of exhibitions as well as review board activities, for example for the German research foundation (DFG).

According to FLI, the institute has intensified attempts at knowledge and technology transfer, resulting in numerous efforts towards commercialization (see Appendix 2). To increase success rates, FLI has launched an internal training and support program for transfer-projects (“SPARK@FLI”), which is based on the concepts of the SPARK program at Stanford University. It is designed to:

- (a) provide seed-funding for translational projects aiming to develop patents and inventions of FLI scientists to a level allowing the transfer of the project to industry partners or spin-out companies. Projects are selected by an external Industry Advisory Board.
- (b) help understanding clinical needs, develop a target product profile and strengthen project management abilities of candidate projects.

The institute currently supports three translational research projects by seed-funding and three other projects with technical support.

Academic events and public relations

In the period 2013-2015, FLI organized altogether 21 conferences and workshops in the field of aging, molecular damages and stem cell research, including Gordon conferences, Else-Kröner Fresenius symposia, the 2nd international meeting on *N. furzeri* as a new model of research on aging, and the annual meetings of the German Foundation for Aging Research (DGfA).

In order to professionalize communications and public relations, FLI established a new staff position (2014) and employed a new head of communications (2015). One major project was to define a corporate identity as the basis of a consistent corporate design and a uniform communication layout (2015). According to the institute, the number of press releases on publications, awards or institutional issues has increased significantly since 2014. FLI participated in a number of events for introducing aging research to a broad audience (Long Night of Sciences, MS Wissenschaft, Girl's & Boy's Days, UniStem Day).

Restructuring of Animal Facilities and compliance crisis

The Institute states that the Animal Facility is instrumental for many groups at FLI for studying basic processes of organismal aging. With the completion of a new research building in 2013, the Mouse Facility has been extended to about twice its former capacity and also the Fish Facility will be restructured and extended during 2017 (see also Chapter 3). Because of this increase in size and changing regulatory requirements (EU legislation), the institute planned to implement a new management structure to the Animal Facilities. Until May 2016, according to FLI, control visits by the state authorities have not indicated any insufficiencies. Also, in March 2016, an evaluation of the Animal Facilities by external reviewers acknowledged high standards of animal husbandry, but also recommended to change the organization and management of the facility.

This need for structural change has been enforced in May 2016 by the start of an investigation by the State Criminal Police Office and the state authorities which was triggered by accuses of misconduct of animal experiments in some cases. According to FLI, these cases are currently under investigation. A detailed and up-to-date progress report will be provided to the review board just before the on-site visit.

In connection with the investigations, the institute received notification from the state authorities that changes to the organization, structure and management of the Animal Facility are immediately required if animal experiments are to be continued at FLI. The institute states that, accordingly, the following structural and personnel changes have either already been implemented or will be implemented soon:

- A veterinarian was recruited from outside the institute as a new head of the Animal Facility.

- A second veterinarian was recruited to head the supervision of animal welfare regulations. This ensures the separation of the Animal Facility management from animal welfare supervision as required by German legislation.
- A third veterinarian will be recruited to implement and monitor standard operating procedures and a quality measurement system for breeding and keeping animals and for conducting animal experiments.
- An External Advisory Board for the Animal Facility was established featuring four experts from major animal facilities in Germany.
- An internal Animal Committee consisting of users, animal caretakers and veterinarians was established to discuss the restructuring of the Animal Facilities.
- Training courses for group leaders, scientists and technical personnel are supposed to ensure that all parties involved in animal experiments have the necessary knowledge.
- An ethics discussion round on the need for animal experiments in aging research and about the possible optimization and reduction of animal experiments is planned.

Strategic work planning for the next few years

In 2014, FLI began to build up a fifth Subdivision on “Systems Biology of Aging” (see Chapter 3). The main focus is the analysis of interactions between different systems in aging at multiple scales (molecules, subcellular structures, cells and tissue). Accordingly, Subdivision 5 is also meant to enhance the cooperation between Subdivisions 1 to 4. As the future head of the Subdivision, it was decided to recruit a senior group leader focusing on “Computational Biology of Aging”; the position is expected to be filled by end of 2016.

In order to focus future work on the functional analysis of molecular damages in aging, NMR- and X-ray-based structural work in Subdivision 3 (“Molecular damages in aging”) was decided to be discontinued. Instead, anticipating the retirement of the “Biochemistry” senior group leader in 2017, FLI intends to recruit a new group continuing functional studies on DNA damage in aging.

Furthermore, FLI plans to apply for additional institutional funding in order to establish a new research area on “Microbiota and Aging” (see below). The respective research groups are supposed to be incorporated into Subdivision 4 about “(Epi)Genetics and Models of Aging” but also meant to contribute to the other Subdivisions.

Appropriateness of facilities, equipment and staffing

In 2015, FLI’s institutional funding (excluding construction projects) was approximately 26.0 M€. Some 4.1 M€ were obtained from project grants (corresponding to 14 % of the overall budget, as compared to 13 % in 2007), including high profile single investigator awards, such as an ERC advanced grant and an Emmy-Noether Research Award from the DFG. Against the background of a recommendation of the last evaluation to increase the proportion of third-party funds in the overall budget (see Chapter 6, recommenda-

tion 14), FLI points out that despite of its high turnover in leadership personnel (see above), third-party funding remained stable over the last years. In order to increase the funds obtained from project grants in third-party funds, FLI introduced a system of performance-dependent budget allocation (cf. Chapter 6) and recruited a staff scientist as coordinator for third-party funding.

No revenue from services such as commissioned work, publications or patents was generated in the reporting period (for details see Appendix 3). The above described SPARK-initiative is supposed to generate revenues in the coming years.

FLI's facilities are distributed over ten buildings on the Beutenberg Campus in southern Jena. The once tense spatial situation significantly improved with completion of a new research building in 2013 (FLI 1), more than doubling the institute's floor space. FLI expects lab and office space to be fully sufficient as soon as the upcoming modernization of two buildings from the 1950s (FLI 2, 3) as well as the conversion of the NMR building (FLI 6) into a new fish facility and a state of the art purchasing and goods receive department is finished.

According to the institute, the technological equipment of its cell and molecular biology laboratories meets the requirements of the research groups and animal facilities. The laboratories are compliant with the constructional and technical prerequisites of safety level S1; additionally, FLI operates three safety level S2 laboratories. Major technology platforms are organized in Core Facilities (see Chapter 3 for details). In order to efficiently handle and analyze the large quantities of scientific data generated e. g. by DNA sequencing, proteomics, bioinformatics or microscopy, FLI maintains a high-performance computing infrastructure and data network as well as a dedicated storage system with regular backups.

Since 2010, the staff appointment scheme applies only to leading positions and non-tariff employees. This flexibility allowed for the establishment of new positions, especially in the service sector (for example in animal keeping and research coordination), and an upgrade to the pay scale of technical assistants, which was necessary due to the change of requirements in the research groups. Nevertheless, no more than 40 % of the institute's total expenses must be spent on permanent staff (current rate: approx. 26 %; for more information on staffing issues see Chapter 5 and Appendix 4).

Temporary extraordinary item of expenditure "Microbiota and Aging"

FLI plans to apply for temporary, additional institutional funding in order to establish a new research area on "Microbiota and Aging". This is supported both by the institute's Board of Trustees and its Scientific Advisory Board. The new research area is supposed to be incorporated into Subdivision 4 about "(Epi)Genetics and Models of Aging" but is also meant to contribute to the other Subdivisions (cf. Chapter 3 and 4.4.) and to bolster the interaction in research on aging at the FLI with neighboring Friedrich Schiller University, Jena University Hospital, MPI for Chemical Ecology and Leibniz Institute for Natural Product Research and Infection Biology (HKI). In addition, FLI envisions the new research area to bridge Jena-based research on aging with research on host-pathogen interactions in infectious diseases and biodiversity – and to support current CRC initia-

tives in these areas and in research on aging as well as the planned application for a Cluster of Excellence in Jena.

According to the institute, both literature and preliminary results from FLI studies show that microbiota have strong effects on stem cell function, organ function and organismal aging. In order to address these in a systematic manner, FLI plans to install three new research groups:

- (1) Senior group on “Metagenomics & Microbiota/Host Interactions in Aging”
- (2) Junior group on “Metabolomics and Metabolite Signaling”
- (3) Junior group on “Microbiota induced Alterations in (Epi)Genetics”

For the implementation of the new research area, FLI estimates overall financial requirements of 4,997 K€ for funding of the senior group and the technical equipment (+ own contribution: 3,081 K€ for funding of the junior groups) in the period 2019-2022. In detail, transient extraordinary funding is required for:

- Senior group – personnel costs of 1,867 K€ for
 - 1 group leader position (E15),
 - 2 Postdoc positions (E13 and E14),
 - 2 PhD positions (E13/2) and
 - 2 Technical assistant positions (E9).
- Senior group – consumables costs of 530 K€
- Costs for technical equipment required for microbiome-linked analysis (mass spectrometry, chromatography, next generation sequencing, laboratory equipment, computers and software) of 2,600 K€

Co-Funding from the Institute’s budgets will cover:

- 2 Junior groups – personnel costs of 2,345K € for
 - 2 group leader positions (E15),
 - 2 Postdoc positions,
 - 2 PhD positions and
 - 2 Technical assistant positions.
- Junior groups – consumables 360 K€
- Animal costs and metabolome analysis costs of 376 K€

The co-funding will be provided by the FLI re-allocating 3 % of its core budget to establish the two junior research groups in succession of Matthias Platzer who is expected to retire in 2018. With the anticipated retirement of another senior group leader in 2023-2025, the institute plans to ensure continuous funding also for the new senior group after temporary additional funding ended.

3. Subdivisions of FLI

Research at FLI is organized in five Subdivisions (cf. Chapter 1). The institute points out that these represent common topics and interests of individual research groups rather than administrative sub-structures. Thus, Subdivisions are strongly interconnected and most of the research groups contribute to more than one Subdivision.

Subdivision 1: Stem Cell Aging (average 2013-2015: 15.5 FTE in research and scientific services, 9.7 FTE doctoral candidates, 7.3 FTE service staff)

Research group (bold: primary groups)	Status	Period	FTE
K. Lenhard Rudolph	senior, head	since 2012	20.2
Julia von Maltzahn	junior	since 2013	2.7
Cristina González-Estévez	fellow	since 2013	1.7
Claudia Waskow	designated W2 tenure track	starting 2017	—
Peter Herrlich	emeritus	since 2012 (scientific director 2003-2011)	4.2
Aspasia Ploubidou	guest group	since 2016 (junior group 2005-2015)	3.5
Heinrich Jasper	cooperating (Buck Institute, USA)	since 2015	0.2
Florian Heidel	cooperating (UKJ)	since 2015	—

Contributing (FLI Subdivision): Christoph Englert (2), Björn von Eyss (2), Zhao-Qi Wang (3), Alessandro Cellerino (4), Francesco Neri (4), Matthias Platzer (4), Alessandro Ori (5)

Subdivision 1 was initiated in 2012 when the newly appointed director started to implement the institute's new research focus on stem cell aging. It is strongly connected to Subdivision 2 ("Organ Maintenance in Aging"). Work in Subdivision 1 aims for delineating basic molecular mechanisms as well as genetic and epigenetic mechanisms that prevent stem and progenitor cell dysfunction or the initiation and clonal dominance of mutant stem and progenitor cells during aging. For this purpose, prominent somatic stem-cell compartments in hematopoietic organs, brain, gut and skeletal muscle are studied using relevant animal models from invertebrates to vertebrates, up to humanized mouse models engrafted with human hematopoietic stem and progenitor cells. Current focus areas in Subdivision 1 are:

- (a) *Cell-intrinsic mechanisms limiting the function of aging stem and progenitor cells*
- (b) *Aging-associated alterations of stem cell niches and the systematic environment limiting stem and progenitor cell function*

In the period 2013-2015, researchers in Subdivision 1 published 62 articles in peer-reviewed journals. Both candidate genes and pathways were studied but researchers also employed unbiased approaches coupled with reverse genetic screens to identify unknown cell-intrinsic factors and signaling pathways that limit the functional capacity of stem cells in the context of aging. Several groups investigated the impact of the micro-environment and systematically acting factors on stem and progenitor cell function during aging.

Work planning in Subdivision 1 aims at extending the analysis of mechanisms of human stem cell aging by focusing on the below projects and by employing humanized mouse models installed by the recruitment of C. Waskow in the beginning of 2017 and the collaboration group of F. Heidel employed at the University Hospital Jena since the beginning of 2016. Both group leaders are third-party funded W2 professors within the ProExcellence program of the state of Thuringia. Most important future projects include:

- Functional analysis of aging-related genes (Gerontogenes) in stem cell aging (ERC advanced grant project)
- Development of humanized animal models, allowing experimental study of the biology of human stem cell aging in vivo
- Exploring the interconnection between cell-extrinsic and cell-intrinsic processes factors that influence stem cell aging in close collaboration with the new Systems Biology of Aging Subdivision

Additionally, the thematic range of Subdivision 1 is supposed to be extended by the topics of “Initiation and clonal dominance of mutant stem and progenitor cells in aging” and “Microbiota impacting on impairments in stem cell function during aging”. For the implementation of the latter, FLI plans to apply for extra funding in the framework of a temporary extraordinary item of expenditure (see Chapter 2 for details).

Subdivision 2: Organ Maintenance in Aging (average 2013-2015: 15.1 FTE in research and scientific services, 10.3 FTE doctoral candidates, 6.7 FTE service staff)

Research group (bold: primary groups)	Status	Period	FTE
Helen Morrison	senior, head	since 2015 (junior 2006-2014)	9.4
Christoph Englert	senior	since 2004	10.3
Björn von Eyss	junior	since 2016	—
Ronny Hänold	provisional head of former Weih group	since 2014 (at FLI since 2004)	7.1
Heike Heuer	former junior	2004-2014	3.3
Cornelius Calkhoven	former junior	2005-2013	1.9
Jan Tuckermann	former junior	2004-2013	0.2
<u>Contributing (FLI Subdivision):</u> Peter Herrlich (1), Julia von Maltzahn (1), K. Lenhard Rudolph (1), Claudia Waskow (1), Florian Heidel (1), Christoph Kaether (3), Zhao-Qi Wang (3), Maria Ermolaeva (4)			

Since the last evaluation, three group leaders of Subdivision 2 were promoted to tenured positions at other institutions. At the same time, one junior group leader was promoted into a tenured position at FLI and became the head of Subdivision 2 in 2015; additionally, one junior group leader was newly recruited. The overarching goal of Subdivision 2 has evolved over recent years to investigate basic mechanisms underlying the failure in organ maintenance during aging rather than disease specific mechanisms. Complementary to Subdivision 1, major subjects are non-stem cell compartments, micro-milieu conditions and systematically acting signaling pathways. Specific organ systems are covered by the expertise of individual group leaders and include skeletal muscle, kidney, brain, the peripheral nervous system, the intestine and the immune system. Focus areas of Subdivision 2 are:

- (a) *Drifts in developmental pathways limiting organ maintenance in aging*
- (b) *Immune aging and inflammation*
- (c) *Systemic and micro-milieu regulators of organ maintenance, regeneration and disease development*

In the period 2013-2015, researchers in Subdivision 2 published 72 articles in peer-reviewed journals. The combined results of research groups working on the central nervous system, skeletal muscle and kidney led to the discovery of a number of developmental pathways that are part of an intrinsic signaling network required for life-long maintenance of different tissues and organs. Research was also devoted to the delineation of how molecular damages and cellular senescence impinge on immune aging and, vice versa, how immune aging influences the accumulation of molecular damages and senescent cells in tissues. Finally, several former groups at FLI investigated the role of

systemic regulators of organ maintenance and how alterations of these maintenance pathways could affect organ maintenance, regeneration and disease development during aging.

Future research in Subdivision 2 is supposed to concentrate on:

- How developmental signaling networks are regulated during aging, what alterations occur and how this impinges on organ maintenance and aging
- The basic mechanism of immune aging as well as on inflammatory response and immune responses triggered by molecular damages and senescent cells
- Investigations on systemic changes that impact on organ maintenance and regeneration of brain, peripheral nerve, muscle, gut and liver
- A new focus on mechanisms that promote aging-associated alterations in the microbiome and its consequences for stem cell function (cf. Subdivision 1), organ maintenance and organismal aging (see Chapter 2 for details)

Subdivision 3: Molecular Damages in Aging (average 2013-2015: 20.0 FTE in research and scientific services, 6.0 FTE doctoral candidates, 11.5 FTE service staff)

Research group (bold: primary groups)	Status	Period	FTE
Zhao-Qi Wang	senior, head	since 2006	10.1
Frank Große	senior	since 1995	7.4
Christoph Kaether	senior	since 2011 (junior 2005-2011)	7.4
Matthias Görlach	former senior, now Head of Core	1999-2015	5.5
Manuel Than	former junior	2006-2015	4.0
Stefan Diekmann	former senior	1992-2014	3.1
<u>Contributing (FLI Subdivision):</u> Peter Herrlich (1), Aspasia Ploubidou (1), K. Lenhard Rudolph (1), Maria Ermolaeva (4), Francesco Neri (4), Alessandro Ori (5)			

The aim of Subdivision 3 is to study causes and consequences of DNA and protein damages in aging cells and tissues, the structure-function relationship of biomolecules relevant to damage processes as well as responses to molecular damage that might lead to pathologies in aging. It is linked to Subdivisions 1 and 2. Since future work in Subdivision 3 is supposed to focus on functional analysis of molecular damages in aging rather than on resolving molecular structures, FLI decided to discontinue NMR- and X-ray-based structural work. The former “Biomolecular NMR spectroscopy” group leader was appointed as the head of Core Facilities and Services (see below). Focus areas of Subdivision 3 are:

(a) *DNA repair and DNA replication*

(b) DNA damage responses

(c) Cellular senescence

(d) Chromosomal stability and ploidy control

(e) Protein trafficking, proteostasis and protein damages

In the period 2013-2015, researchers in Subdivision 3 published 89 articles in peer-reviewed journals. Work in Subdivision 3, among other things, revealed certain essential genes to have a previously unknown function in neurons as well as a new layer of cross-talk between different protein repair pathways. Further subjects included DNA damage-induced senescence and the functional impact of senescence signaling and telomere shortening. Also, chromosome segregation and aneuploidy as well as growth and differentiation pathways regulating tissue architecture were studied. Investigations were conducted on the structure-function relationship and physiologic interaction partners of a protein relevant to the development of Alzheimer's disease.

Planned projects in Subdivision 3 encompass:

- Canonical and non-canonical function of early DNA damage response (DDR) molecules in neurodegeneration
- Characterization of changes of the epigenome and DNA structure in response to DNA damage
- Uncovering novel genes and pathways implicated in DNA damage-induced stress tolerance in *Caenorhabditis elegans*
- The role of the accumulation of damaged proteins, subcellular organelles and other macromolecules in aging

Additionally, based on explorative studies, FLI wants to extend the focus of Subdivision 3 by the topic of "Biophysical parameters related to molecular damages" dealing with biophysical properties in regulating cellular stress responses in the context of molecular damages and during aging. Due to the upcoming retirement of the "Biochemistry" group leader in 2017, FLI plans to recruit a new group continuing functional studies on DNA damage in aging.

Subdivision 4: (Epi)Genetics and Models of Aging (average 2013-2015: 9.2 FTE in research and scientific services, 3.0 FTE doctoral candidates, 7.1 FTE service staff)

Research group (bold: primary groups)	Status	Period	FTE
Matthias Platzer	senior, head	since 2004	14.5
Maria Ermolaeva	junior	since 2015	0.8
Francesco Neri	junior	since 2016	—
Alessandro Cellerino	cooperating (Pisa University, Italy)	since 2010 (junior 2007-2010)	2.3
Ion Cirstea	former fellow	2012-2016	1.6
Manuela Marz	cooperating (FSU)	since 2015	—

Contributing (FLI Subdivision): Cristina González-Estévez (1), Heinrich Jasper (1), Lenhard Rudolph (1), Christoph Englert (2), Hans Kestler (5), Alessandro Ori (5)

After implementing a research program on “Genomics in Aging” in 2004, today’s Subdivision 4 employs comparative genomics and functional genetics to identify genetic and epigenetic factors that influence the accumulation of molecular damages, stem cell function and organ maintenance during organismal aging, thus connecting Subdivisions 1 to 3. Applied short-lived animal models involve nematodes, fish and rodents. In order to also include long-lived species, since 2011, FLI has established collaborations to investigate naked mole-rats and related species through comparative genomic and transcriptomic approaches. Current work is concentrated on two focus areas:

(a) *Comparative (epi)genomics in short- and long-lived models of aging*

(b) *Functional (epi)genetics of aging and aging-related diseases*

In the period 2013-2015, researchers in Subdivision 4 published 86 articles in peer-reviewed journals. Major results were the genomic and functional analysis of the short-lived killifish *N. furzeri* and its establishment as a new model for aging research (see also Chapter 2). According to FLI, in combination with genome editing by CRISPR/Cas, this model provides a platform for rapid exploration of aging and diseases in a short-lived vertebrate. Moreover, *C. elegans* was introduced as an additional model organism, allowing for genome-wide phenotype-based forward genetic screens.

In future work, FLI plans to combine comparative genomics for the identification of new genes and pathways related to stress resistance, aging and longevity in short- and long-lived species with reverse genetic approaches for proving the functional involvement of candidate genes and pathways. Projects in Subdivision 4 will include:

- Forward genetic screens in *C. elegans* in order to identify gene mutations which protect against physiological stressors relevant for aging

- Study of genes positively selected in association with evolutionary lifespan shortening of *Nothobranchii* by genome editing and transgenesis in fish and other models
- Epigenome, transcriptome, translome and proteome analyses of short- and long-lived models to identify and functionally characterize biomarkers predictive for longevity and health span

Furthermore, FLI plans to extend the work program of Subdivision 4 by the topics of “Stochastics and cell-to-cell heterogeneity in aging” and “Microbiota and aging”. For the implementation of the latter, FLI plans to apply for extra funding in the framework of a temporary extraordinary item of expenditure (see Chapter 2 for details).

Subdivision 5: Systems Biology of Aging (average 2013-2015: 3.3 FTE in research and scientific services, 0.1 FTE service staff)

Research group (bold: primary groups)	Status	Period	FTE
N. N.	senior, head	to be recruited	—
Alessandro Ori	junior, provisional head	since 2015	0.3
Jürgen Sühnel	former senior	1993-2014	2.0
Hans Kestler	Cooperation group (University of Ulm)	since 2016 (senior group at FLI 2014-2016)	1.2

Contributing (FLI Subdivision): Heinrich Jasper (1), Julia von Maltzahn (1), K. Lenhard Rudolph (1), Christoph Englert (2), Helen Morrison (2), Christoph Kaether (3), Alessandro Cellerino (4), Maria Ermolaeva (4), Francesco Neri (4), Matthias Platzer (4), Stefan Diekmann (3)

Through its „GerontoSys“ program, the Federal Ministry of Science and Education (BMBF) in 2009-2014 funded a FLI-led collaborative systems biology project with Friedrich Schiller University, Jena University Hospital and Leibniz Institute for Natural Product Research and Infection Biology (HKI). As a consequence, the Jena Centre for Systems Biology of Aging (JenAge) was established in 2009 (cf. Chapter 4), ultimately triggering the implementation of a new research Subdivision in 2014. Subdivision 5 is still under development since the leader of the new “Systems Biology of Aging” senior group accepted a university position shortly after starting at FLI; according to the institute, negotiations with a successor are already under way. Meanwhile, in 2015, a new junior group leader was recruited contributing expertise in mass spectrometry-based proteomics and computational approaches for the analysis and integration of large-scale datasets. His group is currently focusing on proteome alterations that occur in aging organs and adult stem cells.

The aim of Subdivision 5 is the analysis of interactions between different systems in aging at multiple scales (molecules, subcellular structures, cells and tissues). Currently, the Subdivision’s major focus area is:

(a) Multi-species and integrated multi-omics analysis of aging organs and organisms

In the period 2013-2015, researchers in Subdivision 5 published 22 articles in peer-reviewed journals. Major results during recent years were obtained by the JenAge consortium focusing on the identification of conserved networks activated by mild stress and their role in preserving functional integrity in old age.

In order to bridge the gap between research at different biological scales as conducted in the other Subdivisions and to ultimately reveal the impact of specific alterations on the overall organism fitness, future work in Subdivision 5 is planned to contribute to two topics: In a “Multi-scale analysis of aging”, molecular alterations will be studied to understand the impact of genome and chromatin organization, cell organelles and the stoichiometry of protein complexes on aging. Additionally, studies of the “Role of higher order regulation of the genome in aging” will be devoted to basic principles in the area of DNA shape and higher order structure as well as its influence on biological function, such as transport control.

Facilities and Services (average 2013-2015: 8.9 FTE in research and scientific services, 41.3 FTE service staff)

FLI’s scientific services and infrastructures are provided to all research groups (approx. 80-90 % in-house use) as well as to collaborating external users. In the period 2013-2015, all facilities and services contributed to 61 % of FLI’s peer-reviewed research publications. Following a conceptual review by an external scientific panel in 2012, FLI started to reorganize these central units – formerly run by individual research groups – in independent Core Facilities (CF), Core Services (CS) and Animal Facilities. In the course of this restructuring process, FLI decided to discontinue the two former structural biology units (NMR spectroscopy and X-ray crystallography) in favor of new facilities and the further development of existing technologies (see below).

CF and CS are subject to a uniform organizational structure: Altogether, facilities and services are managed by the “Head of Core” who is also a member of the Institute Council and the Group Leader Assembly (cf. Chapter 1). On the next level, both CF and CS are each run by a dedicated manager. Additionally, each CF is supervised by one of the research group leaders.

Currently, FLI provides the following Core Services:

- i) Histology, Pathology & Electron Microscopy
- ii) Protein Production
- iii) Isotope Laboratory
- iv) Gamma Irradiation Chamber
- v) Small Animal Computer Tomography
- vi) S2 Safety Level Laboratories
- vii) Media Preparation

The institute maintains the following Core Facilities:

- i) *CF Bioinformatics* – The facility is currently growing into 2 full time researcher to prove basic and customized analysis of big data sets and screens. Due to the growing adoption of quantitative methods in biomedical research, which leads to an increasing demand for computational biology and the analysis of “big data”, FLI plans to further develop the CF (to be led by the new senior group leader in “Computational Biology of Aging”, see above) for the analysis and integration of high-throughput data.
- ii) *CF DNA Sequencing* – The facility provides next-generation DNA sequencing technology. The institute intends to keep up with the rapid technological development in the field and plans to extend the current methodological focus on transcript based expression in terms of translation, epigenetic regulation, spatial genome organization, metagenomics and metabolomics.
- iii) *CF Proteomics* – The facility provides a complete platform for the identification and quantification of proteins using mass spectrometry. Since December 2015 it is equipped with a state-of-the-art liquid chromatography / mass spectrometer system.
- iv) *CF Imaging* – The CF provides the infrastructure for state-of-the-art light microscopy and is specialised in live cell microscopy to monitor molecular and cellular dynamics in space and time. It maintains several widefield and confocal as well as modern STED and lightsheet microscopes.
- v) *CF Functional Genomics* – The facility performs high-throughput image-based experiments combined with RNAi and provides technical expertise and support in high-content analysis microscopy for the quantitative analysis of cellular phenotypes. The CF’s set-up allows for performing small and large-scale functional screens on the cellular level. The available siRNA libraries will be expanded to include shRNA-based approaches. The CF will also contribute to building up libraries for in vitro and in vivo screens based on CRISP/CAS9 targeting technologies together with the animal facilities (see below).
- vi) *CF Flow Cytometry* – The facility carries out flow cytometric analysis and sorting of cells. It also provides the expertise and instrumentation for sorting of small living organisms and organoids.
- vii) *CF Technology Transfer* – The CF (“SPARK@FLI”) has recently been established following the example of the Stanford University SPARK initiative (cf. Chapter 2). The unit is initially planned for two years and will be reviewed for future continuation.

According to FLI, due to the complexity of organism aging, animal experiments remain essential to understand the role of genes and pathways in organismal aging and to explore the possibility of lifestyle interventions or gene targeting to influence the stem cell function, organ maintenance and health parameters in aging. For this purpose, FLI maintains two Animal Facilities:

- i) *Mouse Facility* – Since 2008, 18 out of 25 FLI research groups have been carrying out experimental studies using mouse models. These include transgenic, knock-

out, knock-in and wild type mice. After a recent extension, the mouse facilities can now host up to 7,200 cages of which approximately 4,500 are currently occupied. In the aftermath of a recent compliance crisis (see Chapter 2), the Mouse Facility is currently being restructured to re-ensure compliance with regulations on documentation and animal welfare.

- ii) *Fish Facility* – The purpose of this facility is the maintenance and breeding of the killifish (*N. furzeri*) species and zebrafish (*Danio rerio*). It is also used to generate and maintain transgenic fish of both species and serves as an experimental area. Currently, the facility houses a total of 12,000 zebrafish and 2,200 killifish and operates at 80 to 90 % occupancy. In order to gain more flexibility and capacities for future experiments as well as for the involvement of additional research groups in the fish program, FLI plans a major reconstruction and expansion of the Fish Facility in 2017/2018.

4. Collaboration and networking

Collaborations in Jena

FLI is closely embedded in the science environment of the Beutenberg Campus in southern Jena and collaborates both with the Friedrich Schiller University (FSU) and the Jena University Hospital (UKJ) – see Chapter 5 for joint appointments, teaching and educational collaboration – as well as with non-university institutions such as the Leibniz Institute for Natural Product Research and Infection Biology (HKI) and the Max Planck Institute for Chemical Ecology (MPI-CE).

The institute highlights the following collaborative projects with FLI involvement:

- Interdisciplinary “Aging Research Center” at FSU, encompassing research activities from life sciences, mathematics, social sciences and humanities with a focus on questions of aging, demographic change and the challenges and opportunities of this change for both society and the individual
- “Jena Centre for Systems Biology of Ageing – JenAge”, a collaborative systems biology project with FSU, UKJ and HKI established in 2009 and funded through the GerontoSys initiative of the German Federal Ministry of Education and Research (BMBF)
- “Leibniz ScienceCampus Regenerative Aging” co-founded by the Leibniz Association and the “ProExzellenz Initiative” of the State of Thuringia, allowing the recruitment of three new W2 associate professorships and one W3 full professorship at FLI, UKJ and FSU (see below)

Other collaborations and networks

FLI is involved in two large Leibniz networks. It co-initiated the Leibniz Research Alliance “Healthy Ageing” with the Leibniz Research Institute for Environmental Medicine (IUF), bringing together 21 Leibniz institutes in the fields of biology, medicine, psychology, education, sociology and economics. Also, the institute is a member of the Leibniz

Research Alliance “Bioactive Compounds and Biotechnology” with 17 institutions performing research on molecules with biological effects. Altogether, 46 publications originated from collaborations with other Leibniz Institutes from 2013 to 2015. Within the Leibniz Association, HKI is FLI’s closest collaboration partner (23 joint publications between 2013 to 2015); other partner institutions are the Leibniz Institute for Zoo and Wildlife Research (IZW), the Leibniz Institute for Neurobiology (LIN), and the Leibniz Institute for Molecular Pharmacology (FMP).

Amongst other networking projects FLI highlights the following:

- “Jena Center for Bioinformatics” – Funded by the BMBF from 2001-2008, the project still continues its work with an emphasis on the organization of seminars and workshops. Involved groups are from FLI (four groups), FSU, HKI, MPI-EC, the University of Applied Sciences Jena and several companies.
- “Naked Mole-Rat Project” – Funded by the Leibniz Association from 2012-2014, the collaborative project with the Leibniz Institute for Zoo and Wildlife Research (IZW) in Berlin and the Washington University in St. Louis, USA, aimed at identifying molecular networks responsible for a long life in good health by employing naked mole-rats as a species with an extraordinary long lifespan.
- “DNA Damage Responses in Aging” – This collaboration with the Leibniz Institute for Molecular Pharmacology in Berlin, the Leibniz Research Institute for Environmental Medicine in Düsseldorf and the Leibniz Institute for Neurobiology in Magdeburg was funded by the Leibniz Association from 2014-2016. Within the same funding line, FLI also participated in the projects “Decline of Cognitive Functions during Physiological Aging” and “Role of Proteostasis in Cellular Aging”.

Additionally, FLI lists international collaborations with institutions in Bulgaria, Canada, China, Denmark, France, Italy, New Zealand, the Netherlands, the UK and the US, featuring e. g. the establishment of an international research campus “LeibnizLink on Healthy Aging” with scientists at Hangzhou Normal University (China). According to FLI, 51 % of its publications include contributing authors from foreign institutions (joint publications).

Between 2013 and 2015, 106 scientists from other institutions stayed at FLI, 20 of these for longer than three months. In the same period, 60 FLI scientists visited other host institutions, four of these for longer than three months.

5. Staff development and promotion of junior researchers

Staff development and personnel structure

On 31 December 2015, FLI employed 268 people. This corresponds to 233.1 full time equivalents, 102.0 of which were assigned to research and scientific services, 111.6 to service positions and 19.6 to administration (see Appendix 4 for details). From 2007 to 2015, the number of employees in science and administration remained largely the same, while FLI increased the staff in facility and building management, team secretariats and coordination (see Chapter 6, recommendation 8).

FLI commits itself to fair and transparent recruitment and appraisal procedures. For this purpose, the institute introduced both operation agreements on job advertisement procedures (*Betriebsvereinbarung Stellenausschreibungen*) and staffing procedures (*Leitfaden Stellenbesetzungsverfahren für Chancengleichheit und Vereinbarkeit Familie und Beruf*).

Due to the retirement of the former director in 2012, a new director was identified by an external selection committee and appointed in March 2012. Including the director, who is also heading a research group, currently, four out of seven senior group leaders hold joint appointments with the FSU. According to FLI, it is planned for three additional group leaders to hold joint appointments in the near future:

- Head of the planned “Computational Biology of Aging” group in Subdivision 5 “Systems Biology of Aging” (W3)
- Head of the planned “(Trans-)Differentiation in Aging and Disease” group in the framework of the “Leibniz ScienceCampus Regenerative Aging” (W3)
- Group leader within Subdivision 1 “Stem Cell Aging” (tenure-track W2, the candidate, C. Waskow, has accepted the position to start in spring 2017)

After the appointment of the new director, an internal search committee was installed and five new junior research group leaders were recruited along the lines of the institute’s new research focus. In general, junior group leaders receive an initial five year contract at FLI, a fixed consumable budget and a group of one postdoc, one PhD student and a technician. The initial contract can be extended for another four years after positive evaluation by outside experts and if supported by the SAB. In principle, all junior group leaders can be tenured upon final evaluation at the end of the eighth year. Additionally, FLI awarded two “Career Development Fellowships” for 3 + 1 years with smaller staff and budget allocations for scientists at the beginning of their independent careers; currently, the fellow program is on hold to evaluate its success before deciding about continuation. One of the two fellows has recently accepted a junior group leader position at a university.

According to FLI, special emphasis is put on the internationalization of the institute staff. For this purpose, FLI places advertisements for PhD positions internationally, provides assistance to foreign researchers and their families when relocating and offers internal language courses in German and English. Between 2013 and 2015 an average of 24 % of all employees came from abroad, as opposed to an average of 16 % between 2008 and 2010. The proportion of PhD students from outside Germany increased from 28 % to 52 %; currently, five out of twelve researchers in leading positions come from abroad.

Promotion of gender equality and family-friendliness

On 31 December 2015, 55 % of the institute’s 268 employees were female (33 % in research and scientific services, 63 % in service positions). Approximately 33 % of the PhD students were women and 35 % of the postdocs (i. e. all scientists holding a PhD but not a group leader position). Currently, three out of twelve research group leaders are female. According to the institute, this ratio will probably change to four out of 15 consid-

ering upcoming changes on the leadership level (see above). Measures taken to enforce gender equality include the definition of flexible target quotas for female scientists using the cascade model as well as a “Welcome Back Fellowship” for female scientists after parental leave.

In order to improve family-friendliness, FLI offers flexible working hours, a parent-child room as well as childcare during institute events. The institute negotiated the allocation of a quota of places to children of institute employees in nearby kindergartens.

Promotion of junior researchers

FLI group leaders as well as postdocs are involved in teaching at FSU (mostly at the Faculty of Biology and Pharmacy) both at undergraduate and graduate level. In turn, bachelor and master students regularly join the institute’s laboratories to conduct their thesis work. Between 2013 and 2015, FLI members supervised 39 bachelor and 52 master or diploma theses from FSU, the Jena University of Applied Sciences (EAH Jena) and other German universities. In order to attract students from abroad, FLI offers master students from three Chinese and one Bulgarian university the opportunity to conduct their thesis work during a twelve to eighteen-months research stay at the institute.

In the period 2013-2015, 46 doctoral degrees were completed at FLI. Initial PhD contracts are issued for one year but usually extended to three years. Further extension to four years is possible if recommended by the internal thesis committee; in special cases, such as parental leave, extension to a maximum of 4.5 years can be conceded. The average duration of a PhD project at FLI until thesis submission is approximately 4.2 years. Irrespective of their financial support, all PhD students are integrated into the “Leibniz Graduate School on Aging and Age-related Diseases” (LGSA), which was initiated in 2007 as a joint initiative of FSU and FLI. The LGSA provides structured training and supervision, e. g. in weekly work-in-progress seminars, scientific or key competence courses. Additionally, FLI groups participate in four structured PhD programs:

- DFG-funded Research Training Group “Molecular Signatures of Adaptive Stress Responses” (since 2012) and
- Research Training Group on Protein Modifications in Aging “ProMoAge” (since 2016)
- EU-funded Marie Curie Initial Training Networks – “Chronic DNA Damage in Ageing” (CodeAge) and the “MARie curie AGEing Network” (MARRIAGE)

Between 2013 and 2015, FLI hosted a total of 114 postdocs. A self-organized PostdocClub, financially supported by FLI, helps to arrange advanced training and information exchange. In 2015, a postdoc network on “Aging Induced Impairments of Regeneration and Stem Cell Functionality – RegenerAging” (funding from the Leibniz Association) with five postdoc positions was established aiming at structuring the period between PhD and a potential junior group leader position. FLI sees this initiative as a blueprint for improving postdoctoral education in the Leibniz Association and other scientific institutions, as it is one of Germany’s first structured postdoctoral programs. In addition, a postdoctoral training network for clinician scientists was initiated recently in

collaboration with the UKJ and with funding from the Kröner-Fresenius Foundation. In this program, FLI intends to train clinician scientists for postdoctoral studies in stem cell aging, organ maintenance and genetics of aging. The institute also highlights its junior groups as an important measure of career development (see above).

Vocational training for non-academic staff

Since 2005, FLI offers a training program for biology laboratory technicians. Since 2009, it also trains animal caretakers in research and clinical practice with two apprentice positions every year. Between 2013 and 2015, four biology laboratory assistants and five animal caretakers completed their vocational training at the institute.

Management personnel, for example in the Core Facilities, is regularly trained on current law amendments. Extra-occupational further training is supported in science management, facility management, personnel management and accounting.

6. Quality assurance

Internal quality management

FLI refers to structured measures of quality control such as weekly in-group lab seminars and institute-wide work-in-progress seminars for all students, postdocs and includes group leader talks in the future; PhD projects are evaluated on a yearly basis by dedicated internal committees. The same system is implemented for postdocs at the Leibniz-funded Postdoc Network. The establishment of a quality management system for grant application is planned.

Rules for good scientific practice were implemented in 2008; compliance with the regulations is supervised by an ombudsperson. Once a year, courses on good scientific practice are offered to students and postdocs. Participation is mandatory for all PhD students at the institute.

Since 2006, FLI maintains a performance-dependent budget allocation, which was reorganized in 2014 so that every group now has a core budget for research, which can be increased or reduced according to publication records and raised third-party funds. In case of newly recruited groups, a 10 % bonus on grant income is paid. These will enter the aforementioned system after completion of 5 years at the institute. Additionally, all research groups are evaluated in five-year intervals by a board of external reviewers.

Quality management by the Scientific Advisory Board and User Advisory Board

The Scientific Advisory Board (SAB) an independent body, which recruits its members according to their own judgment, is responsible for the evaluation of FLI's scientific projects. For its annual meetings, the institute provides reports on achievements, ongoing developments and future plans. The SAB also advises the director on the regular research group evaluations, appoints the external reviewers (see above), and conducts a survey of the institute (called "audit") for the Board of Directors, the Board of Trustees and the Thuringian Ministry for Economic Affairs, Science and Digital Society every year.

Implementation of recommendations from the last external evaluation

FLI responded to the recommendations of the last external evaluation (highlighted in italics, see also statement of the Senate of the Leibniz Association from 27 November 2008) as follows:

1. *The concept of age research is still a rather new feature on the international research landscape. It is in the nature of things that, taken as a whole, the criteria for including or excluding certain issues and topics are currently also controversially discussed in academia. As the leadership and staff are aware, the FLI must play an active role in this process of developing a novel research field. This means that the FLI must remain open to and stay abreast of new developments in the relevant established disciplines on the one hand, while honing its own profile on the other so that it retains its singularity considering the increasing competition in this new research field from other newly established research institutes, such as the Max Planck Institute for the Biology of Aging in Cologne and the Helmholtz Centre for Neurodegenerative Diseases in Bonn. Given all the decisions to be made in connection with contents and personnel, achieving an effective balance is a difficult and challenging task. However, the FLI is well-equipped to deal with this task satisfactorily.*

FLI developed a research program focusing on stem cell aging and impairments in organ maintenance including the basic molecular, genetic and epigenetic factors underlying these processes (see Chapter 2).

2. *Particularly against this backdrop, which requires the FLI to sharpen its profile in the growing area of age research, it is understandable that the institute wants to intensify its links to clinical research in the context of developing its mission. The planned emphasis in the FLI's general concept on investigating age-related diseases, in particular the planned establishment of a Leibniz Research School for Clinician-Scientists, is therefore most welcome and should be pursued.*

Although the planned Leibniz Research School for Clinician-Scientists was not approved, according to FLI, a research focus on aging was successfully pursued together with the Friedrich Schiller University and the University Hospital Jena (UKJ) after the last evaluation. Recently, the establishment of a Leibniz ScienceCampus focusing on "Regenerative Aging" together with UKJ was approved, supporting, among other things, a tenured professorship. Additionally, funding for several graduate schools and a postgraduate program on aging was raised.

3. *Bioinformatics, a technique that is becoming more important, should be applied at FLI more in the coming years. The FLI's idea "to set up a database for aging research" is basically worth pursuing, but is currently still in its infancy and the concept must be prepared more precisely and intensively. Working together with scientists from Jena University is a convincing approach.*

After the last evaluation the Jena Center for Systems Biology of Aging (JenAge) was established with five FLI research groups contributing. Within this effort the aging factor database AgeFactDB (agefactdb.jenage.de) was established and maintained, aiming at the collection and integration of ageing phenotype and lifespan data. After the external

funding had expired, the institute decided to continue and institutionalize its work on bioinformatics by building up a new Subdivision “Systems Biology of Aging” (see Chapter 3).

4. *It is necessary to improve publication performance in some working groups.*

According to FLI, discontinuation of underperforming groups during the refocusing process of the institute as well as performance-dependent budget allocations helped to increase the overall publication performance. The institute states that the annual cumulative impact factor has doubled since the last evaluation and, currently, all groups have strong publication records.

5. *The FLI's national and international contacts should be augmented. It is recommended that the FLI should increase the number of foreign visiting scientists financed by the institute. The number of FLI scientists visiting research institutions abroad should also be increased.*

According to FLI, a frequent exchange of visiting scientists with institutions in several European countries, in China and the US was established (for numbers of guest visits see Chapter 4). In order to increase the numbers of both foreign visiting scientists and FLI scientists visiting institutions abroad, the introduction of mandatory research visits as a measure of career development within the newly established postdoc network is planned by the institute.

6. *On the whole, the present installment, set up and combination of large equipment required for scientific investigations is almost appropriate. Scientifically well-founded arguments to upgrade the present NMR spectroscopy are supported. It is not only the FLI that benefits from NMR spectroscopy, also other research institutions in Jena use the FLI NMR set up in terms of joint projects, as for example via the Collaborative Research Centre 604. Apart from NMR spectroscopy, it has been strongly suggested that the potential synergies of various research institutions in Jena might be exploited more intensively by joint acquisition of large equipment.*

Due to its new research focus, FLI decided to discontinue its NMR program. Access to NMR spectroscopy, e. g. for completion of a remaining NMR project at FLI, is provided by the newly formed NMR center at the University in Jena. According to the institute, redundant resources were instead utilized for establishing state of the art proteomics, functional genomics and microscopy imaging as well as for the expansion of animal facilities.

7. *Automatic sequencing is important for most working groups at the FLI and should therefore be consolidated by the provision of adequate personnel.*

FLI points out that next-generation sequencing was consolidated both with new technical equipment and personnel. A new core facility with one staff scientist, an engineer and a technician was established. In addition to the current head, leader of the Genome Analysis group, the new professor in systems biology of aging is supposed to play a part in running the facility.

8. *The FLI's administration functions extremely effectively and efficiently. The FLI's growth in the last few years legitimates moderate expansion of the administration.*

The administration was subject to a moderate increase in personnel from 17.9 FTE in 2007 to 22.3 FTE in 2015. A need for further expansion was backed by an external evaluation of the institute's administration in April 2016: "[...] the reviewers consider a significant increase in personnel for the Administration for the coordination area between Administration and Science absolutely necessary (inevitable)."

9. *The current director will soon be retiring and stepping back from this position. Ongoing negotiations to appoint a successor must be concluded quickly. The providers of funds are aware that it is essential to fill the position in spring 2009.*

A new director was appointed in the beginning of 2012. Until then, the former director kept his position.

10. *The FLI is planning to set up further junior research groups. This is a welcome development. Care should, however, be taken to ensure that the increase in the number of junior research groups should not introduce an imbalance in relation to the number of working groups already headed by established scientists.*

According to FLI, its target ratio of tenured and non-tenured research groups is 50/50; it is currently almost met.

11. *In the medium term, attempts should be made to recruit younger research group leaders at the FLI.*

FLI points out that the age of the five newly recruited junior group leaders was between 34 and 36 at the time of employment.

12. *The FLI should continue to make efforts to recruit female researchers to executive positions.*

According to FLI, the recruitment of female researchers for leading positions is actively supported. Three out of six tenure track group leaders are female and one female former junior group leader was recently promoted into a tenured position (see Chapter 5).

13. *In order to make appropriate use of the upcoming infrastructure for keeping animals it will be necessary to increase the number of keepers significantly in future. Well-founded scientific arguments have been forwarded which justify eight further positions.*

Due to additional animal facilities and the requirements of a new animal protection law implemented in 2013, the staff in animal care taking was increased from 6.0 FTE in 2007 to 22.4 FTE in 2015 (cf. Chapter 2).

14. *It is remarkable to what extent third-party fund-raising has been increased in the last three years. However, in relation to basic funding the proportion of third-party funds is still too low. The proportion of third-party funds in the overall budget should be increased significantly in future. One of the ways of achieving this would be by utilizing the funding opportunities offered by programs at European level.*

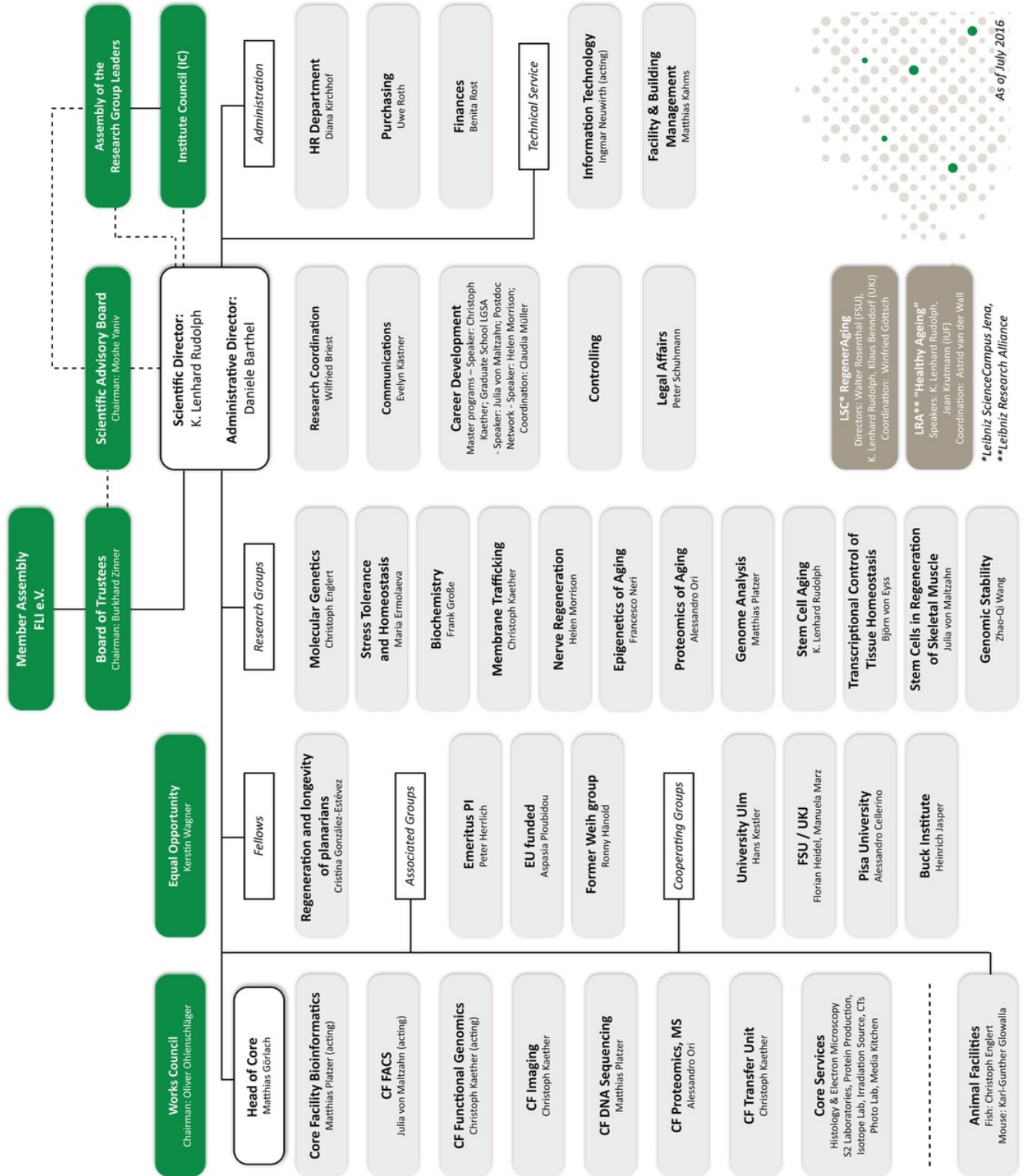
FLI points out that the sum of third-party funds increased to approximately 12 M€ over the period 2013-2015, as compared to some 8 M€ from 2005-2007. The FLI expects that its proportion of approx. 14 % of the overall budget will increase over the next years. Refocusing of the research program of the FLI led to an extensive turnover among the research group leaders with 50 % of the current group leaders being new (with a current average stay for 1.5 years) at the institute. As it takes time to fully install the new research program of new groups, the FLI expects the number of third party funds to increase to 25 % of the global budget. This expectation is supported by the recent success of the newly recruited group leaders in the acquisition of excellence funding, e. g. through the Emmy Noether program of the DFG or the Sofja-Kovalevskaja Award by the AvH foundation. The FLI was also successful in the acquisition of EU projects, e.g. an ERC advanced grant and several Innovative Training Networks on aging (MARRIAGE, CodeAge)

15. In order to enable a sound program budget to be drawn up, the providers of funds should make budgeting more flexible. In particular, the possibility of carrying budget funds forward should be extended and the binding character of staffing schedule should be loosened in accordance with the Federal Government and the Länder's minimum requirements to be met by program budgets.

Program budgeting has been introduced in 2006. The binding character of the staffing schedule was restricted to leading positions and non-tariff employees in 2010 (see Chapter 2). From 2010 onwards the providers of funds allowed up to 20 % of the institutional budget to be carried forward.

Appendix 1

Organizational Chart



Appendix 2

Publications and patents

	Period		
	2013	2014	2015
Total number of publications	88	116	111 (14)
Monographs	0	0	0
Individual contributions to edited volumes	3	3	10
Articles in peer-reviewed journals ¹⁾	84	112	100 (14)
Articles in other journals	1	1	0
Working and discussion papers	0	0	0
Editorship of edited volumes	0	0	1

Industrial property rights (2013-2015) ²⁾	Granted	Registered
Patents	5	22
Other industrial property rights	0	0
Exploitation rights / licences (number)	37	

¹ Contributions that have been accepted for publication but not yet appeared are added in parenthesis.

² Concerning financial expenditures for revenues from patents, other industrial property rights and licences see Appendix 3.

Appendix 3 Revenue and Expenditure

Revenue		2013			2014			2015 ¹⁾		
		K€	% ²⁾	% ³⁾	K€	% ²⁾	% ³⁾	K€	% ²⁾	% ³⁾
Total revenue (sum of I, II. and III.; excluding DFG fees)		41,272			36,647			37,828		
I.	Revenue (sum of I.1., I.2. and I.3)	29,454	100 %		29,325	100 %		30,195	100 %	
1.	<u>INSTITUTIONAL FUNDING (EXCLUDING CONSTRUCTION PROJECTS AND ACQUISITION OF PROPERTY)</u>	25,135	85		25,456	87		26,046	86	
1.1	Institutional funding (excluding construction projects and acquisition of property) by Federal and <i>Länder</i> governments according to AV-WGL	25,135			25,456			26,046		
1.2	Institutional funding (excluding construction projects and acquisition of property) not received in accordance with AV-WGL	0			0			0		
2.	<u>REVENUE FROM PROJECT GRANTS</u>	4,319	15	100 %	3,868	13	100 %	4,149	14	100 %
2.1	DFG	1,203		28	1,258		33	1,186		29
2.2	Leibniz Association (competitive procedure)	333		8	605		16	902		22
2.3	Federal, <i>Länder</i> governments	1,460		34	1,491		39	733		18
2.4	EU	874		20	53		1	793		19
2.5	Industry	12		0	51		1	5		0
2.6	Foundations (e. g. Deutsche Krebshilfe, Children's Tumor Foundation, Velux-Stiftung)	409		9	380		10	472		11
2.7	National and international research organizations / societies / universities	28		1	31		1	59		1
3.	<u>REVENUE FROM SERVICES</u>	0	0		0	0		0	0	
3.1	Revenue from commissioned work	0			0			0		
3.2	Revenue from publications	0			0			0		
3.3	Revenue from exploitation of intellectual property for which the institution holds industrial property rights (patents, utility models etc.)	0			0			0		
3.4	Revenue from exploitation of intellectual property without industrial property rights	0			0			0		
II.	Miscellaneous revenue (e.g. membership fees, donations, rental income, funds drawn from reserves)	7,855			7,322			6,133		
1.	Donations, sponsorship, participation fees for scientific meetings, membership subscriptions	23			66			60		
2.	Revenue from reserve fund and amount carried forward from previous year	7,832			7,256			6,073		
III.	Revenue for construction projects (institutional funding by Federal and <i>Länder</i> governments, EU structural funds, etc.)	3,963			0			1,500		
Expenditures		K€			K€			K€		
Expenditures (excluding DFG fees)		41,272			36,647			37,828		
1.	Personnel	13,105			13,932			14,311		
2.	Material expenses	8,926			8,480			10,422		
2.1	<i>Proportion of these expenditures used for registering industrial property rights (patents, utility models etc.)</i>	35			24			44		
3.	Equipment investments	1,490			4,393			5,715		
4.	Construction projects	10,294			3,437			300		
5.	Reserve, cash assets, unused funds	7,422			6,381			7,036		
DFG fees (if paid for the institution – 2.5% of revenue from institutional funding)		621			631			648		

¹⁾ Preliminary data: no

²⁾ Figures I.1, I.2 and I.3 add up to 100 %. The information requested here is thus the percentage of "Institutional funding (excluding construction projects and acquisition of property)" in relation to "Revenue from project grants" and "Revenue from services".

³⁾ Figures I.2.1 to I.2.7 add up to 100 %. The information requested here is thus the percentage of the various sources of "Revenue from project grants".

Appendix 4

Staff

(Basic financing and third-party funding / proportion of women (as of: 31/12/2015))

	Full time equivalents		Employees ¹⁾		Female employees	
	Total	on third-party funding	Total	on temporary contracts	Total	on temporary contracts
	Number	Percent	Number	Percent	Number	Percent
Research and scientific services (Core Facilities)	102.0	31.7	125.3	86.1	40.9	95.1
Professors / Direct. (C4, W3 or equivalent)	4.3	0.0	4.8	0.0	0.0	0.0
Academic staff in executive positions, including junior group leaders (E15 and E14 or equivalent)	10.3	8.7	11.7	59.4	3.9	74.0
Scientists in non-executive positions including research engineers (E14 and E13 or equivalent)	60.5	31.3	62.8	87.5	22.0	95.5
Doctoral candidates (E13, E13/2 or equiv.)	26.9	46.7	46.0	100.0	15.0	100.0
Service positions (including Core Services and Animal Facilities)	111.6	2.5	121.8			
Executive staff and scientists in Core Services and Animal Facilities	2.5	0.0	2.5			
Laboratory, Core Facilities, Animal Facilities and Core Services including engineers (E9 to E12)	35.3	1.6	37.8			
Laboratory, Core Facilities, Animal Facilities and Core Services including engineers (less than E9)	14.9	6.7	16.0			
Animal care taker	22.4	0.0	22.6			
Adviser with honorarium and commissioner functions (working and biological safety, staff council, equal opportunities, radiation protection, data protection, trainer)	5.6	0.0	9.0			
IT technology (E9 to E12)	7.0	0.0	7.0			
Facility and building management (from E5)	8.0	0.0	8.0			
Staff sections (research coordination, communication, career development, LSC, LRA) (from E13)	5.6	22.9	6.0			
Staff sections (research coordination, communication, career development, LSC, LRA) (less than E13)	0.5	0.0	1.0			
Team secretariats	9.9	0.0	12.0			
Administration	19.6	0.0	21.0			
Head of the administration	1.0	0.0	1.0			
Staff sections (from E13 and honorarium)	1.8	0.0	2.0			
Staff sections (less than E13)	1.9	0.0	2.0			
Internal administration (personnel, finances, purchasing, travel expenses) (less than E13)	15.0	0.0	16.0			
Student assistants	6.6	0.0	23.0			
Trainees	8.0	0.0	8.0			
Scholarship recipients at the institution²⁾	0.0	0.0	2.0		0.0	
Doctoral candidates	0.0	0.0	2.0		0.0	
Post-doctoral researchers	0.0	0.0	0.0		0.0	

¹⁾ Employees with multiple functions are listed in more than one category according to their respective allotment.

²⁾ No regular working hours and hence no FTE are assigned to scholarship recipients with external funding.

Annex B: Evaluation Report

Leibniz Institute on Aging – Fritz Lipmann Institute e. V., Jena (FLI)

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Appendix:

Members of Review Board and guests; representatives of collaborative partners

1. Summary and main recommendations

The Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) successfully conducts fundamental biomedical research with the aim of unravelling the molecular origins of aging. Viewed against the backdrop of demographic trends in many western industrialised countries, FLI's research, which provides the basis for developing new therapies for improving health in old age, is of great relevance both for the future and for society.

Following the retirement of the former director who was highly successful in leading the FLI, a new director was appointed in 2012. The institute's scientific agenda was consequently realigned to focus on impairments in stem cell function and organ maintenance during aging. As recommended at the last evaluation, this has paved the way for FLI to position itself alongside other aging research institutions in Germany. In the context of the continued focussing, seven of FLI's 13 current research groups were newly recruited. In five newly-established subdivisions, work on the molecular, genetic and epigenetic origins of impairments in stem cell function and organ maintenance during aging have now been bundled, allowing the research groups to relate to one another thematically. Since the last evaluation, the institute has enhanced its publication performance very effectively, both in terms of quality and quantity, with numerous publications appearing in the most eminent journals in the field. For example, the FLI established the short-lived fish *Nothobranchius furzeri* as a new vertebrate aging model. This model has now become internationally-recognised. One subdivision was rated as "excellent", one as "very good to excellent" and three as "very good".

FLI cooperates successfully on many projects with its neighbouring institutions on the Beutenberg Campus (Jena University, Jena University Hospital, Leibniz Institute HKI [Leibniz Institute for Natural Product Research and Infection Biology]). Over and above individual projects, there is an increasing tendency to integrate the age-related activities of these four facilities via institutional networks like the newly-established Leibniz ScienceCampus "Regenerative Aging". The outlook of the FLI is international and about half of the institute's publications, are the product of cooperation with foreign partners. Furthermore, more than 50 per cent of FLI's doctoral candidates come from abroad.

Overall, since the last evaluation, FLI has established itself in the maturing field of aging research in Germany. The field of aging-related stem cell research is a unique research area in which both the institute and its director have acquired an international reputation. The institute's ambitious plans for the future are convincing and welcomed.

Experiments involving animals are necessary for much of the work conducted at FLI. The opening of a new research facility in 2013 almost doubled the size of the mouse facility. In May 2016, the regional authorities responsible for authorising animal experiments and the Public Prosecutor's Office initiated an investigation in connection with the breeding and keeping of animals at FLI. In response to these ongoing investigations FLI has fundamentally reconfigured the governance of its animal facilities. The Review Board is of the opinion that the new organizational structure is appropriate to ensure

compliance. It is incumbent upon the FLI leadership, Advisory Board and Board of Trustees to continue to monitor and implement the new structure.

The main recommendations in the evaluation report are highlighted in **bold face** in the following text:

General concept and profile (Chapter 2)

1. Since the last evaluation, the institute's research has been structured in five overarching thematic subdivisions. Every research group is primarily assigned to one subdivision but may also cooperate with others to generate synergy on common topics. In order to exploit this potential to the full, in the future work in some of the subdivisions should be consolidated with greater attention being paid to overarching issues (see also Recommendations on Chapter 3).
2. FLI's ongoing efforts to promote the translation of its basic scientific insights into clinical practice via an internal training and support programme are welcomed and should be resolutely pursued. For this purpose, cooperation with Jena University Hospital in particular should be extended, for example in the field of cohort studies.
3. FLI's plans to initiate the research topic "Microbiota and Aging" are commendable. Start-up financing for this initiative based on additional funding as a temporary extraordinary item of expenditure is expressly endorsed. The total costs of approx. eight million euro estimated for the period 2019-2022 are appropriate. In view of the current relevance of the topic, it is recommended that the institute examines the possible establishment of the planned senior group before 2019. This should precede the establishment of the two proposed junior groups in order to ensure a coherent approach to the research topic.
4. FLI's plans to consolidate its collaboration with its partners on the Beutenberg Campus via the new research topic "Microbiota and Aging" are also welcome. In this context, possible interactions with the Leibniz Institute for Natural Product Research and Infection Biology (HKI), particularly in the field of genomics, should also be investigated.
5. Despite notable success in individual cases, such as the acquisition of an ERC Advanced Grant by the institute director, the contribution of third-party funding to FLI's overall income is still too low. The institute has set itself a potentially achievable target of a 25 per cent contribution from third-party income in the next years.

Subdivisions of FLI (Chapter 3)

6. In view of the institute's overarching focus, the selection of future research topics in Subdivision 3 should more firmly reflect interest in the processes of aging.
7. Subdivision 5: Systems Biology of Aging is likely to have a significant impact on the research of the entire institute. The establishment of this subdivision is crucial for the development of any holistic understanding of aging. It is therefore important that particular attention is paid to ensuring that all relevant levels of systems biology are addressed during the development of this subdivision. In this context, collaboration with Jena University in the field of bioinformatics should be considered.

Collaboration and networking (Chapter 4)

8. FLI is involved in a commendable number of international collaborations. As a result, around half of the institute's publications are joint publications with scientists abroad. This laudable trend might be further improved in future by formal FLI collaborations with foreign institutions.

Staff development and promotion of junior researchers (Chapter 5)

9. Despite the institute's measures to promote gender equality, women account for approx. one third of the scientific staff. At the level of doctoral candidates and post-docs, the proportion of women is significantly lower than at the last evaluation. There are now more female research group leaders, but they nevertheless account for only a quarter of these positions. FLI must take positive steps to improve this unsatisfactory situation.
10. The average length of doctoral studies prior to thesis submission is 4.2 years. This is considerably longer than comparable European institutions. The FLI should strive to reduce the time required significantly. To this end, the provision of more intensive supervision and/or careful selection of research projects for its doctoral candidates may prove effective.
11. In the past, FLI offered two so-called Career Development Fellowships to postdoctoral researchers as a bridge to a regular junior group leader position. The institute is advised to discontinue this programme in favour of a unified, structured postdoctoral qualification of the kind being attempted in the context of the new postdoctoral network.

Quality assurance (Chapter 6)

12. The Review Board is of the opinion that the measures introduced in mid-2016 are appropriate to ensure compliance in animal husbandry and breeding. It will be incumbent upon the leadership, Advisory Board and Board of Trustees to continue monitoring and implementing these measures. The investigations by the authorities and the Public Prosecutor's Office are, however, still ongoing. Once these proceedings are complete, it will be necessary for the leadership, Advisory Board and Board of Trustees to examine whether further changes in the organisation and practice of animal husbandry and breeding at FLI are required to ensure full compliance.

Special mention should also be made of the important issue of FLI staff training. The institute informed the Review Board that the measures already introduced were sufficient to regain permission to keep and breed laboratory animals in August 2016. By the time of the evaluation visit, on this basis five individual fish projects had been relicensed. Further licensing applications are in the pipeline. In the light of these developments, FLI believes that further delays to scientific work will be minimal.

The institute director explained that in a few cases, even if animal experiments are resumed very quickly, some delays to PhD projects are inevitable. The FLI guarantees that the affected doctoral candidates will be given the opportunity to extend

their employment. It is recommended that the institute will consider changing the PhD research topics should this become unavoidable.

13. In future, a comprehensive audit of the entire institute should be conducted once between two external evaluations. This assessment should be submitted together with the evaluation package as recommended by the Senate of the Leibniz Association.

2. General concept and profile

The Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) successfully conducts fundamental biomedical research with the aim of understanding the molecular origins of aging. Viewed against the backdrop of demographic trends in many western industrialised countries, FLI's research, which provides the basis for developing new therapies for improving health in old age, is of great relevance both for the future and for society.

Following the retirement of the former director who was highly successful in leading the FLI, a new director was appointed in 2012. The institute's scientific agenda was consequently realigned to focus on impairments in stem cell function and organ maintenance during aging. As recommended at the last evaluation, this has paved the way for FLI to position itself alongside other aging research institutions in Germany.

Development of the institution since the last evaluation

Since the last evaluation, the institute's research has been structured in five overarching thematic subdivisions. These are points at which the research groups' joint research interests are aggregated and focused rather than administrative units. In principle, FLI differentiates between senior research groups (with tenured leaders) and junior research groups (with fixed-term leaders). **Every research group is primarily assigned to one subdivision but may also cooperate with others to generate synergy on common topics. In order to exploit this potential to the full, in the future work in some of the subdivisions should be consolidated with greater attention being paid to overarching issues (see also Recommendations on Chapter 3).** The research infrastructure available to all research groups has been combined in Core Facilities (CF) and Core Services (CS).

Since the last evaluation, three senior group leaders have retired and some former junior group leaders as well as senior scientists have successfully relocated to leading positions at other institutions. As a consequence, seven of FLI's 13 current research groups have been newly recruited. This has helped to focus research on overarching themes. A welcome innovation is the systematic involvement of all research group leaders in the future development of the scientific agenda via the newly-established Institute Council and the Group Leader Assembly.

In the course of the thematic restructuring, FLI decided to cease structural NMR- and X-ray-based work in order to free up resources for the functional analysis of molecular damage. This strategic decision made sense in view of the large instrumentation investment that would have been required to further develop this structural work. The former

head of the Biomolecular NMR Spectroscopy Group is now in charge of the newly-established Core Facilities and Core Services (see Chapter 3). NMR- and X-ray facilities that are required to successfully complete ongoing (and possibly future) projects, are provided by collaborations with the universities in Jena and Halle.

Results

FLI's results are internationally competitive. A notable example is the establishment of the short-lived fish *Nothobranchius furzeri* as a new vertebrate aging model. This achievement was substantially driven by the institute. The genomic and functional analyses that were conducted at FLI represent a milestone in aging research and an important basis for further studies (see also Chapter 3). The institute's high quality work is reflected in a corresponding publication record. This has improved significantly, both in terms of quality and quantity, since the last evaluation (the annual cumulative impact factor has doubled) and includes publications in the highest impact journals such as Cell, Nature Cell Biology and Cell Stem Cell. It is particularly impressive that the institute has been able to maintain and even slightly improve this level in the last few years despite extensive staff turnover (see above).

Institute scientists are actively involved in organising conferences and workshops. These include the Gordon Conference on Stem Cells & Cancer and the Second International Symposium on *Nothobranchius furzeri*.

FLI's ongoing efforts to promote the translation of its basic scientific insights into clinical practice via an internal training and support programme are welcomed and should be resolutely pursued. For this purpose, cooperation with Jena University Hospital in particular should be extended, for example in the field of cohort studies.

Strategic work planning for the next few years

In the coming years, FLI proposes to include "Microbiota and Aging" in its research programme. The aim is to investigate the effects of microbiota on stem cell function, organ function and organismal aging. In order to implement this proposal, the institute intends to apply to the Federal and *Länder* governments for additional institutional funding for the period 2019-2022 in the form of a temporary extraordinary item of expenditure. To address this new research area, the institute has outline plans to establish a new senior group on "Metagenomics & Microbiota/Host Interactions in Aging" in Subdivision 4: (Epi)Genetics and Models of Aging (see Chapter 3). FLI estimates funding of just under five million euro for human resources and materials for this group. Secondly, FLI will fulfil its co-payment obligation by establishing two additional junior groups on "Metabolomics and Metabolite Signalling" and "Microbiota induced Alternations in (Epi)Genetics" (approx. three million euro for human resources and materials). During the evaluation visit the FLI discussed an alternative arrangement in which the two junior groups would be based in Subdivision 3: Molecular Damages in Aging. At the end of start-up financing, the institute envisages that running costs for human resources and materials will be met from the regular core budget from 2023 onwards.

FLI's plans to initiate the research topic "Microbiota and Aging" are commendable. Start-up financing for this initiative based on additional funding as a temporary extraordinary item of expenditure is expressly endorsed. The total costs of approx. eight million euro estimated for the period 2019-2022 are appropriate. In view of the current relevance of the topic, it is recommended that the institute examines the possible establishment of the planned senior group before 2019. This should precede the establishment of the two proposed junior groups in order to ensure a coherent approach to the research topic.

FLI's plans to consolidate its collaboration with its partners on the Beutenberg Campus via the new research topic "Microbiota and Aging" are also welcome. In this context, possible interactions with the Leibniz Institute for Natural Product Research and Infection Biology (HKI), particularly in the field of genomics, should also be investigated.

The FLI has been developing a subdivision on Systems Biology of Aging since 2014. This initiative represents an important step on the path to a holistic understanding of aging (see Chapter 3). Several research groups plan to build on the success of the *N. furzeri* project by expanding functional studies using this fish model. The necessary extension of the Fish Facility (which is already reaching capacity point) is scheduled for 2017-2018. This methodological focus is welcomed. It underscores an important and unique feature of the institute that contributes significantly to its raised profile. Financing for this measure has already been secured.

Appropriateness of facilities, equipment, and staffing

The provision of institutional funding is adequate for FLI to fulfil its current portfolio of tasks. In this regard, it is gratifying that, in accordance with recommendations made at the last evaluation, the funders have enabled the institute to be more independent and flexible in its budgetary planning. Since 2016, the transfer of a defined amount of its overall budget to the next budgetary year has been allowed.

FLI's income from third-party funding was approx. 4.1 million euro in 2015. This is approx. 14 per cent of the institute's entire budget. At the last evaluation, the institute was enjoined to increase its third-party funding from 13 percent (as of 2007). **Despite notable success in individual cases, such as the acquisition of an ERC Advanced Grant by the institute director, the contribution of third-party funding to FLI's overall income is still too low. The institute has set itself a potentially achievable target of a 25 per cent contribution from third-party income in the next years.**

At the time of the last evaluation it was clear that the institute would suffer from a shortage of space. The opening of a new research facility in 2013 improved the situation significantly and more than doubled the usable space. It is pleasing to note that within the next few years, the planned modernisation of two buildings from the 1950s and the conversion of the NMR building (see above) will provide the institute with adequate office and laboratory space.

The FLI boasts state of the art equipment that is appropriate for the research work it conducts.

3. Subdivisions of FLI

FLI's research work has been bundled in five thematic subdivisions (see Chapter 2). These are points at which the research groups' joint research interests are aggregated and focused rather than administrative units.

Subdivision 1: Stem Cell Aging (AVERAGE 2013-2015: 15.5 FULL-TIME EQUIVALENTS [FTE] IN RESEARCH AND SCIENTIFIC SERVICES, 9.7 FTE DOCTORAL CANDIDATES, 7.3 FTE SERVICE STAFF)

With the appointment of the new institute director K. Lenhard Rudolph in 2012, Subdivision 1 was completely reconstituted. This subdivision now investigates cell-intrinsic mechanisms limiting the function of aging stem and progenitor cells, aging-associated alterations of stem cell niches and the systematic environment limiting stem and progenitor cell function.

As the largest research group at FLI, the Rudolph Group has a decisive impact on the profile of the entire institute as well as a shaping influence on the subdivision. Its excellent work on the causes, processes and consequences of stem cell aging makes it a world leader in this field. The group's outstanding publication record is demonstrated by articles in top international journals like *Cell*, *Nature Cell Biology* and *Cell Stem Cell*. The Rudolph Group is also highly successful in attracting third-party funding. The director's award of an Advanced Grant by the European Research Council is particularly noteworthy in this regard.

Since 2013, Subdivision 1 has been enhanced by Julia von Maltzahn's junior group which is funded under the DFG's Emmy Noether Programme. With its impressive work on the role of stem cells in regenerating skeletal muscle, the von Maltzahn Group has already developed a strong research profile of its own and integrated very well into the subdivision by forming close ties with the Rudolph Group. Moreover, it cooperates closely with the group headed by Cristina González-Estévez (also at FLI since 2013) who studies planarians (flatworms) as an important model for tissue repair. As a "fellow group" (to the general concept "fellow group" see Chapter 5) she is less well endowed than the junior groups at FLI but was supported by the institute during the group leader's pregnancy and parental leave by providing, amongst other things, an additional laboratory technician. When the group leader returns from parental leave she should be encouraged to work more independently to establish herself in her field.

In addition to this, two "cooperation groups" are integrated in Subdivision 1. The work on the development of myeloid neoplasms by Florian Heidel's group at Jena University Hospital builds an important bridge between fundamental research at FLI and clinical research. In addition, two postdocs are working at FLI under the direction of Heinrich Jasper (Buck Institute for Research on Aging, Novato, CA, USA) to establish the fruit fly (*Drosophila melanogaster*) as a model system for stem cell biology. The work of the Jasper Group is particularly significant in connection with "Microbiota in Aging" (see Chapter 2) and, the institute's plans to consolidate the project in the form of an independent junior group are welcomed. Equally pleasing is the additional creation of a W2 position for Immunology and Aging under the State of Thuringia's ProExcellence Programme. FLI expects appointment procedures to be completed shortly.

Overall, Subdivision 1: Stem Cell Aging, is rated as “excellent”.

Subdivision 2: Organ Maintenance in Aging (AVERAGE 2013-2015: 15.1 FULL-TIME EQUIVALENTS [FTE] IN RESEARCH AND SCIENTIFIC SERVICES, 10.3 FTE DOCTORAL CANDIDATES, 6.7 FTE SERVICE STAFF)

Subdivision 2 has experienced a number of changes in personnel. Three junior group leaders relocated to other institutions. Former junior group leader Helen Morrison assumed leadership of a senior group and of the subdivision in 2015. Today, Subdivision 2 concentrates on researching drifts in developmental pathways limiting organ maintenance in aging, immune aging and inflammation, and systemic and micro-milieu regulators of organ maintenance, regeneration and disease development.

Helen Morrison's senior group focuses on the regeneration of nerves in the context of tumour biology. The group's innovative work opens up interesting perspectives, not least for translating research results into clinical practice, particularly in connection with the Schwann cells model. Christoph Englert's senior group researches the molecular genetics of aging particularly in the *Nothobranchius furzeri* (see Subdivision 4) model, which was substantially developed at FLI. His work is an excellent fit with the institute's overall strategy. Both of these senior groups have a superb publication record and have been very successful in raising third-party funding in the last few years.

Since the beginning of 2016, Björn von Eyß's junior group has complemented the profile of Subdivision 2 with investigations into the transcriptional control of tissue preservation. The topic and the broad methodological spectrum employed dovetail very well with the interests of the subdivision. Following the early death of the group leader Falk Weih, the Immunology research group which is quite currently heterogeneous is experiencing a period of transition. The institute's plans to continue to support the group under new leadership from 2017, are welcomed.

Overall, Subdivision 2: Organ Maintenance in Aging, is currently rated as “very good”. The extremely promising approaches in the newly-formed groups may raise achievements to an even higher level.

Subdivision 3: Molecular Damages in Aging (AVERAGE 2013-2015: 20.0 FULL-TIME EQUIVALENTS [FTE] IN RESEARCH AND SCIENTIFIC SERVICES, 6.0 FTE DOCTORAL CANDIDATES, 11.5 FTE SERVICE STAFF)

Subsequent to the last evaluation, FLI decided to cease structural NMR- and X-ray work in order to free-up resources to fund functional analysis of molecular damages (Subdivision 3). This strategic decision is fully justified and has been efficiently implemented (see Chapter 2).

Subdivision 3 thus now has three senior groups: The “Genomic Stability” group headed by Zhao-Qi Wang successfully employs cellular and molecular tools together with animal models to dissect how dysfunctional DNA damage signalling and repair pathways contribute to pathological changes in human aging. The “Biochemistry” group headed by Frank Große examines basic aspects of DNA replication and the prevention of replication errors. Finally, the “Membrane Trafficking” group headed by Christoph Kaether ad-

dresses issues related to trafficking and localisation of proteins within cells. Their aim is to identify basic cell biological processes as possible targets for treating age-related diseases. All three groups conduct important, internationally-competitive fundamental research in the field of molecular damages. **In view of the institute's overarching focus, the selection of future research topics in Subdivision 3 should more firmly reflect interest in the processes of aging.**

In view of the expected retirement of Frank Große in 2017, the FLI plans to continue research on the effects of DNA damage with a stronger focus on aging. This shift of emphasis is welcomed. In addition, the work of the subdivision will be reinforced with the addition of two new junior groups (Microbiota and Aging, see Chapter 2) on metabolomics and signalling. Here, too, it is essential to ensure a clear connection between the research topics and aging.

Overall, Subdivision 3: Molecular Damages in Aging, is rated as "very good".

Subdivision 4: (Epi)Genetics and Models of Aging (AVERAGE 2013-2015: 9.2 FULL-TIME EQUIVALENTS [FTE] IN RESEARCH AND SCIENTIFIC SERVICES, 3.0 FTE DOCTORAL CANDIDATES, 7.1 FTE SERVICE STAFF)

Subdivision 4 develops fundamental models in aging research by identifying relevant (epi)genetic factors for stem cell function, organ maintenance and accumulation of molecular damages. Activities focus on the fields of comparative (epi)genomics in short- and long-lived aging models and functional (epi)genetics of aging and aging-related diseases.

This subdivision is substantially driven by the group headed by Matthias Platzer which addresses (epi)genetic aspects of aging. A key milestone of the last few years was the establishment of the short-lived killifish *N. furzeri* as a new model for aging research and its genomic and functional analysis. The use of short-lived and long-lived species to identify factors in stress resistance, aging and longevity is an extremely promising approach. The Platzer Group's results are reflected in their impressive publication record and their success in attracting an exceptionally high proportion of third-party funding.

Subdivision 4 also comprises two junior groups. Since 2015, Maria Ermolaeva's group has been studying stress-related cell death and its impact on organ maintenance. In order to continue developing this innovative and promising work, it is recommended that the group makes greater efforts to acquire third-party funding. In addition, FLI should examine the possibility of supporting additional group members. Francesco Neri is a Humboldt Fellow. Although he has only been at FLI since 2016, results on stem cell epigenetics from this group are already promising and fit in well with the institute's agenda.

Collaboration with the group headed by Manja Marz at Jena University Hospital has been important in establishing high throughput analysis, especially in relation to epigenetics. An additional institutional alliance links FLI with Alessandro Cellerino who was one of the main drivers in establishing the *N. furzeri* fish model (see above) when he was a junior group leader at FLI and also afterwards: Since 2010, he leads a research group at the University of Pisa but continues his commitment to the institute by pursuing relevant

work in the context of the JenAge Project (see Chapter 4). In this way, the institute has succeeded in retaining valuable expertise which will be essential for the development of plans to extend functional studies based the fish model (see Chapter 2).

When Matthias Platzer is due to retire in 2018 FLI plans that Subdivision 4 will adopt a new thematic focus with a new senior group on “Metagenomics and Microbiota/Host Interactions in Aging”. This measure is fully endorsed and will require temporary additional institutional funding (see Chapter 2 for details).

Overall, Subdivision 4: (Epi)Genetics and Models of Aging, is rated as “very good to excellent”.

Subdivision 5: Systems Biology of Aging (AVERAGE 2013-2015: 3.3 FULL-TIME EQUIVALENTS [FTE] IN RESEARCH AND SCIENTIFIC SERVICES, 0.1 FTE SERVICE STAFF)

Subdivision 5 aims to bridge the gap between research on molecules, subcellular structures, cells and tissues as conducted in the other subdivisions, and overall organism fitness.

This subdivision came into existence in 2014 and is still under development. At the moment, it comprises the junior group of Alessandro Ori, (since 2015) who conducts very promising work on the proteomics of aging organs and adult stem cells. It is complemented by a “cooperation group” consisting of two postdocs that is maintained by Hans Kestler using his own independent funding. He moved from the FLI to the University of Ulm in 2016. This temporary arrangement will remain in place until a new senior group leader/subdivision head is appointed. Gratifyingly, it became clear during the evaluation visit that recruitment efforts were already well advanced.

Subdivision 5: Systems Biology of Aging is likely to have a significant impact on the research of the entire institute. The establishment of this subdivision is crucial for the development of any holistic understanding of aging. It is therefore important that particular attention is paid to ensuring that all relevant levels of systems biology are addressed during the development of this subdivision. In this context, collaboration with Jena University in the field of bioinformatics should be considered.

Overall, the strategy and activities in Subdivision 5: Systems Biology of Aging are rated as “very good”.

Facilities and Services (AVERAGE 2013-2015: 8.9 FULL-TIME EQUIVALENTS [FTE] IN RESEARCH AND SCIENTIFIC SERVICES, 41.3 FTE SERVICE STAFF)

FLI initiated a reorganization of its scientific infrastructures and services following a conceptual review by an external scientific panel in 2012. Centrally organized Core Facilities (CF) and Core Services (CS) are independent of research groups. This highly welcomed reorganization is beneficial to research groups and helps to optimise operations and utilisation.

CF and CS are very well equipped and provide the institute with an impressive array of services. The sector is excellently managed by the former head of the NMR Spectroscopy

group. As need arises, additional human resources should be made available in facilities that are in particularly great demand such as the CS Histology, Pathology & Electron Microscopy (here especially the field of electron microscopy) and the CF Bioinformatics. With regard to the CF Proteomics, attention should be paid to aligning instrumental and human resource capacity to changing needs, for example in the course of building Sub-division 5. The capacity required for the planned work on metabolomics (see above) should be bundled in a dedicated facility.

4. Collaboration and networking

Collaboration in Jena

FLI cooperates successfully on many projects with its neighbouring institutions on the Beutenberg Campus (Jena University, Jena University Hospital, Leibniz Institute HKI [Leibniz Institute for Natural Product Research and Infection Biology]). Over and above individual projects, there is an increasing tendency to integrate the aging-related activities of the four facilities on an institutional level, for example via networks like the Jena Centre for Systems Biology of Aging (JenAge), the interdisciplinary Aging Research Center at Jena University and the newly-established Leibniz ScienceCampus “Regenerative Aging” (2015-2018). Primarily with regard to the joint use of infrastructure, further opportunities for cooperation should be investigated (as described in Chapter 2). This is particularly important in relation to the transfer of fundamental research results into clinical practice, for example, or in the context of the planned research topic “Microbiota and Aging”. For joint appointments and teaching activities by leading FLI staff as well as joint promotion of junior researchers, see Chapter 5.

Other collaborations and networks

Within the Leibniz Association, the institute’s particularly close cooperation with the neighbouring HKI (see above) is reflected in numerous publications. Over and above this, FLI is encouraged to extend further its collaborative relations with other Leibniz Institutes.

FLI is involved in a commendable number of international collaborations. As a result, around half of the institute’s publications are joint publications with scientists abroad. This laudable trend might be further improved in future by formal FLI collaborations with foreign institutions.

5. Staff development and promotion of junior researchers

Staff development and personnel structure

During the evaluation visit, staff expressed high levels of job satisfaction.

FLI’s personnel structure, particularly in the scientific sector, is characterised by a flat hierarchy (see Chapter 2) appropriate for fulfilling the institute’s mission. It is welcomed that in accordance with a recommendation made at the last evaluation, the responsible

state authorities have given flexibility to the staffing plan. This allowed the institute to create the new positions it required.

Currently, four of the seven senior group leaders hold joint appointments with Jena University. Moreover, in the coming years, FLI plans to establish three additional joint appointments (two W3 professorships and one tenure track W2 professorship). In this context it is gratifying that, in the interests of greater coordination of aging-related work in Jena (see Chapter 4), future increasing numbers of joint appointments between institutions are envisaged. According to FLI and Jena University Hospital plans, for example, a new W3 professorship for “(Trans-)Differentiation in Aging and Disease” (with the focus of work at University Hospital) is foreseen in the context of the Leibniz Science-Campus “Regenerative Aging”. In addition, following the retirement of Frank Große in 2017, his successor as Biochemistry Group leader will be based equally at FLI and Jena University.

It is welcomed that FLI has created clear and uniform conditions with regard to length of employment and the allocation of human and material resources, especially for new junior group leaders. It is also pleasing that, in principle, all junior group leader positions are tenure-track positions. Since 2004, 20 per cent of junior group leaders were given tenured positions at the institute. Since the last evaluation, four of six junior group leaders have transferred to leading positions at other institutions.

Promotion of gender equality

Equal opportunity issues, such as work-family balance, play an important role at FLI. This is welcomed. A number of measures such as anchoring the cascade model in the programme budget, flexitime arrangements, the introduction of a Welcome Back Fellowship for female scientists after maternity leave and reserved places for the children of institute staff at local kindergartens are commendable.

Despite the institute’s measures to promote gender equality, women account for approx. one third of the scientific staff. At the level of doctoral candidates and postdocs, the proportion of women is significantly lower than at the last evaluation. There are now more female research group leaders, but they nevertheless account for only a quarter of these positions. FLI must take positive steps to improve this unsatisfactory situation.

Promotion of junior researchers

The training of junior researchers is a priority at FLI. FLI research group leaders and postdocs are involved in undergraduate level teaching at Jena University. They also mentor Bachelor and Master students in the institute.

Since 2007, the structured supervision and training of all doctoral candidates has been conducted via the Leibniz Graduate School on Aging and Age-related Diseases, which is operated jointly with Jena University. A particularly high percentage of foreign doctoral candidates (2015: 52 %) testifies to the institute’s intensive internationalisation efforts. PhD positions are advertised internationally and German and English language courses

are offered internally. Doctoral candidates are given the opportunity to attend one international conference per year.

The average length of doctoral studies prior to thesis submission is 4.2 years. This is considerably longer than comparable European institutions. The FLI should strive to reduce the time required significantly. To this end, the provision of more intensive supervision and/or careful selection of research projects for its doctoral candidates may prove effective.

Since 2015, FLI has operated a postdoc network “RegenerAging” funded by the Leibniz Association. Its aim is to structure the qualification phase between doctorate and potential group leadership. With this programme, FLI has assumed a pioneering role in Germany and is encouraged to continue along this path. In order to broaden the horizons of its postdocs, the network should take greater account of aspects of career planning in its future activities.

In the past, FLI offered two so-called Career Development Fellowships to postdoctoral researchers as a bridge to a regular junior group leader position. The institute is advised to discontinue this programme in favour of a unified, structured postdoctoral qualification of the kind being attempted in the context of the new postdoctoral network.

Vocational training for non-academic staff

It is welcomed that FLI has extended its training programme since the last evaluation. Since 2009 it has also offered training not only to biology laboratory technicians, but has also trained animal caretakers in research and clinical practice. The institute also supports in-service training measures for its staff in fields including science management and human resources management.

6. Quality assurance

Restructuring of animal facilities and compliance crisis

The opening of the new research facility in 2013 (see Chapter 2) almost doubled the capacity for breeding and keeping mice. An external evaluation of the animal facilities in March 2016 recommended reconstituting the organisational and management structure. The pressure for change grew massively in May 2016, when the regional authorities responsible for authorising animal experiments and the Public Prosecutor’s Office initiated comprehensive enquiries and investigations in connection with the breeding and keeping of animals. In mid-2016, the institute’s permission to keep and breed animals was withdrawn together with 25 individual animal research project licences.

The measures taken by FLI and its committees are set out in the Status Report (see p. A-8). Particular attention is drawn to the separation of animal welfare and animal house leadership. There are changes in organisation and personnel as well as the establishment of an internal Animal Committee and an external Animal Advisory Board.

The Review Board is of the opinion that the measures introduced in mid-2016 are appropriate to ensure compliance in animal husbandry and breeding. It will be incumbent upon the leadership, Advisory Board and Board of Trustees to continue monitoring and implementing these measures. The investigations by the authorities and the Public Prosecutor's Office are, however, still ongoing. Once these proceedings are complete, it will be necessary for the leadership, Advisory Board and Board of Trustees to examine whether further changes in the organisation and practice of animal husbandry and breeding at FLI are required to ensure full compliance.

Special mention should also be made of the important issue of FLI staff training. The institute informed the Review Board that the measures already introduced were sufficient to regain permission to keep and breed laboratory animals in August 2016. By the time of the evaluation visit, on this basis five individual fish projects had been relicensed. Further licensing applications are in the pipeline. In the light of these developments, FLI believes that further delays to scientific work will be minimal.

The institute director explained that in a few cases, even if animal experiments are resumed very quickly, some delays to PhD projects are inevitable. The FLI guarantees that the affected doctoral candidates will be given the opportunity to extend their employment. It is recommended that the institute will consider changing the PhD research topics should this become unavoidable.

Internal and external quality management

The institute's publication record is evidence of the FLI's convincing system of internal scientific quality assurance. One component of this system is the performance-related award of funding with a basic budget for each established research group (for new groups special regulations apply), which is adjusted annually in accordance with the group's publication record and third-party fund-raising. An ombudsperson monitors compliance with the rules of good scientific practice.

The Scientific Advisory Board successfully contributes to FLI's quality management by producing a critical evaluation of the institute's scientific and organisational development and planning at its annual meeting. Moreover, it appoints reviewers who evaluate the work of FLI's individual research groups every five years. **In future, a comprehensive audit of the entire institute should be conducted once between two external evaluations. This assessment should be submitted together with the evaluation package as recommended by the Senate of the Leibniz Association.**

The Board of Trustees fulfils its role as a supervisory body in accordance with its statutory duties.

Implementation of recommendations from the last external evaluation

FLI has largely been successful in implementing the recommendations issued by the Senate of the Leibniz Association in 2008. The following points (numbered according to the Status Report, pp. A-24-A-28) still need to be addressed by the institute:

2. Although the planned Leibniz Research School for Clinician-Scientists had not been approved at the time of the last evaluation, as recommended, FLI is still seeking closer cooperation with Jena University Hospital in the framework of the Leibniz ResearchCampus “Regenerative Aging” (see Chapter 4), for example, which is still under construction. Particularly with regard to the translation of fundamental results into clinical practice, the institute should resolutely continue its efforts in this regard (see Chapter 2 and 4).
5. The institute has obviously made further progress in internationalisation in the last few years. With regard to cooperating with scientists abroad, in addition to individual collaborations, in future, more institutional collaborations with foreign institutions should be sought (see Chapter 4).
12. At the level of research group leader, FLI has managed to slightly increase the proportion of women from approx. a fifth to a quarter since the last evaluation. However, the small proportion of female scientists at all qualification and hierarchy levels must be increased significantly (see Chapter 5).
14. The proportion of third-party funding in FLI’s overall budget is too small. The institute is expected to achieve the envisaged target of 25 per cent of the overall budget in the coming years (see Chapter 2).

Appendix

1. Review Board

Chair (Member of the Senate Evaluation Committee)

Annette **Beck-Sickinger** Institute of Biochemistry, Leipzig University

Vice Chair (Member of the Senate Evaluation Committee)

Tanja **Weil** Max Planck Institute for Polymer Research, Mainz

Experts

Ingo B. **Autenrieth** Institute of Medical Microbiology and Hygiene, University Hospital Tübingen

Allison **Bardin** Department of Developmental Biology and Cancer, Institut Curie, Paris (FR)

Wolfgang **Driever** Institute of Biology I, University of Freiburg

Christopher **Heeschen** Barts Cancer Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London (UK)

Peter **Karran** The Francis Crick Institute, South Mimms (UK)

Joachim **Krug** Institute of Theoretical Physics, University of Cologne

Nektarios **Tavernarakis** Institute of Molecular Biology and Biotechnology, Heraklion (GR)

Rudolf **Wiesner** Department of Physiology, University of Cologne

Representative of the Länder Governments (Member of the Senate Evaluation Committee)

Woldemar **Venohr** Ministry of Education, Science and Culture of the State of Mecklenburg-Vorpommern, Schwerin

2. Guests

Representative of the responsible federal government department

Joachim **Klein** Federal Ministry of Education and Research, Berlin

Representative of the responsible Länder department

Bernd **Ebersold** Thuringian Ministry of Education, Science and Culture, Erfurt

Representative of the Leibniz Association

Rolf **Horstmann** Molecular Medicine Department, Bernhard Nocht Institute for Tropical Medicine, Hamburg

Representative of the Scientific Advisory Board

Magdalena **Götz** Institute of Stem Cell Research, Helmholtz Zentrum München German Research Center for Environmental Health

3. Representatives of collaborative partners (one-hour interview)

Walter **Rosenthal** President, Friedrich Schiller University Jena

Andreas **Hochhaus** Department of Haematology and Medical Oncology, Jena University Hospital

Thorsten **Heinzel** Institute of Biochemistry and Biophysics, Friedrich Schiller University Jena

Voler **Haucke** Managing Director, Leibniz-Institut für Molekulare Pharmakologie, Berlin

John **Sedivy** Department of Molecular Biology, Cell Biology and Biochemistry, Brown University, Providence, RI (USA)

13 March 2017

Annex C: Statement of the Institution on the Evaluation Report

**Leibniz Institute on Aging –
Fritz Lipmann Institute e. V., Jena (FLI)**

Wir danken dem Gutachtergremium für die sehr gute bis exzellente Einschätzung unserer wissenschaftlichen Arbeiten in allen Teilbereichen. Insbesondere freut uns, dass das Gremium unsere Wissenschaft als hochrelevant für die Gesellschaft einschätzt und in der Fokussierung auf „Stammzellaltern und Organerhalt“ ein Alleinstellungsmerkmal mit internationaler Sichtbarkeit sieht. Wir teilen die Einschätzung, dass die vom Institut getroffenen organisatorischen, strukturellen und personellen Maßnahmen eine tier-schutzgerechte und im Einklang mit den gesetzlichen Vorgaben stehende Durchführung von Tierversuchen dauerhaft ermöglichen. Die aktuelle Wiedergenehmigung von 11 Tierversuchsvorhaben zeigt, dass auch die Behörden dies anerkennen.

Wir empfinden die Kommentare des Gutachtergremiums zur zukünftigen Entwicklung des FLIs als außerordentlich konstruktiv und sehen diese im Einklang mit unseren Zukunftsplänen, die in weiten Teilen bereits in der konkreten Umsetzung sind. So wurde:

- die Vernetzung mit der Friedrich-Schiller-Universität durch die gemeinsame Gründung eines universitären „Zentrums für Alternsforschung“ und durch die Einwerbung eines Leibniz-WissenschaftsCampus zum Thema „Regeneratives Altern“ auf dem Campus der Medizinischen Fakultät gestärkt (Punkt 2),
- durch die anstehende Besetzung einer W3-Professur der empfohlene Ausbau der Subdivision „Computational Biology of Aging“ über alle Bereiche der Systembiologie zur Stärkung übergreifender Forschungsprojekte eingeleitet (Punkte 1 und 8),
- aufgrund der sehr positiven Bewertung des beantragten, transienten Sondertatbestands zum Aufbau des neuen Forschungsgebietes zu „Mikrobiota und Altern“ der Gutachter-Empfehlung zur vorgezogenen Umsetzung gefolgt und die Implementierung einer aus Institutsmitteln gegenfinanzierten W3-Professur in diesem Bereich begonnen (Punkt 3 und 4); diese wird im Institutionen-übergreifenden „Jena Center for Microbial Communication - JSCM“ eingebunden und so unsere Vernetzung am Standort weiter verstärken (Punkte 2-4),
- zur Verwirklichung der Erhöhung unserer Drittmittelinwerbungen auf 25% des Institutsetats bis 2024 eine Stabsstelle zur Akquise und Assistenz bei der Einwerbung von Drittmittelprojekten eingerichtet (Punkt 5),
- zur Erhöhung des Anteils von Frauen in Führungspositionen in der diesjährigen, ersten Runde des neuen Leibniz-Professorinnen Programms eine Kandidatin zur Etablierung einer W3-Seniorgruppe am Institut vorgeschlagen (Punkt 9); zusätzlich wurden 4 von 5 Positionen im neu etablierten Postdoc-Netzwerk am FLI – dem ersten strukturierten Postdoktorand/innen Programm innerhalb der Leibniz-Gemeinschaft - mit Frauen besetzt,
- die Fertigstellung aller Projekte von Doktorand/innen und Postdoktorand/innen, deren Projekte durch die stattgefundenen Umstrukturierungen im tierexperimentellen Bereich Verzögerungen erfahren haben, durch die Rückstellung von Institutsmitteln sichergestellt (Punkt 12),
- im Einklang mit der späteren Beschlusslage durch die WGL hinsichtlich eines eingehenden Audits zwischen 2 Evaluationen eine solche Zwischenevaluation bereits

im Jahr 2012 im Zuge des Direktorenwechsels am FLI durchgeführt und als außerordentlich nützlich empfunden (Punkt 13).

Insgesamt wurden die wissenschaftliche Ausrichtung, die Alleinstellung und die gesellschaftliche Bedeutung des FLIs durch die sehr positive Evaluierung bestärkt und dem Institut wertvolle Anregungen für Weiterentwicklung gegeben. Wir danken dem Gutachtergremium hierfür und den Mitarbeiter/innen des SAEs für die in allen Punkten professionelle und effektive Begleitung unseres Institutes im Evaluierungsverfahren.