

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

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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 17. und 18. September 2019 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 15. Juli 2020 auf dieser Grundlage die vorliegende Stellungnahme. Der Senat dankt den Mitgliedern der Bewertungsgruppe und des Senatsausschusses Evaluierung für ihre Arbeit.

1. Beurteilung und Empfehlungen

Der Senat schließt sich den Beurteilungen und Empfehlungen der Bewertungsgruppe an. Das Leibniz-Institut für Alternsforschung – Fritz Lipmann Institut (FLI) betreibt Forschung zu den molekularen Grundlagen des Alterns und der Entstehung von alternsassozierten Erkrankungen. Die Arbeiten zielen ab auf die Translation von Forschungsergebnissen in die klinische Anwendung, um die Entwicklung neuer Therapien zur Verbesserung der Gesundheit im Alter zu ermöglichen.

Bei der **letzten Evaluierung** waren die wissenschaftlichen Leistungen des FLI zunächst äußerst positiv bewertet worden (Evaluierungsbesuch im Oktober 2016). Jedoch veröffentlichte das Präsidium der Leibniz-Gemeinschaft im Juni 2017, kurz vor der Verabschiedung der Stellungnahme des Senates der Leibniz-Gemeinschaft im Juli, die Ergebnisse einer Überprüfung von Vorwürfen wissenschaftlichen Fehlverhaltens gegen den damaligen Direktor des FLI. Ein vom Präsidium eingesetzter Untersuchungsausschuss stellte schwerwiegende Verstöße gegen die Regeln guter wissenschaftlicher Praxis in Publikationen fest, für die der Direktor hauptverantwortlich war. Vor diesem Hintergrund waren wesentliche Grundlagen für die im Rahmen der Evaluierung vorgenommene Bewertung einer der fünf Teilbereiche des FLI entfallen. Der Senat hielt fest, dass die sehr positiven Bewertungen der übrigen Leistungen und Pläne am FLI davon unberührt blieben.

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

Darüber hinaus hatten die zuständigen Behörden aufgrund von Defiziten in der Tierhaltung im Jahr 2016 alle Genehmigungen für Tierversuche zurückgezogen. Das Institut hatte zwar bereits einen Prozess zur Wiedergenehmigung der Lizenzen eingeleitet, diesen jedoch noch nicht abgeschlossen.

Aufgrund dieser gravierenden und grundlegenden Krise des FLI empfahl der Senat eine erneute Evaluierung in drei Jahren. Er sah es als notwendig an, dass eine neue wissenschaftliche Leitung unverzüglich Maßnahmen einführt, die die Einhaltung der Regeln guter wissenschaftlicher Praxis am FLI sichern. Im Anschluss daran sollten zudem die wissenschaftlichen und organisatorischen Strukturen des Instituts angemessen reformiert werden. Daraufhin zog der damalige Direktor die erwartete Konsequenz und trat von seinem Posten zurück. Er leitet jedoch nach wie vor eine Forschungsgruppe am FLI und ist Professor an der Universität Jena.

Im März 2018 bestellte das Aufsichtsgremium einen hoch anerkannten und erfahrenen Wissenschaftler von außerhalb zum **kommisarisichen Direktor**. Er hat herausragende Arbeit geleistet. Unter seiner Führung wurden entschlossen und zügig alle Instrumente des Qualitätsmanagements überarbeitet und in einem auch international stark wahrgenommenen *Compliance Management System* (CMS) zusammengeführt. Dieses beinhaltet u. a. neue Regeln guter wissenschaftlicher Praxis, die vorsehen, alle Publikationen vor der Veröffentlichung durch einen externen Anbieter prüfen zu lassen. Auch die Maßnahmen zur Sicherung des Tierwohls sind Teil des CMS. Die Tierhaltung wurde zudem personell und strukturell neu aufgestellt. Mittlerweile hat das FLI alle notwendigen Genehmigungen für Tierversuche wiedererhalten.

Alle Beschäftigten des FLI haben sich hervorragend in den organisatorischen Veränderungsprozess eingebracht und setzen die verschiedenen Maßnahmen sehr gut um. Darüber hinaus ist es gelungen, die **wissenschaftlichen Leistungen** des FLI trotz der Führungskrise, die das Institut vor drei Jahren traf, auf einem hohen Niveau zu halten. Die fünf Teilbereiche des FLI werden einmal als „sehr gut bis exzellent“ und je zwei Mal als „sehr gut“ und „gut bis sehr gut“ bewertet.

Die Arbeitsgruppen am FLI erhalten nach klar definierten Kriterien vergleichbare Mittel der institutionellen Förderung. Eine Ausnahme bildet allerdings die Gruppe des früheren Direktors, die aufgrund der Berufungszusage von 2012 nach wie vor eine erheblich umfangreichere Grundausstattung erhält. Diese Ungleichbehandlung muss wie vom Kuratorium bereits fest vorgesehen umgehend geändert werden. Sie schwächt die ansonsten überzeugende Institutsstruktur und ist ein gravierender Nachteil auch mit Blick auf die anstehende **Besetzung der Position der wissenschaftlichen Leitung** des FLI. Die Stelle wurde bereits im Oktober 2018 als gemeinsame Berufung mit der Universität Jena ausgeschrieben, ist aber bedauerlicherweise noch vakant. Die Besetzung mit einer wissenschaftlich exzellent ausgewiesenen, von außen an das Institut zu berufenden Persönlichkeit muss nun wie geplant bis zum 1. Januar 2021 erfolgen. Der Senat bittet das Kuratorium darum, bis zu diesem Datum über das Ergebnis des Verfahrens zu berichten.

Dem FLI wurden nach der letzten Evaluierung zusätzliche Mittel in Höhe von insgesamt 5 Mio. € bewilligt, die zwischen 2019 und 2022 an das Institut fließen, um einen **neuen Bereich „Microbiota and Aging“ aufzubauen**. Mit diesem Aufbau konnte jedoch noch

nicht begonnen werden, weil die für die Leitung des Bereichs vorgesehene und gemeinsam mit der Universität Jena zu berufene Professur noch vakant ist. Die Professur muss nun wie vorgesehen möglichst zügig besetzt werden, auch weil in den vergangenen Jahren andere Einrichtungen Arbeiten auf diesem oder angrenzenden Gebieten ausgeweitet haben.

Dem FLI steht eine herausragende Ausstattung mit **Core Facilities** (inkl. Tierhaltung) zur Verfügung, die ein Alleinstellungsmerkmal des Institutes ist. Vor dem Hintergrund der hohen Mittel, die für den Betrieb notwendig sind, sollte das FLI Maßnahmen entwickeln, um die Kosten-Nutzen-Relation der einzelnen *Facilities* regelmäßig zu überprüfen. Zudem sollten die Umlagekosten für die Nutzung angehoben werden. Dies gilt insbesondere für die Tierhaltung, da damit auch ein höherer Anreiz gesetzt wird, die Tierversuche auf die minimal notwendige Anzahl zu beschränken.

Die Ausstattung des FLI mit **Mitteln** der institutionellen Förderung ist für das Aufgabenspektrum auskömmlich. Die Drittmiteinnahmen betragen zwischen 2016 und 2018 10-13 % des Gesamtbudgets. Es ist sehr zu begrüßen, dass das FLI einen Großteil der Förderungen über kompetitive Programme der DFG oder der EU erzielt. Jedoch muss das FLI seine Drittmiteinnahmen insgesamt erhöhen, wie es vor drei Jahren empfohlen wurde.

Der **wissenschaftliche Nachwuchs** findet am FLI sehr gute Bedingungen vor. Die *Leibniz Graduate School on Aging* bietet einen angemessenen Rahmen für die Betreuung der Promovierenden. Es wird begrüßt, dass das FLI wie empfohlen Dissertationsprojekte verlängerte, die durch die fehlenden Genehmigungen für Tierversuche in Verzug gerieten. Um dem bereits promovierten Personal eine längerfristige Perspektive zu bieten, hat das FLI ein überzeugendes Verfahren etabliert, um mit eigenen Mitteln Nachwuchsgruppen einzurichten. Das FLI sollte jedoch auch drittmittelfinanzierte Nachwuchsgruppen am Institut etablieren. Im Vergleich zur vergangenen Evaluierung stieg der Anteil von Frauen am wissenschaftlichen Personal von 33 % auf 40 %. Von den 15 wissenschaftlich leitend tätigen Personen sind inzwischen 6 Frauen und 9 Männer. Das FLI sollte diesen positiven Trend bei der **Gleichstellung der Geschlechter** fortsetzen.

Die Pläne für die Intensivierung der **Zusammenarbeit am Standort Jena** unter dem Dach des *Leibniz ScienceCampus Regenerative Aging* sind sehr zu begrüßen. Dadurch wird die Vernetzung am Standort deutlich verbessert, insbesondere auch im Hinblick auf die Translation von Forschungsergebnissen in die klinische Anwendung. Zudem ergeben sich bessere Möglichkeiten für das Einwerben drittmittelgeförderter Verbundvorhaben. Es wird eine wichtige Aufgabe der neuen Leitung sein, die Pläne weiter voranzutreiben.

Das FLI widmet sich mit seinen Arbeiten zu wesentlichen Fragen der Altersforschung sehr erfolgreich einem Thema von hoher gesellschaftlicher Relevanz, die in dieser Form nicht an einer Hochschule erbracht werden können. Eine Eingliederung in eine Hochschule wird daher nicht empfohlen. Das FLI erfüllt derzeit auch die Anforderungen, die an eine Einrichtung von überregionaler Bedeutung und gesamtstaatlichem wissenschaftspolitischen Interesse zu stellen sind. Das Institut hat über viele Jahre hin hervorragend gearbeitet. Vor diesem Hintergrund wurden trotz der Krise, die das Institut vor drei Jahren traf, von den Beschäftigten unter der hervorragenden Leitung des kommissarischen Direktors seit der letzten Evaluierung nach wie vor sehr gute Leistungen erarbeitet. Es ist

allerdings von entscheidender Bedeutung, dass die offene Leitungsfrage nun zügig geklärt wird, um die Leistungsfähigkeit des Instituts nachhaltig zu sichern.

2. Zur Stellungnahme des FLI

Der Senat begrüßt, dass das FLI beabsichtigt, die Empfehlungen und Hinweise aus dem Bewertungsbericht bei seiner weiteren Arbeit zu berücksichtigen.

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.

Annex A: Status report

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

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1. Key data, structure and tasks

Key data

The FLI originates from the German Democratic Republic Academy of Sciences institute ZIMET (“Zentral-institut für Mikrobiologie und experimentelle Therapie”).

Admission to joint funding by Federal and <i>Länder</i> Governments:	1991
Admission to the Leibniz Association:	1997
Last statement by the Leibniz Senate:	2017
Legal form:	‘Registered Association’ (“eingetragener Verein”, e.V.).
Responsible department at <i>Länder</i> level:	Thuringian Ministry of Economy, Science and the Digital Society (TMWWDG)
Responsible department at Federal level:	Federal Ministry of Education and Research (BMBF)

Total budget (2018)

25.86 M€ institutional funding

3.78 M€ revenue from project grants (in addition 0.39 M€ externally administered grants)

Number of staff (2018)

124 individuals in research (incl. 43 PhD candidates)

126 individuals in the research service sector

29 individuals in administration

Mission and tasks

Statutory mission: “The purpose of the association is to promote research and science, focusing on the field of age research. In particular, the purpose of the Articles of Association is realized by the following:

- The association maintains a research institute in which research groups collaborate in joint research and development programs.
- The results of the research activities performed at the institute shall be published or made accessible to the general public in another manner.
- The association supports junior researchers, especially in the aforementioned field.”

(Quoted from § 2 of the Articles of the Association of the FLI)

Research Structure

The research structure of the FLI is divided in two Research Areas (I and II), each comprising of two conceptual Subareas (Subareas 1 – 4). Additionally, a fifth overarching

computational Subarea exists. Additionally, scientific infrastructure and service units are provided (see Appendix 1). Each Subarea has a chair responsible for its scientific performance and strategic development. Within the interconnected Subareas individual Research Groups mainly contribute to the research focus of the superordinate Subarea, however connections between the distinct groups exist (details Chapter 7). Three types of groups are currently discriminated at FLI (details see Chapter 4): Senior Research Groups (SRG), Junior Research Groups (JRG) and Associated Research Groups (ARG).

2. Overall concept: activities and results

Topics

FLI has a dedicated research focus on aging biology which aims at a better understanding of the basic mechanisms that cause the aging of an organism and contributing to improved therapies of age-associated diseases. The FLI is primarily a research institution. However, it engages in offering infrastructures to outside users and also in transferring its knowledge and insights toward medical or industrial applications as well as into society (schools, universities, politicians, press organs, etc.).

Central to the aims of Research Area I (*Stem cells, Regeneration and Organ Homeostasis in Aging*) is the cellular and molecular biology of adult stem cells (Subarea 1), which play an important role for lifelong maintenance of organ homeostasis and regeneration (Subarea 2). Thus, an age-associated decline in stem cell activity, associated with a reduced potential for organ regeneration, is central to age-dependent changes in organ function. The roles of such alterations in disease development are also investigated.

At the molecular level, and central to the aims of Research Area II (*Genetics, Epigenetics and Molecular Cell Dynamics of Aging*), are genetic and epigenetic determinants (Subarea 3) that have an impact on the dynamical cellular activities of an aging system (Subarea 4). These activities are subject to molecular damages that an aging system accumulates with time.

All research projects performed at FLI entail large sets of experimental data, the mining and modelling of which requires improved computational and bioinformatic strategies (Subarea 5).

Moreover, the FLI provides Core Facilities and Core Services as well as Animal Facilities to all research groups.

Model organisms

At the FLI aging process of living systems is studied by investigating model organisms. The institute uses rodents (*M. musculus*, *F. mechowii*) and fish (*D. rerio*, *N. furzeri*) as vertebrate model organisms, while invertebrate species used for aging research include flies (*D. melanogaster*), worms (*C. elegans*), planarians (*S. mediterranea*) and hydra (*H. vulgaris*). "Human-

ized mice”, i.e. mice equipped with genes of human origin and/or stably engrafted with human stem cells, are used to translate basic mechanisms of stem cell and organism aging from animal models into human aging at FLI.

FLI emphasizes the importance of the African turquoise killifish *Nothobranchius furzeri* (*N. furzeri*) in the context of FLI aging research. This fish model for aging research was introduced to the scientific community by A. Cellerino in 2004. The FLI embarked on establishing *N. furzeri* as an additional model for research on aging and contributed to generating functional insights into killifish aging biology, including the compilation of a reference sequence of the *N. furzeri* genome in 2015. Generation of transgenic fish by classical and CRISPR/Cas-enabled strategies has now been established at FLI and presents the killifish model as a versatile system for both basic aging research and pharmacological drug discovery.

With the advent of modern CRISPR/Cas9 strategies, the institute restructured and improved activities toward the generation of transgenic animals in 2018. A dedicated Animal Transgenesis Facility (ATF) (see Chapter 7) was established, where engineered animal models are being created (initially mouse models, projected are models of killifish and zebrafish).

Technologies

According to the FLI it invests significant financial resources and personnel allocations toward maintaining strong Core Facility units to provide its scientists with immediate access to competent, state-of-the-art technologies. These units were established during the reporting period and services and training in the methodologies of genomics/DNA sequencing, proteomics, bioinformatics/life science computing, functional genomics, imaging, flow cytometry and technology transfer are being offered.

The FLI Core Facilities are overseen by the Head of Core, who also maintains 6 Core Service units, which provide, e.g., support in protein purification, S2 level biosafety areas, histological and electron microscopy services, or three radiation safety areas (Isotope Laboratory, Gamma Irradiator, and Small Animal CTs). The respective units are described in Chapter 7.

Results

Research

FLI considers novel scientific insights and the resulting publications in peer-reviewed journals as its primary products of relevance. Between 2016 and 2018 FLI researchers contributed to 365 publications, including 305 articles in peer-review journals (see Appendix 2). 46 of the FLI publications involved more than one FLI research group and 101 publications were results of cooperative efforts with the neighbouring Friedrich Schiller University Jena or the University Hospital Jena. Moreover, 175 publications resulted from international collaborations. The scientific results generated in the five Subareas are described in Chapter 7.

Provision of research infrastructures to external users

To promote collaborative interactions, FLI offers external users a share in the use of the Core Facilities. So far, these external users are primarily located at the Friedrich Schiller

University Jena (FSU) or the University Hospital Jena (UKJ). Details are given in Chapters 6 and 7.

Transfer activities

Transfer activities at the FLI are being oriented towards three aims described in the following.

Translation of insights from basic research to clinical use: According to the FLI the translation of basic insights into a clinical application requires intense interactions between basic and clinical researchers. Thus, the FLI maintains close ties to its clinical partners. To this end, FLI and UKJ engage in the recently approved, joint DFG-funded program *OrganAge*, which is designed to train Clinician Scientists along the topic *Organ dysfunction in old age*. For further collaborations see Chapter 6.

Commercial applications: The institute established the Core Facility *Technology Transfer*, which scouts for scientific insights with potential for application. The patenting of potential uses is facilitated and the exploitation by licensing of patents is promoted by the facility. In addition, many products of FLI research are made available to academic and industrial partners via the formulation of exploitation rights. Integrated into the Core Facility *Technology Transfer* is the so-called “SPARK@FLI” program. This program was originally developed at Stanford University with the goal to decrease time and costs in developing new therapeutics and diagnostics toward market release. SPARK was started at FLI in 2016.

Outreach to society: FLI researchers participated in numerous appearances at public events organized at schools, universities, industries and ministries, as well as in radio and TV broadcasts. The FLI also contributed to numerous articles and commentaries published by media of the national press. The media resonance has almost doubled compared to the previous evaluation period.

3. Changes and planning

Development since the previous evaluation

Subsequent to the last evaluation the FLI had to deal with two issues of concern, one regarding Mouse Husbandry and the other regarding accusations of scientific misconduct against the scientific director.

Mouse Husbandry

In May 2016, legal authorities and members of the Public Prosecutor’s Office inspected the Animal Facilities of FLI and uncovered inappropriate procedures linked to the FLI Animal Facility (Mouse). Deficiencies in the animal facilities that became apparent included (i) insufficient documentation of experimental animals, (ii) incomplete licensing for genetically manipulated lines and intercrosses, (iii) insufficient monitoring of animals in experiments, (iv) deficiencies in keeping standards of animal husbandry, (v) excessive breeding of animals, and (vi) inappropriate storage and documentation of animal medication. As a consequence, authorities withdrew all animal licenses.

The FLI states that the use of animal model systems is absolutely necessary to functionally understand the aging process. Therefore, FLI implemented the following organizational measures to regain the permissions for animal handling, breeding, and experimentation:

- Replacement of the Head of Animal Facility (Mouse) by a qualified veterinarian.
- Setting up of a new and independently acting unit of Animal Welfare in accordance with the stipulations of the animal protection law (*Tierschutzgesetz*).
- Employment within the unit of Animal Welfare of two additional veterinary doctors to establish a regime for the continuous monitoring of FLI animal husbandry, animal health, experimental animal handling by performing scientists, and strict abidance by the experimenters of the stipulations linked to project permissions.
- Setting up of a comprehensive training scheme to educate all relevant staff in the required expertise of animal handling (126 FELASA-B courses and 44 FELASA-C courses).
- In 2017, four team-building workshops taught by external experts were attended by all staff members.

As of Dec. 2018, the legal status of animal experimentation is summarized by the FLI as follows: (i) FLI is fully accepted by the legal authorities as one of high competence in animal experimentation, (ii) follow-up applications regarding all previously withdrawn permissions have been approved, (iii) current applications for new projects are routinely approved by the authorities without delay (usually requiring a processing time of approx. 2 months).

Details about the work of the Animal Facilities are described in Chapter 7.

Accusations of Scientific Misconduct

Following accusations of scientific misconduct against the scientific director of the FLI in 2016 the Executive Board of the Leibniz Association published the results of a review of these allegations in 2017. A Committee of Enquiry, appointed by the Executive Board, identified violations of the Rules of Good Scientific Practice in publications. In consequence, the FLI did not prolong the appointment of the scientific director in October 2017, however the SRG leader position at FLI and the joint appointment with the Friedrich Schiller University Jena were not withdrawn. In March 2018 an interim scientific director was appointed part time at the FLI with a contract ending 2020. The search for a new scientific director of the FLI has been initiated in September 2018 and is ongoing. Details are described in the strategic work planning below.

The FLI was instructed by the Leibniz Executive Board to implement safeguard mechanisms to ensure strict future compliance with the standards of Good Scientific Practice for any scientific work at FLI. According to the FLI immediate actions were taken and the current measures can be summarized as following:

- Tightening and advertising written statutes of FLI for safeguarding the standards of Good Scientific Practice.

- Expanding regular training courses on Good Scientific Practice rules for all FLI scientific staff.
- Tightening PhD student supervision (Thesis Advisory Committees) and instructions of the Leibniz Graduate School on Aging regarding Good Scientific Practice standards.
- Introducing a central, comprehensive electronic archive for all FLI scientific data related to publications and PhD dissertations.
- Establishing mandatory use of an Electronic Laboratory Notebook to keep detailed electronic records of all experimental steps taken in any scientific project.
- Mandatory assessment before submission of all research manuscripts (not review articles) regarding integrity and statistical plausibility of data presented. This analysis is outsourced to an external provider.
- Mandatory assessment before submission of all dissertations regarding potential plagiarism, as well as integrity and statistical plausibility of all data presented. This analysis is outsourced to an external provider.

The mouse husbandry issues and the violations against good scientific practice resulted in the instalment of a new Compliance Management System at the FLI. It is described in detail in Chapter 4.

Strategic work planning for the coming years

Appointing a new scientific director

After the FLI did not prolong the position of the scientific director in October 2017 the Board of Directors of FLI initiated a search for a new scientific director in summer 2018. According to the FLI, top candidates for filling the position have been identified by an international Selection Committee and negotiations have begun. The FLI plans to appoint the new scientific director also as head of a Senior Research Group, thus introducing a candidate dependent research field to the institute, which is stated by the FLI to complement the research structure of the institute.

Expansion of Subarea 2: New research program Microbiota and Aging

The plans of the FLI to expand prior work done at the institute in a new area of investigation (*Microbiota and Aging*) were positively evaluated by the review panel during the last evaluation 2016 and accordingly the Senate of the Leibniz Association approved its implementation. This new activity is thus financed by additional institutional funding provided by the federal and Länder governments and the FLI will contribute partially with its core budget. The research program will be endowed with one Senior and two Junior Research Groups. The SRG is a joint appointment with the Friedrich Schiller University Jena and the search for a candidate was initiated in February 2018 by a public call for a W3 professorship *Functional Microbiota-Host Interactions in Aging*. The FLI will start the search for the two JRG leaders after the SRG leader is appointed. The scientific focus will be on the influence of the microbiome on organ function.

Expansion of Subarea 4

In 2018 the SRG *Biochemistry* was discontinued due to retirement of the group leader. The FLI plans to fill this W3 professorship in a joint appointment with the Friedrich Schiller University Jena again and extend its denomination from *Biochemistry* to *Biochemistry of Aging*. This professorship is intended to be jointly financed by the University and the Institute and thus encompass more teaching activities than other professors at the FLI. The institute states that the call for this professorship is expected to be published in the fourth quarter of 2019. Moreover the FLI plans to intensify its efforts towards studying the topics proteostasis/autophagy in aging in Subarea 4, as it perceives this topic of high importance for the concepts of aging and longevity.

Expansion of Subarea 5

The institute expects the number of high-throughput data-driven research projects to increase and considers expanding the capacities of both Subarea 5 and the Core Facility *Life Science Computing* to meet the increasing demands for research data management. The FLI intends to develop strategies to facilitate primary data archiving and to appoint data stewards who will help the research groups to organize the data and to simplify the publication of articles and data resources.

Further future plans of the FLI include advancing the translation toward “Healthy Aging” by intensifying the collaborations with clinical partners and strengthening the *Leibniz ScienceCampus Jena – Regenerative Aging* (see Chapter 6). Moreover, the FLI intends to strengthen the local cooperation with neighbouring Leibniz institutes and intensify international networking efforts.

4. Controlling and quality management

Facilities, equipment and funding

Funding (see Appendix 3)

In 2018, FLI’s institutional funding was approx. 25.86 M€.

Additionally, 3.78 M€ were spent from revenues from project grants (corresponding to 13 % of the overall budget). The revenues split into 1.44 M€ from the German Science Foundation (DFG), 764 K€ from EU grants, 576 K€ from foundations, 507 K€ from Federal or *Länder* governments and 495 K€ from the competitive procedure of the Leibniz Association. Moreover, the FLI acquired revenue from scholarships and externally administered funds, which are not part of total revenue, of 395 K€.

The institute envisages an increase of third-party funds to about 17-20 % of the total revenue for the subsequent years and has developed a dedicated strategy towards this aim.

Buildings and laboratories

The FLI is located at the Beutenberg Campus in Jena together with a number of research institutes and faculties of the Friedrich Schiller University Jena and the University Hospital Jena. After a new FLI laboratory building (FLI 1) had been put into operation in 2013,

an extensive restoration and refurbishment program of the old buildings of FLI was started. This restoration program proceeds in three stages and the completion of planned restoration activities is scheduled for 2022. According to FLI, the current operating costs of 1.1 M€ for the new building FLI 1 can only be covered within FLI's core budget until 2023. To cover the operational costs for the building FLI 1 from 2024 on, FLI sees the need for an increase of its core budget by 1.1 M€.

The FLI states that, in general, the equipment of FLI meets the infrastructure requirements of a state-of-the-art cell and molecular biology laboratory to satisfaction. Major technology platforms of the FLI are organized as Core Facilities (Chapter 7).

IT strategy

In order to ensure complete documentation of data used in publications, and to facilitate compliance with the standards of Good Scientific Practice, the FLI has established a primary research data archive. This depository mirrors and archives all FLI-generated data referred to or used within FLI publications. The Core Facility *Life Science Computing* improves and facilitates the archiving process in conjunction with the establishment of the Electronic Lab Notebook (ELN) and its associated databases.

Organisational and operational structure

Organizational structure

FLI operations are governed by the Board of Directors (Scientific Director, Administrative Director).

The governance of the Board of Directors is controlled by the Board of Trustees, where the two responsible ministries (federal and regional level) are represented with one seat each. All personnel changes at FLI, from group leader level and above, are to be approved of by the Board of Trustees.

Scientific performance and future scientific directions of the FLI are overseen by the 12-membered, international Scientific Advisory Board (SAB). The SAB advises on scientific perspectives of the Institute and engages in regular evaluations of group leader performance, Core Facility productivity, and compliance standards regarding Good Scientific Practice and Animal Welfare.

Operational structure

At the FLI currently three types of Research Group are distinguished; Senior Research Groups (SRG), Junior Research Groups (JRG) and Associated Research Groups (ARG). Within the conceptual Research Areas currently 7 SRG, 5 JRG and 8 ARG support the research goals.

Senior Research Group (SRG): The head of a senior group is tenured and the position is often combined with a professorship at the neighbouring Friedrich Schiller University in Jena (5 out of 7 group leaders are professors). The FLI offers each SRG leader a personnel support of 2:2:2 (2 Postdocs, 2 PhD candidates and 2 Technicians).

Junior Research Groups (JRG): The chairs of JRG are offered an initial 5 year contract with an optional 4 year contract extension. The FLI usually provides 1:1:1 personnel support (1 Postdoc, 1 PhD candidate and 1 Technician). Two of the current SRGs leaders previously headed JRGs at the FLI.

Associated Research Groups (ARG): According to the FLI, the idea of the ARGs is to provide outside expertise and to connect the FLI research to other institutions. Individual arrangements are made with each group leader regarding the granted resources in terms of personnel support, laboratory space and consumables. The ARGs are always entitled to access to the Core Facilities (see Chapter 7).

Fellows: The FLI initiated in 2012 the *Career Development Fellowship*, a program to provide young Postdocs with the opportunity of taking early responsibility for independent research projects. The program offers a 3-4 year working contract for the Fellow, supported by funding for one technician and one PhD candidate. After the SAB had recommended discontinuation of the last fellowship (closed June 2019), no subsequent Fellow arrangements were initiated yet at FLI.

Altogether, the FLI states that the research at the institute is structured to maximize the complementarity between research groups, thereby eliciting maximal levels of cooperativity and synergy.

FLI operations are conducted in close interaction of the Directors and the Group Leaders. These interactions are formalized by two bodies: the Group Leader Assembly and the Institute Council. According to the FLI, both bodies meet with the Directors on a monthly schedule. The Group Leader Assembly contributes input into all major institutional decisions made by the Directors. It consists of all Senior and Junior Group Leaders, and the Head of Core Facilities. The Institute Council consists of representatives of Senior Group Leaders and Junior Group Leaders, and the Head of Core Facilities. It acts in a solely advisory function to aid decisions of the Directors. The Head of Core Facilities and the heads of Animal Facilities report directly to the Scientific Director.

Changes in the research structure

During the reporting period, one recruitment was made at the Senior and one at the Associate Group Leader level. Additionally, one SRG Leader, three JRG Leaders and one ARG leader who were recruited shortly before the last evaluation 2016 have finalized the establishment of their groups at the FLI. At the same time two SRG leaders retired as well as one ARG and the Fellow Group.

Quality Management

The FLI states that, since the last evaluation it has re-evaluated and optimized all of its quality assurance measures. The institute conceived a Compliance Management System (CMS) in 2018, which is currently being implemented and optimized. The CMS oversees and coordinates all individual measures that had previously been implemented separately, in order to comply with regulations associated with different aspects of scientific work. Each of the Compliance Segments is overseen by a dedicated Compliance Expert,

who monitors and assures concurrence with the specific rules of the segment. The Compliance Experts report to, and are supervised by, the newly formed Compliance Board. The Compliance Board reports directly, and regularly, to the Board of Directors.

Quality management by advisory boards and supervisory board

The Scientific Advisory Board advises the Board of Trustees and the FLI Directors on issues of scientific performance and productivity of FLI, as well as the annual Program Budget. Chair and Deputy Chair of the SAB attend the meetings of the Board of Trustees as guests. The SAB assesses the scientific quality of the research performed at FLI and offers advice on future perspectives. In particular, individual Senior Group Leaders are evaluated by the SAB every five years (Quinquennial Review). Junior Group Leaders are evaluated at the end of the fourth year of their contract and recommendations are reached by the SAB regarding potential prolongation of the group by four more years (up to a total of max. nine years). In exceptional cases, before completion of the ninth year, the SAB may recommend tenure offers.

5. Human Resources

Management

The FLI is led by the Board of Directors, consisting of the Administrative Director and the Scientific Director. The next level of the hierarchy is represented by the scientific group leaders. In terms of managing the FLI, no formal distinctions are made between Senior and Junior Group Leaders. The directors consult with the Group Leaders through the Institute Council and reach final agreements on future decisions through exchanges with the Group Leader Assembly, which is formed by all SRGs and JRGs.

Common appointments of professorships

Professorships at FLI are jointly recruited by the local Friedrich Schiller University Jena (FSU) and the FLI. The FLI has a fixed contingent of eight W3 professor positions at FSU. Currently, five W3 professorships are filled. In the near future, the FLI intends to recruit four additional professors. Toward that aim, FSU has offered to provide one additional allotment when filling the W3 professorship *Biochemistry of Aging*.

The positions to be filled are:

- W3 professorship for the next Scientific Director; preliminary negotiations are ongoing.
- W3 professorship *Functional Microbiota-Host Interactions in Aging*; ranked list of candidates is established.
- W3 professorship *Biochemistry of Aging*; call is expected to be published after October 2019.
- W3 professorship *Neurobiology and Aging*; ad personam appointment of the chair of Subarea 2.

Additionally, two appointments are planned at the University Hospital Jena (UKJ) which will cooperate strongly with the FLI; these, however, are not joint appointments:

- W3 professorship *Translational Geriatric Medicine*.
- W3 professorship *Cellular Reprogramming and Transdifferentiation in Aging* or Junior Group with possibility for promotion to Junior Professorship (tenure track); endowed start-up funding from the Leibniz Association to the ScienceCampus (see Chapter 6).

Postdoctoral staff

On 31. December 2018, the FLI hosted 48 Postdocs (28 male, 20 female).

Postdoctoral scientists (Postdocs) at FLI are researchers with a PhD degree, employed with time-limited contracts. According to the institute, Postdocs can usually devote their work entirely to individual scientific projects and are not obliged to carry out routine services. Career support that complies with the Leibniz Guidelines shall help Postdoctoral researchers to develop their scientific profile. The institute supports and engages in initiatives and programs to establish Postdoc networks for biomedical sciences on aging, career development of female scientists, and international connectivity. Additionally, the FLI offers a skills-development program. This program covers all aspects of professional development, including research management, grant writing, Good Scientific Practice, leadership training and courses on career promotion. Each Postdoc may take two courses per year. The program also offers 2-day courses on career promotion.

The FLI offers to FLI Postdocs the *Welcome Back-Fellowship*, which provides up to twelve months of salary support after parental leave.

Doctoral Candidates

Between 2016 and 2018, 39 doctoral degrees were completed at the FLI. The PhD candidates are organized within the Leibniz Graduate School on Aging (LGSA) established in 2007. The LGSA offers a structured qualification program for all PhD candidates. Currently, LGSA lists 56 PhD candidates (as of December 31, 2018; including guest Doctoral candidates). All graduates of LGSA are either financed through an FLI work contract (1st year: 50% E13 contract, subsequently: 65% E13) or are supported by either a full PhD stipend or a work contract from external sources (or a combination of both). The LGSA Training Guidelines incorporate all objectives of the Leibniz guidelines on career development. Almost all PhD students receiving training at FLI are registered with Friedrich Schiller University Jena, which is also awarding the doctoral degrees and certificates.

All PhD candidates select a thesis advisory committee consisting of three to four PIs. The committee offers advice to the candidate and evaluates the progress of the work in yearly meetings. The completed theses are checked for plagiarism and other issues of data integrity.

Between 2016 and 2018 the average PhD project took 4.4 years, while the time including thesis defense was 5.4 years. The FLI states to have implemented steps to reduce the time to completion of theses.

The FLI currently develops an Alumni network.

Non-scientific staff

Since 1998, the FLI provides vocational training for biology lab technicians (Biologielaborant/innen), and, since 2009 for animal caretakers (Tierpfleger/in für Klinik und Forschung) in the field of animal husbandry (different species, primarily fish and rodents). In total, the FLI offers eight trainee positions, with usually two new trainees getting accepted for vocational training each year.

Between 2016 and 2018, seven technicians and seven animal caretakers were trained. Of these, four technicians and four animal caretakers completed their training so far. Six of them were offered subsequent employment at FLI.

Equal opportunities and work-life balance

The FLI lists a 40 % share of female staff in research and scientific services including doctoral candidates. Details are listed in Appendix 4.

According to the FLI, the institute's leadership strives to increase the share of women scientists in leadership positions and will put a special emphasis on this ambition. Since 2011, the FLI has appointed a dedicated officer for gender equality. The FLI has fully implemented the DFG's *Research-oriented Standards on Gender Equality*, as well as the *Leibniz Gleichstellungsstandards*, and thus supports its employees with numerous programs and measures supporting equal opportunity and facilitating diversity.

The FLI has agreed on target rates to increase the percentage of women in science. Since 2015, those rates are laid down as binding guidance principles in the FLI's Program Budget and are specified with detailed measures in the institute's equality plan. Compared to previous years, the percentage of newly recruited women has increased, in detail the share of female PhD students has risen from 50 % in 2017 to 60 % in 2018 and the share of newly recruited female Postdocs increased from 14 % in 2017 to 45 % in 2018.

Regarding external certification, the FLI has been repeatedly awarded the *Total E-Quality Certificate for Equal Opportunity*. A recertification of FLI was approved on July 8, 2019.

At the FLI operation agreements (Betriebsvereinbarungen) facilitate work and family life. These agreements include models for the reintegration of scientists after family leave, various working time models, maintenance of a parent-child office, the cooperation with neighbouring day care centers, children emergency care, and workshops on nursing care for relatives. On average, two female Postdocs per year make use of the *Welcome back Fellowship* provided by FLI, facilitating reintegration into scientific work after a parental leave.

6. Cooperation and environment

Cooperation

Cooperation with local universities

The FLI engages in close collaborations with the Friedrich Schiller University Jena (FSU) and the University Hospital Jena (UKJ). Most SRG leaders at FLI have joint appointments with the FSU and fulfil a teaching obligation of 2 hr per week at the university. In addition,

on a voluntary basis, the FSU and UKJ offer the JRG leaders and Postdocs to engage in training of the different student programs. Projects for BSc and MSc theses are supervised by FLI scientists. The close collaboration is additionally strengthened by the appointment of 2 ARG leaders from the FSU and 1 ARG from the UKJ at the FLI. The FLI and the FSU share facilities for mouse husbandry and the restructuring of the mouse facilities in 2016 was organized by a member of the FSU. Together with the UKJ the FLI develops most of its clinically applied projects.

Cooperative Networks

The FLI is engaged in numerous cooperative networks:

Computational Network *DigLeben*: This regional network intends to develop and apply machine learning strategies to handle large data sets for uses in personalized medicine and related industrial applications.

Excellence Cluster *Balance in the Microverse*: In 2018, the FSU was awarded with a Cluster of Excellence and a leader of a JRG at FLI is involved in the Cluster activity as an associated group.

The *Leibniz ScienceCampus Jena – Regenerative Aging*: This ScienceCampus was formally initiated at the beginning of 2016. It joins FSU, UKJ, and FLI in their mutual interest to advance basic and clinically applied aging research.

The National Leibniz Research Alliance *Healthy Ageing*: The Alliance constitutes of 21 Leibniz institutes and the FLI acts as the central coordinating institute. The aim is to decipher the causes and effects of age-related dysfunctions and to develop measures and therapies that will reduce the negative impacts of aging on individuals and on the society.

National Network for Bioinformatics Infrastructure (de.NBI): With the establishment of the Computational Biology SRG in late 2017, the FLI has become a member of the German Network on Bioinformatics Infrastructure (de.NBI). The BMBF-funded initiative aims at developing and providing tools, services, and training for life scientists to carry out complex bioinformatic analyses.

International Network *International Cancer Genome Consortium (ICGC)*: The International Cancer Genome Consortium (ICGC) is a global initiative to unravel the molecular mechanisms of cancers. With this participation, the FLI strives to sharpen its profile in cancer research and to invite more collaborations in this aging-relevant research field.

Institution's status in the specialist environment

The FLI names the following institutions that also work on aging:

- Max Planck Institute for Biology of Aging / CECAD (Cologne, Germany),
- Buck Institute for Research on Aging (Novato, CA-USA),
- European Research Institute for the Biology of Aging (Groningen, Netherlands),
- Center for Healthy Aging at the University of Copenhagen (Denmark),
- The Paul F. Glenn Center for Aging Research at University California Berkeley and University of California San Francisco (CA-USA)

In comparison to above-mentioned aging centers, FLI distinguishes itself with regard to several characteristics: (i) strong focus on stem cell biology and stem cell aging, (ii) numerous, intense collaborative interactions with clinical partners, (iii) high capacity resources for animal experimentation (especially mice and fish), including humanized mice, (iv) pioneering expertise in using the *Nothobranchius furzeri* (killifish) model of aging, (v) early engagement in the novel research topic *Microbiota and Aging* and (vi) access to high-capacity and high-competence technology infrastructure (Core Facilities).

7. Subareas of FLI

In the following, a description is provided of the five FLI research Subareas (1 to 5), the research Core Facilities, and the research Animal Facilities (including the Animal Welfare unit).

Subarea 1: Stem Cell Aging

[Average 2016-2018: 30.2 FTE, thereof 12.6 FTE Research and scientific services, 9.8 FTE Doctoral candidates, and 7.8 FTE Service staff (including student assistants).]

The individual research groups within Subarea 1 investigate the causes and consequences of stem cell aging. The research work spans from basic model organisms over genetic mouse models up to humanized mouse models engrafted with human stem cells. According to the FLI, with the closure of two groups since 2016 the representation of invertebrate models of stem cell research was reduced in Subarea 1. The institute presumes that the recruitment of new groups should fill this gap. The research is defined by four focus areas:

- Cell-intrinsic mechanisms limiting the function of aging stem and progenitor cells,
- Aging-associated alterations of stem cell niches and the systemic environment,
- Mechanisms of clonal selection and epigenetic drifts in stem cell aging, and
- Microbiota- and metabolism-induced impairments in stem cell function during aging (in context of the new focus area *Microbiota and Aging* currently being built up within Subarea 2).

Since the last evaluation Research Area I was renamed from formerly *Stem Cell Aging and Organ Maintenance* to now more clearly reflect the overarching topics addressed.

Currently 2 SRGs, 1 JRG and 1 ARG contribute to the research in Subarea 1. Since the last evaluation 1 ARG and 1 Fellow Group were discontinued. An overview of the individual groups supporting the research in Subarea 1 since 2016 is listed below.

Research group (chair of subarea in bold)	Research Focus	FTE (2016-2018)
SRG Rudolph	Stem Cell Aging	17.0
SRG Waskow (since 11/2017)	Regeneration in Hematopoiesis / Immunology of Aging	1.7
JRG von Maltzahn	Stem Cells of Skeletal Muscle	5.4
Fellow Group González-Estévez (closed 2019)	Stem Cells / Regeneration of Plannarians	2.6
ARG Heidel (Medical Faculty; UKJ)	Stem Cell Aging / Myeloid Neoplasia	-
ARG Jasper (closed 2018, Buck Institute, Novato, CA, USA)	Stem Cell Signaling in Aging and Inflammation	3.5

Contributing FLI Subareas: SRG Morrison, JRG von Eyss (Subarea 2), JRG Neri (Subarea 3), JRG Ermolaeva, SRG Wang (Subarea 4), SRG Hoffmann, JRG Ori (Subarea 5).

Between 2016 and 2018 Subarea 1 published 53 articles in peer-reviewed journals, 2 articles in other journals as well as 1 individual contribution to an edited volume. Nine exploitation rights were granted. In the same time period the institutional funding was 5.7 M€. The revenue from project grants totalled 3.2 M€, with 1.13 M€ spent from the German Science Foundation (DFG), 1.1 M€ from EU grants, 438 K€ from the competitive procedure of the Leibniz Association and 209 K€ from Federal or Länder governments. 5 doctoral degrees were completed between 2016 and 2018 in Subarea 1.

The research highlights of Subarea 1 between 2016 and 2018 include the identification of aging-associated alterations in the epigenome of aging muscle stem cells in response to injury, which leads to an aberrant activation of developmental signals that impair the regenerative capacity in aging skeletal muscle. Through the ARG findings from animal models about the pathophysiologic consequences of hematopoietic stem cell aging are translated onto humans and mice. Several new insights were generated in terms of the investigation of the role of niche factors and systemically acting hormones in regulating self-renewal of muscle stem cells and function during aging. A study showed that dietary restriction, which influences the microbiome, delays early aging of hematopoietic stem cells by reducing Igf1 expression and the division rates of hematopoietic stem cells. Moreover, it was revealed that *Setd1a* controls DNA damage responses through epigenetic modifications in hematopoietic stem and progenitor cells. Researchers from Subarea 1 contributed to dissecting the role of the transcription factor CEBP β /LIP in controlling the lifespan of mice.

Transfer activities of Subarea 1 were pursued via the SPARK@FLI Core Facility (see Core Facilities below). This also included translational efforts together with the ARG from the University Hospital Jena to investigate whether new mechanisms identified in animal models contribute to human aging.

The future plans of Subarea 1 include research on the genetics of stem cell aging based on several model systems. The epigenetics of stem cell aging as well as the proteostasis in aging stem cells will also be pursued within the research focus area cell intrinsic factors.

Within another research focus the cell-extrinsic factors inducing stem cell-intrinsic alteration during aging will be investigated with the aim to dissect their impact disturbing the regulation of the epigenome, the proteome and of signal transduction pathways. Another research direction will further concentrate on the aging-associated changes in metabolism.

Subarea 2: Regeneration and Homeostasis of Organs in Aging

[Average 2016-2018: 21.2 FTE, thereof 11.9 FTE Research and scientific services, 3.4 FTE Doctoral candidates, and 5.9 FTE Service staff (including student assistants).]

The main goal of Subarea 2 is to identify cellular and molecular pathways used to ensure effective organ maintenance and repair, and to unravel the mechanisms of their deterioration during aging. While stem cells are important for organ homeostasis, this Subarea does not *per se* directly addresses stem cell aging but rather focusses on the following focus areas:

- Drifts in developmental pathways limiting organ maintenance in aging,
- Immune aging and inflammation,
- Systemic and micro-milieu regulators of organ maintenance, regeneration, and disease development.

Subarea 2 was renamed (formerly: *Organ Maintenance in Aging*) since the last evaluation. Due to the retirement of the chair of Subarea 3 the SRG Englert working on molecular genetics of aging transferred from Subarea 2 to Subarea 3. Moreover the SRG Weih working on Immunology, which was provisionally headed after the death of the group leader in 2014, was discontinued. This topic is being continued at the FLI within the research of the SRG Waskow in Subarea 1. According to the FLI the JRG von Eyss established shortly before the last evaluation in 2016 has successfully integrated into Subarea 2 and the institute profits from the added expertise in functional genome screening, e.g. genome-wide and targeted CRISPR screening. The FLI will place the new research focus *Microbiota and Aging* (see Chapter 3) within Subarea 2. This will expand the Subarea by one SRG and two JRGs.

Currently one SRGs, two JRG and two ARGs contribute to the research in Subarea 2. An overview of the individual groups supporting the research in Subarea 2 since 2016 is listed below.

Research group (chair of subarea in bold)	Research Focus	FTE (2016-2018)
SRG Morrison	Nerve Regeneration	10.7
JRG von Eyss	Transcriptional Control of Tissue Homeostasis	3.8
ARG Herrlich (Emeritus)	Cancer Cell Biology	1.7
ARG Ploubidou (guest status at FLI, EU funded)	Virus Induced Oncogenesis	3.0
SRG Weih (closed 2018)	Immunology	2.0

Contributing FLI Subareas: SRG Rudolph, JRG von Maltzahn, ARG Heidel (Subarea 1), SRG Englert (Subarea 3), SRG Kaether, JRG Ermolaeva (Subarea 4), SRG Hoffmann, JRG Ori (Subarea 5).

Between 2016 and 2018 Subarea 2 published 59 articles in peer-reviewed journals. 13 exploitation rights were granted and 5 patents applied for. In the same time period the institutional funding was 3.5 M€. The revenue from project grants totalled 2.3 M€, with 1.2 M€ spent from EU grants, 426 K€ spent from the German Science Foundation (DFG), 436 K€ spent from national or international foundations or associations and 234 K€ from the competitive procedure of the Leibniz Association. 14 doctoral degrees and 1 habilitation were completed between 2016 and 2018 in Subarea 2.

The research highlights of Subarea 2 between 2016 and 2018 include the discovery of the importance of the *NF2* gene for neuronal differentiation and maturation, as well as maintenance and regeneration of adult neurons. Another work proves that peripheral nervous system regeneration also shows an age-dependent regenerative decline, with “repair-aiding” Schwann cells (SC) exhibiting alterations within the Ras signaling pathway, limiting “repair-aiding” cell responses. Work on the Receptor for Hyaluronic Acid Mediated Motility (RHAMM) discovered that it localizes to the mitotic spindle and regulates orientation. Disruption of this function in the testis resulted in hypofertility and seminoma while disruption in neuronal progenitors resulted in megalencephaly. The repressive transcription factor tricho-rhino-phalangeal syndrome 1 (TRPS1) was identified as potent repressor of YAP/TAZ activity. TRPS1 acts as an oncogene in breast epithelial cells and cancer by limiting YAP/TAZ, which surprisingly has tumor suppressive properties in this cancer entity. Also within the research of Subarea 2 a contribution to the understanding of micro-environmental signaling events by studying metalloprotease cleavage regulation was made.

Transfer activities of Subarea 2 were pursued via the SPARK@FLI Core Facility (see Core Facilities below) and included the development of a potential protein replacement therapy to prevent schwannoma formation. This technique was patented.

The future plans of Subarea 2 are committed to further substantiate and uncover new knowledge on the age-dependent mechanisms leading to organ dysfunction and regenerative decline. After the detection of the systemic pro-inflammatory cytokine CCL11 as a nerve-aging factor the CCL11-CCR5-CCL2 axis as an inducer and/or mediator of peripheral nerve aging will be investigated. Another research focus will be on intrinsic age-dependent changes in the systemic altered immune response (macrophages) that might contribute to the aged nerve. How tissue stiffening leads to aging-associated defects in tissue architecture

and cellular differentiation and how modulation of YAP/TAZ can be exploited to counteract those dysfunctions will be addressed. Extensive use of the novelty established 10x Chromium single-cell analysis platform at the Core Facility *Functional Genomics* is planned to analyze the heterogeneity of aging organs on the transcriptional (scRNA-Seq) and chromatin level, e.g. scATAC-Seq.

Subarea 3: Genetics and Epigenetics of Aging

[Average 2016-2018: 22.9 FTE, thereof 12.5 FTE Research and scientific services, 3.6 FTE Doctoral candidates, and 6.8 FTE Service staff (including student assistants).]

The focus of Subarea 3 is on genetic and epigenetic determinants of life- and health span as well as aging in fish, rodents and humans. This line of research builds on the expertise of the institute in comparative and functional genomics. The research is defined by five focus areas:

- Comparative genomics in short- and long-lived models of aging,
- Genomic engineering in *N. furzeri*,
- Epigenetics of aging,
- Non-coding RNAs in aging,
- Comparative transcriptomics of aging.

Subarea 3 was renamed from previously *(Epi)Genetics and Models of Aging*. According to the FLI, since the last evaluation other essential developments have been the final establishment of the JRG Neri at FLI as well as recruiting a new ARG in 2017. On the other hand, a SRG leader and previous chair of Subarea 3 retired in August 2018. FLI transferred unpublished data of this SRG to the collaborators where the research will potentially be followed up and/or utilized in future publications. The institute is engaged in recruiting a senior group leader with expertise in genomics, e.g., within the call for a W3 professorship on *Functional Microbiota Host-Interactions in Aging* (to be located in Subarea 2). The SRG of the new chair of Subarea 3 was previously located in Subarea 2, however the scientific focus of the SRG on the genetics of aging, in particular in the *N. furzeri* and *D. rerio*, also complete the research in Subarea 3.

Currently one SRG, one JRG and three ARGs contribute to the research in Subarea 3. An overview of the individual groups supporting the research in Subarea 3 since 2016 is listed below.

Research group (chair of subarea in bold)	Research Focus	FTE (2016-2018)
SRG Englert	Molecular Genetics	8.8
JRG Neri	Epigenetics of Aging / Damage Accumulation	5.3
ARG Bierhoff (Faculty of Biological Sciences, FSU Jena)	Epigenetics of Aging / Chromatin Landscape	-
ARG Cellierino (Scuola Normale Superiore, Pisa, Italy)	Biology of Aging	2.1
ARG Marz (Faculty of Mathematics, FSU Jena)	Non-coding RNAs in Aging	-
SRG Platzer (closed 2018)	Genome Analysis	6.2

Contributing FLI Subareas: JRG von Maltzahn, SRG Rudolph, ARG Heidel (Subarea 1), SRG Morrison, JRG von Eyss (Subarea 2), JRG Ermolaeva, SRG Wang (Subarea 4), JRG Ori, ARG Kestler (Subarea 5).

Between 2016 and 2018 Subarea 3 published 105 articles in peer-reviewed journals and 7 articles in other journals as well as 5 individual contributions to edited volumes. 5 exploitation rights and 3 licenses were granted. In the same time period the institutional funding was 4.7 M€. The revenue from project grants totalled 1.8 M€, with 929 K€ spent from national or international foundations or associations, 521 K€ spent from the German Science Foundation (DFG) and 180 K€ from the competitive procedure of the Leibniz Association. 12 doctoral degrees were completed between 2016 and 2018 in Subarea 3.

The research highlights of Subarea 3 between 2016 and 2018 include work on the Wilms tumour suppressor protein Wt1 as well as establishing *N. furzeri* as a useful model to study tumour development. A transparent *N. furzeri* line was generated which will serve as a tool for various analyses including the *in vivo* observation of tumor growth and metastasis formation as well as regeneration. The laboratory on epigenetics of aging was established within Subarea 3 and genome-wide epigenetic analysis implemented at FLI. With a newly developed method called *triplex recognition in cell* (TRIC) it was found that an RNA:DNA tripe helix at the *Kras* promoter regulates gene activity. MicroRNA-29 was identified as a regulator of iron homeostasis and brain aging as well as a mediator of oxidative stress and a regulator of cardiac aging. In agreement with evolutionary theories of aging in eusocial organisms, transcriptome patterns in naked mole-rat breeders were identified that, in contrast to the disposable soma theory of aging, may slow down aging rates and potentially contribute to their exceptional long life- and health span.

In terms of transfer activities Subarea 3 engages in a collaboration with the Hospital Weimar and the University Hospital Heidelberg. The cooperation with the University Hospital Jena is very strong and in some works the aim is to translate the research into a diagnostic tool.

The future plans of Subarea 3 include generating knock-in mutations in *N. furzeri* to investigate the role of candidate genes that were positively selected during lifespan shortening of *N. furzeri*. The knock-in experiments aim to replace genomic sequences of short-lived *N.*

furzeri with homologous sequences of long-lived species, to determine whether the manipulated region contributes to changes in lifespan of *N. furzeri*. Furthermore, the efforts to analyse the role of the microbiome for aging and regeneration in fish will be intensified.

Subarea 4: Cell Dynamics and Molecular Damages in Aging

[Average 2016-2018: 29.4 FTE, thereof 15.4 FTE Research and scientific services, 5.6 FTE Doctoral candidates, and 8.3 FTE Service staff (including student assistants).]

The research focus of Subarea 4 is on studying damages of macromolecules (proteins, nucleic acids) and determining the structure-function relationship of biomolecules relevant to damage and damage repair processes and responses to molecular damage that might lead to aging and aging-associated pathologies. The studies are focused on the following research areas: DNA replication, DNA damage responses (DDR); stress responses; metabolic stresses; protein trafficking and protein damages. The research is defined by four focus areas:

- DNA damage response in tissue homeostasis and neuropathies,
- The quality control in the endoplasmic reticulum for secretory pathway in aging processes,
- Intrinsic and extrinsic factors implicated in cellular decline during aging,
- DNA replication and genomic integrity preventing premature aging and diseases.

Since the last evaluation one SRG leader working on Biochemistry within Subarea 4 retired and the JRG Ermolaeva was transferred from Subarea 3 to Subarea 4 to contribute studies in cell dynamics of aging. Subarea 4 was also renamed (formerly: *Molecular Damages in Aging*). The institute intends to place the SRG of the planned recruitment of a W3 professorship *Biochemistry of Aging* within Subarea 4 (see Chapter 3).

Currently 2 SRGs and 1 JRG contribute to the research in Subarea 4. An overview of the individual groups supporting the research in Subarea 2 since 2016 is listed below.

Research group (chair of subarea in bold)	Research Focus	FTE (2016-2018)
SRG Wang	Genome Stability	11.9
SRG Kaether	Membrane Trafficking in Aging	6.9
JRG Ermolaeva	Stress Tolerance and Homeostasis	5.4
SRG Große (closed 2018)	Biochemistry	5.2

Contributing FLI Subareas: SRG Rudolph (Subarea 1), SRG Morrison, JRG von Eyss, ARG Herrlich (Subarea 2), JRG Neri, ARG Cellarino (Subarea 3), JRG Ori (Subarea 5).

Between 2016 and 2018 Subarea 4 published 65 articles in peer-reviewed journals and 2 individual contributions to edited volumes. 3 exploitation rights and 4 licenses were granted as well as 6 patents. In the same time period the institutional funding was 5.5 M€. The revenue from project grants totalled 1.94 M€, with 933 K€ spent from the German

Science Foundation (DFG), 564 K€ from the competitive procedure of the Leibniz Association and 275 K€ spent from national or international foundations or associations. 7 doctoral degrees were completed between 2016 and 2018 in Subarea 4.

The research highlights of Subarea 4 between 2016 and 2018 include the discovery of a novel regulatory mechanism how poly(ADP-ribose) polymerase protects cells and organisms from acute DNA damage. Another study identified that axonopathy-causing mutations in Atlantin (ATL) 3 affect ER-morphology, ER-Golgi transport and autophagy, potentially contributing to axon degeneration. From proteomics analysis of young and old animals treated with metformin the conclusion was drawn that adaptive stress responses become inhibited in late life limiting effectiveness of anti-aging treatments in the elderly. In terms of the investigations of DNA replication an important result was the identification that Cdc45 is limiting for DNA replication and serves as a loading factor for human RPA protein onto single stranded DNA.

In the sense of transfer activities Subarea 4 collaborates with the FMP Leibniz Institute (Leibniz-Forschungsinstitut für Molekulare Pharmakologie in Berlin). Also within Subarea 4 screens for gene mutations and compounds that alleviate endoplasmic reticulum stress counteracting inflammatory bowel disease are conducted. Moreover, in collaboration with an industrial partner novel drugs for cancer therapy are developed.

The future plans of Subarea 4 are to study the mechanism through which neuron functionality as well as cellular metabolism is regulated. The role of PARP1 enzymatic activity and PARP1 protein in tissue homeostasis will be deciphered as well as the role of YIPF5, Golt1A and Golt1B in endoplasmic reticulum export and in senescence-associated changes of the secretory pathway. The role of Klotho in the brain and in the choroid plexus will also be investigated. Mitochondrial decline and distorted energy metabolism in the aging process will be studied as well as host effects of age- and disease-associated microbes. Genetic screens are planned to identify genes implicated in resistance to aging relevant stresses. DNA replication stress in aging and age-related pathologies will be investigated and pharmacological tools to intervene the consequences of genomic destabilization during aging and cancer developed.

Subarea 5: Computational and Systems Biology of Aging

[Average 2016-2018: 5.9 FTE, thereof 2.8 FTE Research and scientific services, 1.7 FTE Doctoral candidates, and 1.4 FTE Service staff (including student assistants).]

Subarea 5 focuses on the development of methods to analyse and understand complex biological systems. This work includes the design of computer algorithms and biostatistical approaches as well as the development of novel Omic strategies (i.e. genomics/epigenomics, transcriptomics, proteomics, and metabolomics) to study aging and aging-related diseases. According to the FLI, due to the Subarea's expertise in computational data analysis, it is deeply interconnected with all other Subareas. The Subarea hosts two critical core facilities (Life Science Computing, Proteomics) and provides consulting services in statistics. Furthermore, it organizes courses on data analysis and statistics. The research is defined by five focus areas:

- Mapping extrinsic and intrinsic factors influencing stem cells during aging,

- Integration of spatiotemporal proteomics and transcriptomics data,
- Comprehensive evaluation of qualitative and quantitative expression changes,
- Identification and analysis of epigenomic alterations during aging and age-related diseases,
- Network analysis of genomic, transcriptomic and epigenomic alterations during aging.

Subarea 5 was newly established at the time of the previous evaluation and was then composed of the SRG Kestler and the JRG Ori. Since the last evaluation the SRG Kestler has returned to the University of Ulm and remained affiliated to FLI as an ARG. The new SRG Hoffmann was set up in late 2017, and all critical staff positions were filled by mid-2018.

Currently 1 SRG, 1 JRG and 1 ARG contribute to the research in Subarea 5. An overview of the individual groups supporting the research in Subarea 5 since 2016 is listed below.

Research group (chair of subarea in bold)	Research Focus	FTE (2016-2018)
SRG Hoffmann (since 09/2017)	Computational Biology of Aging	1.7
JRG Ori	Aging of Protein Complexes	3.8
ARG Kestler (Ulm University)	Bioinformatics and Systems Biology of Aging	-

Contributing (FLI Subdivision): SRG Rudolph, JRG von Maltzahn (Subarea 1), SRG Morrison, JRG von Eyss, SRG Platzer, ARG Bierhoff, ARG Cellarino (Subarea 3), SRG Wang, JRG Ermolaeva (Subarea 4).

Between 2016 and 2018 Subarea 5 published 37 articles in peer-reviewed journals and 1 individual contribution to edited volumes. In the same time period the institutional funding was 1.25 M€. The revenue from project grants totalled 296 K€, with 183 K€ spent from the German Science Foundation (DFG) and 90 K€ from Government (Bund).

According to the institute the research highlights of Subarea 5 between 2016 and 2018 include the development of proteomic strategies to comprehensively map cell extrinsic and intrinsic factors influencing muscle and intestinal stem cells during aging. A new line of research was also developed that combines transcriptomics and proteomics to study determinants of longevity. Work was done on the analysis of transcriptomic data and its integration with other sources of biological and clinical information. Novel methods have been developed for the detection of alternative differential splicing in large RNA-Seq data sets data and are used within the FLI and in cooperation projects.

Subarea 5 has engaged in transfer activities in the sense that it has actively participated in the development and operation of other research infrastructures, especially the Core Facilities *Life Science Computing* and *Proteomics*.

The future plans of Subarea 5 involve the investigation of regulatory mechanisms governing transcription, translation, and protein abundance in different cellular compartments as well as mechanisms of inter-cellular communication in aging. On the computational side Boolean networks and multi-agent systems will be leveraged to better infer potential

epigenome-transcriptome interactions from next-generation sequencing experiments including single-cell analyses. Furthermore, Subarea 5 is working on methodological improvements for big data analysis in close collaboration with other FLI groups.

Core Facilities and Core Services

[Average 2016-2018: 33.3 FTE, thereof 13.3 FTE Research and scientific services, 0.6 FTE Doctoral candidates, and 19.5 FTE Service staff (including student assistants).]

In order to provide FLI researchers with state-of-the-art research infrastructures, starting January 2016 the FLI established central technology platforms (Core Facilities, CF). The institute states that the defining considerations for the built-up of these infrastructures were the scientific needs of the FLI research groups, recommendations by external experts, incl. the SAB, and the potential to foster high-profile publications at the FLI. Currently seven Core Facilities exist. In addition, FLI operates a Core Service (CS) support structure, providing different laboratory services.

The operation of Core Facilities and Core Services is overseen by the Head of Core. Each individual CF is scientifically guided by an FLI group leader, the Scientific Supervisor of the CF. A dedicated CF Manager organizes the day-to-day operation of each CF.

While the Core Facilities are mainly designed for FLI internal use (including use by ARGs), external partners also use the facilities. Between 2016 and 2018 the external usage (workload) of the CFs averages to 21.5 % of total usage. The Core Facilities and Services have significantly contributed to publications of the FLI. During the reporting period, close to 50% of all research articles from FLI acknowledged a CF or were co-authored by CF members.

Currently, the FLI provides the following Core Facilities:

DNA Sequencing providing sequencing service. During the reporting period a yearly average of 1418 samples was processed. The CF currently extends available methods and implements new approaches, in particular for single-cell analysis.

Proteomics: The facility developed a dedicated pipeline for quantitative proteomic measurement of rare primary cell populations, a full pipeline for Thermal Proteome Profiling (TPP) in both one and two dimensions. Development continues on post-translational modification enrichment pipelines, with acetylation virtually finalized and phosphorylation underway.

Life Science Computing: This CF has been established in 2018. It provides consulting services in biostatistics, offers training courses in bioinformatics, develops and adjusts best-practices and carries out bioinformatics analyses. Its portfolio of data analyses encompasses qualitative and quantitative expression studies (RNA, protein), variation/mutation analysis, CHIP- and ATAC-Seq studies.

Functional Genomics: This CF provides human and murine genome-wide siRNA libraries, human lentiviral genome-wide CRISPR/CAS9 inactivation and activation (SAM) libraries. It offers service for small and large-scale functional screens on the cellular level. The CF also supports *in vivo* screens based on CRISPR/CAS9 targeting technologies, in collaboration with the Animal Transgenesis Facility (ATF) to support transgenic mouse line generation.

Imaging: The CF provides training and support for an average of 176 users per year for 14 light microscope platforms. Equipment was brought up-to-date by several acquisitions. Various super-resolution technologies (STED, HyVolution II, Airyscan) were introduced.

Flow Cytometry: All Flow Cytometers (6 sorters, 4 analyzers) are managed by facility personnel. The CF provided introductory training in applying flow cytometric analysis software as well as hands-on training in flow cytometric sorting on-demand.

Technology Transfer "SPARK@FLI": This CF has been established in 2016 following the example of the Stanford University SPARK initiative. The CF aims to assess and support technology transfer of research results towards potential commercial applications. An external advisory board was established and includes 24 experts from pharmaceutical companies, transfer units from other Leibniz Institutes, academic institutions, and SPARK units elsewhere. Also, the former founder of SPARK@Stanford is on the panel. Twice per year, the panel evaluates all project proposals and the progress of running projects. Seven out of 13 projects were selected by the panel for seed funding between 2016 and 2018. Additionally, early-stage transfer projects receive technical and advisory support by the CF personnel.

The Core Services (CSs) provide general laboratory support. The CSs are supervised directly by the Head of Core. The support offered and their annual average usages (in parentheses) are as follows: Histology/Electron Microscopy (10 FLI groups, 7 external groups; external usage 16 %), Protein Production (9 FLI groups, 4 external groups; external usage: 23%), S2 safety level labs (83 users from FLI; no external users), Isotope Lab (62 individual usages; no external users), Gamma Irradiation Source / Small animal CT (160 irradiations for FLI groups; external usage: 17%), Media Kitchen and Autoclave Service (only FLI groups).

Animal Facilities and Animal Welfare

[Average 2016-2018: 43.3 FTE Service staff (including student assistants).]

The FLI states that aging research at the institute depends heavily on the study of model organisms. Primarily, rodents (*M. musculus*) and fish (*D. rerio*, *N. furzeri*) are used, for which separate animal facilities are established. To a lesser extent, the following animal models were also used during the reporting period: *S. mediterranea* (a planarian), *H. vulgaris* (hydra), *C. elegans*, *D. melanogaster*, and *F. mechowii* (giant mole-rat). The generation of genetically modified organisms is being pursued in the newly established Animal Transgenesis Facility (ATF). According to FLI, all animal experimentation is overseen by an independently operating Animal Welfare unit.

Following Animal Facilities are currently maintained at the FLI:

Animal Facility (Mouse): This facility is a medium-sized animal unit with approximately 12,500 mice. More than 90 % of the research groups at FLI perform experiments with mice or investigate organs of over 340 genetically modified mouse lines. The FLI houses mice until an age of 36 months. The mouse facility is equipped with surgery rooms, metabolic cages, two small animal CTs and equipment for behavioral studies. Embryo transfer

and mouse line cryopreservation complete the service offered to the scientists. The mouse facility implemented a new mouse database for real-time monitoring of the mice and documentation of experiments.

Animal Facility (Fish): Since December 2016, the Animal Facility (Fish) is an independent animal care unit providing a maximum of 4,500 *N. furzeri* and 24,000 *D. rerio* fish for scientific purposes. Over the last years, the team improved and refined the housing protocols and established standardization in fish husbandry. The service provided to the fish users includes management of the stock center for established fish lines, centrally organized wild type breeding, and supply of aging cohorts of different fish strains. Health monitoring is performed, with daily visual inspections and quarterly comprehensive pathogenic testing.

Animal Transgenesis Facility (ATF): The FLI explains that, with the advent of CRISPR-based genome engineering, the generation of genetically modified mice has substantially accelerated in recent years. To this end, the institute has installed a new Animal Transgenesis Facility (ATF) in order to provide scientists with a competitive facility that generates new mouse lines using CRISPR-based technologies. Currently, the ATF has initiated several projects to generate new lines in-house. In the future, it aims to provide various services (e.g. pronuclear injection, embryo electroporation, genome-editing via oviductal nucleic acid delivery (GONAD) system, etc.). It is foreseen that the ATF will also engage in generating genetically modified lines of *N. furzeri* and *D. rerio* in the future.

Animal Welfare: The Animal Welfare unit was established in 2016 and is run by the head animal welfare officer who is a veterinarian. One other full-time veterinarian and a part-time veterinarian, who also oversees the FLI veterinary pharmacy, constitute the staff of the unit. The unit oversees all three animal facilities (mouse, fish, ATF). Major activities and tasks include: monitoring of animal health and hygiene, controlling of all animal experimentations, optimization of animal husbandry (e.g. testing of new enrichments), training and further education of animal experimentation, advisory work and mediation of all communication between FLI scientists and legal authorities.

8. Handling of recommendations from the previous evaluation

The recommendations of the reviewers and the Senate of the Leibniz Association are shown in *italics*.

- 1. Since the last evaluation, the institute's research has been structured in five overarching thematic subareas. 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.*

The five subdivisions, now termed Subareas, have been consolidated thematically to each address more distinctly a specific overarching issue of aging. In accordance, new Group Leaders have been recruited to the Subareas to strengthen these overarching issues. The changes are outlined in Chapter 7.

2. *FLI's ongoing efforts to promote the translation of its basic scientific insights into clinical practice via an internal training and support program 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.*

According to the institute, the interactions with UKJ have been intensified considerably. These collaborations are all within basic, clinically applied research, although not yet including cohort studies. However, it is expected that the imminent appointment of the new W3 professorship *Translational Geriatric Medicine* at the UKJ will catalyze such cohort studies with the FLI.

Further collaborations are outlined in Chapter 6.

In addition, joint literature seminars have been established among FLI and UKJ researchers (partly including the Leibniz HKI), which address neurology and aging (Neuro-Club), the aging hematopoietic system (Haemato-Club), and the microbiome and aging (Intestine and Microbiome Club).

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.*

The FLI followed the reviewer's recommendation and first started the recruitment of the W3 professorship *Microbiota-Host Interactions in Aging*. Details are given in Chapter 3.

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.*

According to FLI, during the current reporting period, the existing contacts with HKI have been intensified and new ones were initiated. In 2018, the 'Intestine and Microbiome Club' has been established. It is an interest group that on a monthly basis brings together groups from FLI, HKI and UKJ with the aim of intensifying scientific exchange on topic of host-microbiome interaction in aging.

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.*

The Institute has revised its target on third party funding and a share of 17 – 20 % third party income is expected until 2020 (relative to total budget), which may be considered

an intermediate goal. The new Group Leaders recruited in 2016/2017 have begun to contribute to the institute's third party income and will further strengthen the institutes' budget. The figures of 2018 (i.e., 13.9 %) already show improvements over those of 2016 and 2017. To consolidate this trend, FLI is increasing its efforts to optimize the application process. A grant acquisition officer has been installed to stimulate application activities. Also, the existing incentive system was improved.

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.*

The previous Subdivision 3 is now Subarea 4. The FLI transferred JRG Ermolaeva with expertise in the field of cellular longevity to Subarea 4 to strengthen the aging focus. The institute states that, the SRG Wang has intensified its efforts to unravel the contributions of DNA damages to aging-associated neurodegeneration and the inclusion of the W3 professorship on the *Biochemistry of Aging* will sharpen the aging profile of Subarea 4.

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.*

According to the FLI the recruitment of the chair of Subdivision 5 in late 2017 has strengthened the FLI's profile in the field of bioinformatics and computational biology. Also a Core Facility *Life Science Computing*, supporting bioinformatics analyses of all scientists at the FLI, has been established. Collaborations with the Friedrich Schiller University Jena have been intensified through the network *DigLeben*.

With the recruitment A. Ori and his JRG, the Subarea 5 has substantially improved its expertise in high-throughput proteomics and proteome bioinformatics.

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.***

The FLI explains that, the trend for intensified international cooperations has indeed been strengthened by FLI group leader initiatives, specifically regarding new one-to-one collaborative interactions (a total of 45 collaborations). On the level of formal institutional collaboration, active exchange contacts exist between FLI and the Buck Institute for Research in Aging (Novato, CA, USA). A memorandum of understanding (MOU) for mutual cooperative exchanges has been filed. New institutional contacts are being established with the Glenn Center for Biology of Aging Research at UC Berkeley.

Regarding PhD training, four FLI group leaders are involved in a joint program between FSU Jena and Shenzhen University (China), which has been initiated in 2017.

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.*

With deadline December 31, 2018, at the Postdoc level, 42 % are women (end of 2015: 40 %). At the level of doctoral candidates, 50 % are women (end of 2015: 37 %). Overall, at the level 'employees in science': 40 % (end of 2015: 33 %).

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.*

A number of PhDs were affected by the closure of the Animal Facilities in 2016 causing prolongation of the projects. As this issue is solved, the following two major measures are being taken by the FLI to reduce PhD project times: discontinuation of financial support after 4 years and guidance by thesis advisor and advisory committee. Details are described in Chapter 5.

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 program in favor of a **unified, structured postdoctoral qualification** of the kind being attempted in the context of the new postdoctoral network.*

Upon this recommendation and a comparable one by the SAB, FLI did not recruit any new Fellow Groups after 2013. Instead, a structured Postdoc qualification program was implemented (see Chapter 5).

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 organization 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.

The FLI has established a Compliance Management System. The institute describes that, the FLI Board of Directors is continuously monitoring compliance with all regulations of Animal Welfare and that this process is actively supported by the Supervisory Board (meetings November 2017, January 2018, October 2018, May 2019), and the SAB (June 2016, June 2017, June 2018, and June 2019). The measures implemented in 2016 and thereafter included the restructuring of the Animal Facility (Mouse) and the formation of an Animal Welfare unit with several Animal Welfare Officers and professional veterinarians. Details are described in Chapter 3. Thirteen PhD candidates were affected by withdrawal of licenses and their contracts were prolonged by 12 months beyond the initially planned duration.

*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.*

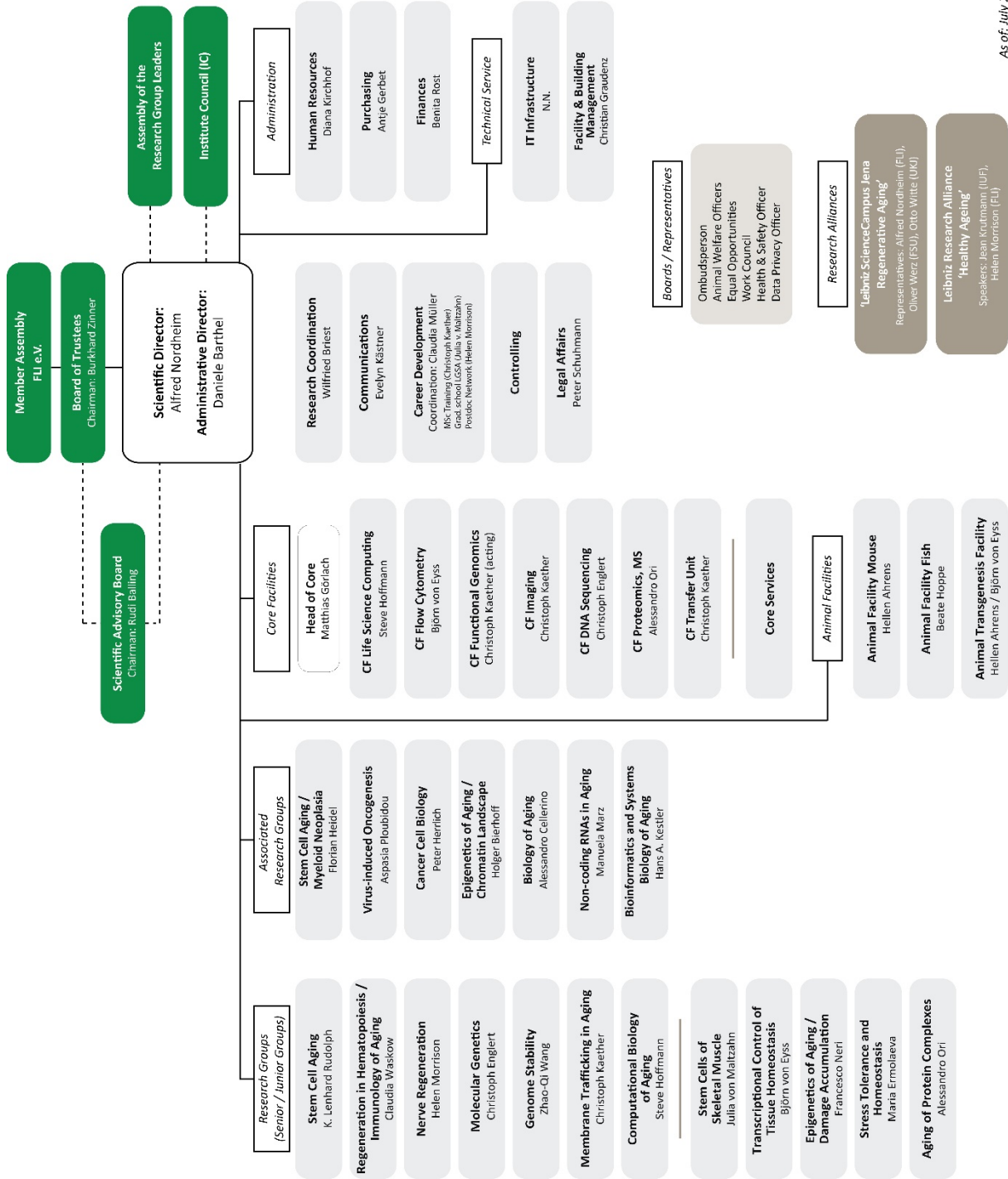
The institute states to implement this recommendation for the evaluations in a 7-year cycle.

Appendix 1

Organisational Chart



Star (*) indicates Chair of Subarea.



Appendix 2

Publications and patents

	Period		
	2016	2017	2018
Total number of publications	131	114	120 (11)
Monographs (PhD theses)	13	11	15
Individual contributions to edited volumes	6	2	2
Articles in peer-reviewed journals ¹⁾	111	100	94 (11)
Articles in other journals	0	1	9
Editorship of edited volumes	1	0	0

Industrial property rights (2016-2018) ²⁾	Granted	Registered
Patents (newly granted / newly applied)	6/5	12
Exploitation rights / licences (number)	44/19	

¹ Additional contributions which have been published in status "Epub ahead of print" in the past year in parentheses.

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

Appendix 3 Revenue and Expenditure

Revenue		2016			2017			2018 ¹⁾		
		k€	% ²⁾	% ³⁾	k€	% ²⁾	% ³⁾	k€	% ²⁾	% ³⁾
Total revenue (sum of I, II, and III; excluding DFG fees)		30,158.0			30,564.3			30,558.4		
I.	Revenue (sum of I.1., I.2. and I.3)	28,582.0	100 %		28,480.1	100 %		29,646.0	100 %	
1.	<u>INSTITUTIONAL FUNDING (EXCLUDING CONSTRUCTION PROJECTS AND ACQUISITION OF PROPERTY)</u>	25,062.7	88 %		25,494.4	90 %		25,857.9	87 %	
1.1	Institutional funding (excluding construction projects and acquisition of property) by Federal and <i>Länder</i> governments according to AV-WGL	25,062.7			25,494.4			25,857.9		
1.2	Institutional funding (excluding construction projects and acquisition of property) not received in accordance with AV-WGL	0.0			0.0			0.0		
2.	<u>REVENUE FROM PROJECT GRANTS</u>	3,519.0	12 %	100 %	2,985.0	10 %	100 %	3,783.0	13 %	100 %
2.1	DFG	915.0		26 %	971.0		33 %	1,440.0		38 %
2.2	Leibniz Association (competitive procedure)	514.0		15 %	612.0		21 %	495.0		13 %
2.3	Federal, <i>Länder</i> governments	456.0		13 %	402.0		13 %	507.0		13 %
2.4	EU	1,178.0		33 %	301.0		10 %	764.0		20 %
2.5	Industry	0.0		0 %	0.0		0 %	0.0		0 %
2.6	Foundations	402.0		11 %	673.0		23 %	576.0		15 %
2.7	Other sponsors (DAAD, ZA), International)	54.0		2 %	26.0		1 %	1.0		0 %
3.	<u>REVENUE FROM SERVICES</u>	0.3	0 %		0.7	0 %		5.1	0 %	
3.1	Revenue from commissioned work	0.0			0.0			0.0		
3.2	Revenue from publications	0.0			0.0			0.0		
3.3	Revenue from exploitation of intellectual property for which the institution holds industrial property rights (patents, utility models etc.)	0.3			0.7			0.5		
3.4	Revenue from exploitation of intellectual property without industrial property rights	0.0			0.0			4.6		
II.	Miscellaneous revenue (e.g. membership fees, donations, rental income)	76.0			99.2			112.4		
III.	Revenue for construction projects (institutional funding by Federal and <i>Länder</i> governments, EU structural funds, etc.)	1,500.0			1,985.0			800.0		
Expenditures		k€			k€			k€		
Expenditures (excluding DFG fees)		30,158.0			30,564.3			30,558.4		
1.	Personnel	14,917.1			15,528.1			16,472.9		
2.	Material expenses (Sachausgaben) ⁴⁾	9,026.4			8,170.5			9,449.8		
2.1	<i>Proportion of these expenditures used for registering industrial property rights (patents, utility models etc.)</i>	33.9			41.2			25.0		
3.	Equipment investments	2,856.3			2,418.7			3,005.4		
4.	Construction projects, acquisition of property	1,993.2			2,692.3			1,176.1		
5.	Revenues of previous years carried forward	1,365.0			1,754.7			454.2		
DFG fees (if paid for the institution – 2.5% of revenue from institutional funding)		622.3			630.6			643.1		

¹ Preliminary data: yes.

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 “Revenues 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 resources of “Revenue from project grants”.

⁴ Including: consumables, travel expenses, membership fees (WGL, SAW), maintenance and building running costs

Appendix 4

Staff (Basic financing and third-party funding / proportion of women (as of: 31.12.2018))

	Full time equivalents		Employees ⁵⁾		Female employees		foreigners
	Total	on third-party funding	Total	on temporary contracts	Total	on temporary contracts	Total
	Number	Percent	Number	Percent	Number	Percent	Number
Research and scientific services	98.1	33.2	124	85.5	50	88.0	68
1 st level scientific director	0.5	0.0	1	100.0	0	0.0	0
2 nd level -senior research group leaders ⁶⁾	7.0	14.3	7	14.3	2	0.0	2
2 nd level -junior research group leaders	5.0	0.0	5	100.0	2	100.0	3
Further academic staff in executive positions	2.9	35.1	3	66.7	2	100.0	2
Scientists in non-executive positions	59.7	36.4	65	83.1	24	83.3	30
Doctoral candidates	23.1	38.5	43	100.0	20	100.0	31
Service positions	116.0	1.2	126				
Service positions in Research and Facilities:	88.6	1.1	96				
Laboratory (E9 to E12)	24.0	4.2	26				
Laboratory (below E9)	2.5	0.0	3				
Services (CF/CS) (E9 to E12)	17.0	0.0	18				
Services (CF/CS) (below E9)	3.5	0.0	3				
Executive staff/scientists/advisors in Animal Facilities	6.8	0.0	11				
Animal Care (below E10)	34.8	0.0	35				
Service positions in Management:	27.4	1.3	30				
Advisers and Commissioner functions ⁷⁾	3.8	9.1	4				
Information technology – IT (E10 to E12)	5.0	0.0	5				
Building Management (E4 to E12)	8.5	0.0	9				
Secretariats	10.1	0.0	12				
Administration	27.2	6.9	29				
Administrative director	1.0	0.0	1				
Staff positions (from E13, senior service) ⁸⁾	6.8	27.6	7				
Staff positions (E9 to E12) ⁸⁾	4.1	0.0	5				
Internal administration (E6 to E12) Personnel, Finances, Purchasing	15.3	0.0	16				
Student and research assistants	2.2	22.1	10				
Trainees	7.0	0.0	7				
Scholarship recipients at the institution ⁹⁾	0.0	100.0	4		3		3
Doctoral candidates		100.0	3		2		2
Post-doctoral researchers		100.0	1		1		1

⁵ 16 employees with more than one position are counted in the position with the highest FTE or in the first mentioned category within this table

⁶ The FLI has a flat hierarchy. Junior Group Leaders lead their research groups at the same level as Senior Group Leaders.

⁷ 2 advisers with honorarium, 2 commissioners (working and biological safety); additional FTEs come from 9 employees with part time commissioner functions (Working and biological safety, Staff Council, Equal Opportunities, Radiation Protection, Data protection) counted in other categories.

⁸ Research coordination, PR, Career Development, Legal Affairs, Directors office, Controlling

⁹ The FLI does not award own scholarships for Postdocs or Doctoral candidates. Scholarship holders from other funding organizations have no regular working hours and therefore no FTE.

Dormant staff (e.g. parental leave, early retirement plan; 13 in total) are not included in the numbers above.

Annex B: Evaluation Report

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

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Appendix:

Members of Review Board

1. Summary and main recommendations

The Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) conducts research on the causative mechanisms of organismal ageing. FLI's activities aim to translate research results into clinical practice in order to facilitate the development of new therapies to improve health during ageing. Given the demographic developments in many western industrialised countries, this work is of major relevance to society.

At the last evaluation, FLI's scientific performance was initially rated extremely positively (evaluation visit: October 2016). In June 2017, however, shortly before the Statement by the Leibniz Association Senate was adopted in July, the Executive Board of the Leibniz Association published the findings of a review of accusations of scientific misconduct against FLI's director at the time. A Committee of Enquiry commissioned by the Executive Board identified serious violations of good scientific practice in publications for which the director was primarily responsible. Against this backdrop, essential fundamentals on which the 2016 evaluation of one of FLI's five subdivisions had been founded were no longer valid. The Senate stated that the very positive assessment of FLI's performance and plans in other areas were unaffected by this.

Moreover, at the time of the last evaluation, FLI was also experiencing problems in the field of animal husbandry. Even before the evaluation visit, legal authorities and members of the Public Prosecutor's Office had inspected FLI's animal facilities and identified inappropriate procedures with regard to mouse husbandry. As a consequence, the authorities withdrew all animal welfare licences. Whilst FLI had already started proceedings to have its licences re-issued, the procedure had not yet been completed by the time of the Statement by the Leibniz Association Senate.

The Senate considered the institute to be experiencing a serious, fundamental crisis and recommended a re-evaluation in three years' time. It called upon the Supervisory Board to find ways of solving FLI's management crisis as soon as possible. To this end, a new, uninvolved director should immediately introduce measures to ensure that the rules of good scientific practice were observed and to appropriately reform the institute's scientific and organisational structures.

The incumbent director consequently drew the necessary conclusions and resigned. He still, however, heads a Senior Research Group (SRG) at FLI and is a professor at Friedrich Schiller University Jena. In March 2018, the Supervisory Board appointed an interim scientific director at FLI who acted quickly and decisively. Under his leadership, all quality assurance measures were re-evaluated, optimised and compiled in an excellent Compliance Management System (CMS). Amongst others, this includes new rules of good scientific practice and envisages all FLI publications being checked by an external provider prior to publication. The CMS also contains the revised measures with regard to animal welfare. Furthermore, changes have been made in the staffing and structure of animal husbandry. FLI now again holds all the necessary licences required for animal experiments.

In accordance with their respective duties, all of the staff at FLI have positively embraced the process of reorganisation and comply outstandingly to implement the various measures. Moreover, the staff have managed to maintain FLI's scientific performance at a high level. The institute's five subareas are rated as "very good to excellent" in one case and "very good" or "good to very good" in two other cases respectively.

The interim scientific director has done an excellent job and has successfully put an end to the crisis FLI was experiencing at the last evaluation. Furthermore, under his leadership, the process of appointing a new permanent director has been initiated. The call was published in October 2018, again as a joint appointment with Friedrich Schiller University Jena.

Special consideration should be given to the following main recommendations in the evaluation report (highlighted in **bold face** in the text):

Changes and planning (Chapter 3)

1. Absolute top priority must now be given to **filling the position of director** with an internationally recognised scientist. The new director's SRG should be furnished in a way that will allow her/him to establish her/his research focus at FLI as quickly as possible and thus also decisively shape FLI's scientific image. In this context it is a disadvantage that the former director, still working with FLI, heads the largest SRG at the institute. It is of high importance that the responsible bodies, especially the Board of Trustees, communicate and manage in a binding way that his position at the FLI is now different from his former tasks. The resources being used by the former director due to earlier commitments should be reduced at the earliest opportunity, as planned but not realised until now.
2. The plans FLI presented at the last evaluation to establish a **new field of "Microbiota and Aging"** were evaluated positively. FLI envisaged financing a new SRG and equipment to the tune of EUR 5 m (temporary extraordinary item of expenditure 2019-2022). In addition, EUR 3 m were supposed to be used for two JRGs. As recommended at the time, FLI initially planned to appoint the head of the SRG jointly with Friedrich Schiller University Jena (FSU) as a W3 professorship in Functional Microbiota-Host Interactions in Aging. Subsequently, two JRGs were scheduled to be established. So far, however, it has not been possible to fill the post. The topic still fits extremely well into FLI's portfolio and would help to strengthen the institute significantly. The plans for filling the professorship must be vigorously pursued and implemented as quickly as possible especially as other institutions have expanded their activities in this or neighbouring fields in recent years.

Controlling and quality management (Chapter 4)

3. In 2018, income from **revenues for project grants** totalled EUR 3.78 m. This equates to 13 percent of the overall budget. It is greatly welcomed that FLI acquires a large percentage of these revenues through the DFG's and EU's competitive programmes. As recommended at the last evaluation, however, FLI must increase its third-party income as a whole. For this purpose, much stronger incentives should be offered inhouse for obtaining third party funding, especially to junior researchers.

4. FLI has outstanding **core and animal facilities** at its disposal. They are a unique feature and form the indispensable basis for the institute's very successful work as a whole. Given the volume of funding that is required to operate the extensive facilities, FLI should elaborate measures to permanently monitor the cost-benefit relationship of the individual technologies. As also recommended by the SAB, the overheads for using the facilities should be increased. This means that all SRG's should be obliged to pay especially for the animal facilities to have an incentive for reducing their use to the lowest necessary level.

Cooperation and environment (Chapter 6)

5. The plans for intensifying **cooperation within Jena** under the umbrella of the Leibniz ScienceCampus Regenerative Aging combined with the various executive positions due to be filled at FLI, FSU and Jena University Hospital (UKJ) are greatly welcomed. As recommended, this will significantly improve local networking, especially with regard to translating research results into clinical applications. Moreover, it will generate better opportunities for acquiring major third-party funded collaborative projects. It will be one of the new FLI director's important tasks to drive plans to intensify institutional cooperation locally.

2. Results

Evaluation of the five subareas

FLI's scientific activities are conducted in five subareas comprising seven Senior Research Groups (SRG), five Junior Research Groups (JRG) and seven Associated Research Groups (ARG). Since the last evaluation in 2016, collaboration amongst the individual groups has been reinforced and, as a result of restructuring, the research profile has been sharpened to focus on the biochemical aspects of ageing. These were the first successful steps in implementing the recommendation issued at the last evaluation to consolidate some of the subareas with greater attention being paid to overarching issues. FLI should continue along this path. The institute's scientific performance is rated as "very good to excellent" in one case and "very good" or "good to very good" in two other cases respectively (see Chapter 7 for the evaluation of subareas). At the level of the institute as a whole, the following assessments have been made of the three areas: i) research, ii) scientific services and iii) transfer.

Research

FLI's research results continue at a high level as evidenced by its publication record. The institute regularly publishes in very high-ranking journals.

Scientific services

FLI has outstanding core facilities at its disposal which are also used by external scientists. They are composed of seven facilities, including DNA sequencing, proteomics and life science computing as well as a service unit to provide general laboratory support. In addition, FLI has three animal facilities (see Chapter 7). For details of the financing of the core and animal facilities, see Chapter 4.

Transfer

In the field of transfer, the translation of research results into clinical applications is of particular importance. In this context, FLI can boast success in various respects, especially in its collaboration with Jena University Hospital (UKJ). The Associated Research Group at UKJ contributes to the collaboration. FLI should further intensify translation, as planned (see recommendation in Chapter 6).

It is welcomed that FLI has established a core facility for technology that scouts for scientific insights with potential for applications. It facilitates the patenting of potential uses and promotes exploitation by licensing patents. Integrated into the facility is a new programme that aims to assess and financially support technology transfer of research results. An external advisory board has been established to evaluate proposals.

3. Changes and planning

Development since the last evaluation

At the last evaluation, FLI's scientific performance was initially rated extremely positively (evaluation visit: October 2016). In June 2017, however, shortly before the Statement by the Leibniz Association Senate was adopted in July, the Executive Board of the Leibniz Association published the findings of a review of accusations of scientific misconduct against FLI's director at the time. A Committee of Enquiry commissioned by the Executive Board identified serious violations of good scientific practice in publications for which the director was primarily responsible. Against this backdrop, essential fundamentals on which the 2016 evaluation of one of FLI's five subdivisions had been founded were no longer valid. The Senate stated that the very positive assessment of FLI's performance and plans in other areas were unaffected by this.

Moreover, at the time of the last evaluation, FLI was also experiencing problems in the field of animal husbandry. Even before the evaluation visit, legal authorities and members of the Public Prosecutor's Office had inspected FLI's animal facilities and identified inappropriate procedures with regard to mouse husbandry. As a consequence, the authorities withdrew all animal welfare licences. Whilst FLI had already started proceedings to have its licences re-issued, the procedure had not yet been completed by the time of the Statement by the Leibniz Association Senate.

The Senate considered the institute to be experiencing a serious, fundamental crisis and recommended a re-evaluation in three years' time. It called upon the Supervisory Board to find ways of solving FLI's management crisis as soon as possible. To this end, a new, uninvolved director should immediately introduce measures to ensure that the rules of good scientific practice were observed and to appropriately reform the institute's scientific and organisational structures.

The incumbent director consequently drew the necessary conclusions and resigned. He still, however, heads a Senior Research Group (SRG) at FLI and is a professor at Friedrich Schiller University Jena. In March 2018, the Supervisory Board appointed an interim scientific director at FLI who acted quickly and decisively. Under his leadership, all quality

assurance measures were re-evaluated, optimised and compiled in an excellent Compliance Management System (CMS). Amongst others, this includes new rules of good scientific practice and envisages all FLI publications being checked by an external provider prior to publication. The CMS also contains the revised measures with regard to animal welfare. Furthermore, changes have been made in the staffing and structure of animal husbandry. FLI now again holds all the necessary licences required for animal experiments. All in all, FLI's CMS is exemplary and similar structures are already being introduced at other institutions (see Chapter 4 for details).

The interim scientific director has done an excellent job and has successfully put an end to the crisis FLI was experiencing at the last evaluation. Furthermore, under his leadership, the process of appointing a new permanent director has been initiated. The call was published in October 2018, again as a joint appointment with Friedrich Schiller University Jena.

Plans for the coming years

Absolute top priority must now be given to filling the position of director with an internationally recognised scientist. The new director's SRG should be furnished in a way that will allow her/him to establish her/his research focus at FLI as quickly as possible and thus also decisively shape FLI's scientific image. In this context it is a disadvantage that the former director, still working with FLI, heads the largest SRG at the institute. It is of high importance that the responsible bodies, especially the Board of Trustees, communicate and manage in a binding way that his position at the FLI is now different from his former tasks. The resources being used by the former director due to earlier commitments should be reduced at the earliest opportunity, as planned but not realised until now.

The plans FLI presented at the last evaluation to establish a new field of "Microbiota and Aging" were evaluated positively. FLI envisaged financing a new SRG and equipment to the tune of EUR 5 m (temporary extraordinary item of expenditure 2019-2022). In addition, EUR 3 m were supposed to be used for two JRGs. As recommended at the time, FLI initially planned to appoint the head of the SRG jointly with Friedrich Schiller University Jena (FSU) as a W3 professorship in Functional Microbiota-Host Interactions in Aging. Subsequently, two JRGs were scheduled to be established. So far, however, it has not been possible to fill the post. The topic still fits extremely well into FLI's portfolio and would help to strengthen the institute significantly. The plans for filling the professorship must be vigorously pursued and implemented as quickly as possible especially as other institutions have expanded their activities in this or neighbouring fields in recent years.

4. Controlling and quality management

Facilities, equipment and funding

Funding

FLI's institutional funding is adequate. In 2018, it was approx. EUR 26 m.

In 2018, income from revenues for project grants totalled EUR 3.78 m. This equates to 13 percent of the overall budget. It is greatly welcomed that FLI acquires a large percentage of these revenues through the DFG's and EU's competitive programmes. As recommended at the last evaluation, however, FLI must increase its third-party income as a whole. For this purpose, much stronger incentives should be offered inhouse for obtaining third party funding, especially to junior researchers.

Buildings and facilities

FLI's very good location on the Beutenberg Campus in Jena promotes collaboration with institutions in the immediate vicinity, especially with a number of research institutes and faculties at FSU and UKJ. It is welcomed that FLI has been operating a new laboratory building since 2013 and that its old buildings are undergoing extensive renovation. Restoration work is scheduled to be completed in 2022. According to FLI, it is only able to cover the operating costs of EUR 1.1 m for the new laboratory building until 2023. As of 2024, a permanent increase in its core budget would be required. The members of the review board do not consider themselves able to judge on this matter.

FLI has outstanding core and animal facilities at its disposal (see Chapter 7). They are a unique feature and form the indispensable basis for the institute's very successful work as a whole. Given the volume of funding that is required to operate the extensive facilities, FLI should elaborate measures to permanently monitor the cost-benefit relationship of the individual technologies. As also recommended by the SAB, the overheads for using the facilities should be increased. This means that all SRG's should be obliged to pay especially for the animal facilities to have an incentive for reducing their use to the lowest necessary level.

Organisational and operational structure

FLI's research activities are conducted in five subareas comprising seven SRGs, five JRGs and seven ARGs. This structure has proven its worth. It is welcomed that the SRGs and the JRGs, respectively, are assigned the same basic number of staff. The composition of the ARGs is determined individually. As a tool, ARGs function very well and FLI benefits from the diverse expertise in the external groups. For its communication, FLI has established appropriate committees and formats at the institute which have proved their value, especially in the recent difficult years.

Quality Management

As a consequence of the former director's scientific misconduct and the problems relating to mouse husbandry, the institute re-evaluated and optimised all of its quality assurance measures under the leadership of the interim scientific director and compiled them in an excellent Compliance Management System (CMS). The CMS is composed of eight different segments, including good scientific practice (GSP), animal welfare, data security and laboratory safety. Each of the segments is overseen by a dedicated compliance expert who reports to the newly formed Compliance Board. The Compliance Board reports directly to the Board of Directors. The measures stipulated in the CMS refer to handling data archiving, keeping electronic laboratory records and pre-screening publications. Whilst carrying

out the various measures is time-consuming, it is both necessary and expedient. FLI's CMS is exemplary and similar structures are already being introduced at other institutions

With regard to the rules of GSP (Segment 1 of CMS), FLI has introduced or improved various measures, such as regular training courses on GSP rules for all FLI scientific staff, a central electronic archive for all FLI scientific data related to publications and dissertations and the mandatory use of an electronic laboratory notebook to keep detailed electronic records of all experimental steps taken in any scientific project. Special mention should be made of the provision for all FLI publications to be checked by an external provider prior to publication. As planned, FLI should utilise the insights gained from these measures to further enhance its scientific staff's awareness to work self dependently in accordance with the scientific standards.

With regard to animal welfare (Segment 2 of CMS), too, FLI has adopted various very good measures. Amongst others, a qualified veterinarian has been newly appointed to head the Animal Facility (mouse). Furthermore, in 2016, an independent Animal Welfare Unit was established (see Chapter 7) in accordance with the stipulations contained in the Animal Welfare Act (*Tierschutzgesetz*). It monitors all three animal facilities (mouse, fish, transgenic animals). Two additional veterinary doctors were employed in the unit to establish a regime for the continuous monitoring of FLI animal husbandry. Moreover, a scheme was introduced to continuously train all relevant staff. As planned, the new structures should be sustainably anchored at the institute. FLI and its committees should continue to keep a watchful eye on the topic of animal welfare. For this purpose, the institute should consider whether regular external assessments should be obtained.

It is welcomed that FLI is implementing strategies to help researchers handle the new CMS regulations. This is particularly necessary in the case of applications for activities in S1 and S2 laboratories as well as licences for animal experiments. Many researchers who do not speak German are employed at FLI; particularly for this group, the institute should communicate the support measures more effectively.

Quality management by the Scientific Advisory Board and Board of Trustees

FLI's Board of Trustees (BoT) carries out its supervisory function very well. This is particularly true of the way in which it has designed the necessary reforms since the last evaluation. Currently, great demands are still being made on the BoT due to the ongoing process of appointing a new director.

The Scientific Advisory Board advises the Board of Trustees and the FLI directors on issues pertaining to scientific performance and productivity. Amongst others, it is involved in appointments or extensions of executive positions. Attention is drawn to the recommendation issued at the last evaluation to hold an audit, as is usual at Leibniz institutions, evaluating both the institute as a whole and the individual groups between two evaluations.

5. Human Resources

Management

Since March 2018, FLI has been managed by an interim scientific director. It is remarkable how quickly he has established new structures at the institute. His dedication, which goes well beyond what could be expected, has made a crucial contribution to overcoming the crisis at the last evaluation.

The other senior scientists have also dealt with the situation remarkably well. It is to their great credit that FLI continued to maintain its performance almost unimpaired despite the delays caused to their work by the temporary absence of licences for animal experiments. The continuation of good cooperation amongst themselves as well as with the new director will be crucial for the institute's development.

Postdoctoral staff

As of 31 December 2018, FLI hosted 48 postdoctoral researchers (postdocs). FLI's excellent scientific infrastructure, in particular, offers postdocs outstanding opportunities for development. Moreover, they have access to an appropriate skills-development programme that covers all aspects of professional development, including research management, grant writing, good scientific practice, leadership training and courses on career promotion.

It is welcomed that FLI utilises its own funding to establish fixed-term Junior Research groups (5+4 years) in order to specifically establish promising research topics at the institute and offer junior researchers longer-term prospects. FLI should, however, strive to also establish third-party funded junior research groups at the institute, financed, for example, by the DFG or EU. It should overhaul the existing incentive system with the aim, on the one hand, of motivating internal junior researchers to make greater efforts to acquire external funding and, on the other, of encouraging external junior researchers with existing third-party funding to come to FLI.

Doctoral candidates

As of 31 December 2018, 43 doctoral candidates were employed at FLI, including a remarkably high number of foreign researchers. Between 2016 and 2018, 30 doctorates were successfully completed, taking an average of 4.4 years. Due to the absence of licences for animal experiments some doctoral projects fell behind schedule. It is very good that, as recommended, FLI offered to extend the contracts of the 13 candidates affected. Now that FLI has full access to animal models once again, it should reduce the average time taken to complete a doctorate, as recommended.

Doctorates at FLI are organised in the Leibniz Graduate School on Aging (LGSA). As of 31 December 2018, LGSA listed 56 doctoral candidates (including guests). LGSA training guidelines incorporate all the objectives of the Leibniz guidelines on career development. Every doctoral candidate has a Thesis Advisory Committee and is required to participate in a one-and-a-half-day workshop on good scientific practice. During the initial phase, it

is positive that doctoral candidates get to know all the groups working at FLI. It is welcomed that the institute plans to establish an alumni network.

Non-scientific staff

As of 31 December 2018, 155 individuals were employed at FLI in the service and administrative sectors. FLI staff have actively engaged in introducing the new system of quality management as well as the restructuring of animal husbandry; the new measures have also been very well embraced and implemented by non-scientific staff. It is welcomed that FLI has established structures for training and continuing education. Between 2016 and 2018, seven technicians and seven animal caretakers were trained. Of these, four technicians and four animal caretakers have completed their training so far.

Equal opportunities and work-life balance

It is very pleasing that, since the last evaluation, FLI has increased the proportion of women in research and scientific services from 33 percent to 40 percent, also at executive level. As of 31 December 2018, out of 15 executive scientists 6 were female (two of seven SRG heads, two of five JRG heads and two of three other executive positions). FLI should continue this positive trend.

Of the seven SRG heads, five hold joint professorships at Friedrich Schiller University Jena, of whom four are male (W3) and one female (W2). The planned appointments to executive positions (see Chapter 6) offer FLI an opportunity to increase both the number of women employed as SRG heads as well as those appointed to joint university professorships on the W3 salary scale.

FLI has adopted appropriate measures to promote the reconciliation of work and family life. These agreements include various working time models, the maintenance of a parent-child office and cooperation with neighbouring day care centres. It is welcomed that FLI offers a Welcome Back Fellowship which provides up to twelve months of salary support after parental leave. On average, two scientists per year make use of the Fellowship.

6. Cooperation and environment

National cooperation

FLI cooperates closely with Friedrich Schiller University Jena (FSU). Professors at FLI hold joint appointments at FSU. Currently, there are five such professorships (four W3 and one W2). In the near future, FLI plans the following four additional appointments (W3):

- The new Scientific Director (see Chapter 2).
- The head of the new Microbiota research area (see Chapter 2).
- Appointment of a professor for the Biochemistry of Aging, due to retirement, jointly financed with FSU (see Chapter 7, Subarea 4).
- The promotion of the chair of Subarea 2 to a professorship for Neurobiology and Aging (see Chapter 7).

Additionally, two W3 professorships (Translational Geriatric Medicine and Cellular Re-programming and Transdifferentiation in Aging) are planned at Jena University Hospital (UKJ) which will become important collaborative partners.

In the context of changes in personnel, various activities taking place in Jena are scheduled to be pooled under the umbrella of the Leibniz ScienceCampus Regenerative Aging which was established in 2016. In addition to FLI, the institutions involved include FSU and UKJ as well as the two other Leibniz institutes on the Beutenberg Campus in Jena, the Leibniz Institute of Photonic Technology (IPHT) and the Leibniz Institute for Natural Product Research and Infection Biology – Hans Knöll Institute (HKI). **The plans for intensifying cooperation within Jena under the umbrella of the Leibniz ScienceCampus Regenerative Aging combined with the various executive positions due to be filled at FLI, FSU and Jena University Hospital (UKJ) are greatly welcomed. As recommended, this will significantly improve local networking, especially with regard to translating research results into clinical applications. Moreover, it will generate better opportunities for acquiring major third-party funded collaborative projects. It will be one of the new FLI director's important tasks to drive plans to intensify institutional cooperation locally.**

In addition to joint professorships, FLI is linked to FSU by two ARGs and to UKJ by one ARG. This kind of collaboration has proved very worthwhile.

International cooperation

FLI can boast many joint publications with scientists abroad and diverse individual international collaborations. The institute is, moreover, very active in international consortia, such as the International Cancer Genome Consortium (ICGC) and the European LifeTime Consortium (LifeTime). FLI's plans to develop institutional cooperation with various international institutions are welcomed.

7. Subareas of FLI

Subarea 1: Stem Cell Aging

[Average 2016-2018: 30.2 FTE, thereof 12.6 FTE Research and scientific services, 9.8 FTE Doctoral candidates, and 7.8 FTE Service staff (including student assistants)]

In Subarea 1, two SRGs, one JRG and one ARG very successfully investigate the causes and impacts of stem cell ageing. The main scientific focus targets the fundamental molecular mechanisms that influence ageing and lead to ageing-related diseases. The subarea is headed by the former director of the institute.

SRG Rudolph focusses on the fundamental principles of stem cell ageing. At the last evaluation, activities were originally rated very positively. Due to the confirmed violations of good scientific practice within the SRG, however, the essential fundamentals on which the evaluation had been founded were no longer valid. The head of the SRG resigned from his position as director of FLI and has intensively dedicated himself to reappraising the violations, for example by publishing corrigenda. In other respects, the SRG's scientific performance is of high quality and internationally extremely visible. At present, the group is

the largest at FLI. It is welcomed that it is supposed to be reduced in size in the course of the continued development of the institute as a whole.

As planned at the last evaluation, under the “ProExzellenz-Programm”, run by the *Land Thüringen*, research on the regeneration of haematopoiesis was reinforced in 2017 by the extremely successful SRG Waskow. Even by international standards, activities are outstanding. The head of the group has brought her unique expertise to the institute and FLI should do everything in its power to retain her long-term.

From 2013 to 2018, JRG von Maltzahn was financed as an Emmy Noether Group by the DFG, and since then by FLI. The JRG conducts extremely successful research on the ageing of stem cells in skeletal muscle. As noted at the last evaluation, the JRG fits excellently into the profile of the subarea and cooperates particularly closely with the SRG Rudolph. Due to the problems in the mouse husbandry, it shifted its focus on new model organisms and managed to even enhance its performance since the last evaluation.

In 2018, ARG Heidel (Jena University Hospital) was established under the ProExzellenz-Programm (see above). Even before this, close, highly successful cooperation had been undertaken by FLI with the group. Moreover, it also complements the newly established SRG Waskow very well. As a result, the whole subarea has an excellent basis for continuing to strengthen especially the translation of research results into clinical practice.

Since the last evaluation, the subarea’s third-party funding has dropped slightly but is still at a very high level. It includes extensive funding from the DFG and EU. Even though certain projects were delayed by the temporary absence of access to mouse models, excellent research results have been produced and appropriately published in high-ranking journals

Subarea 1 is rated as “very good to excellent”.

Subarea 2: Regeneration and Homeostasis of Organs in Aging

[Average 2016-2018: 21.2 FTE, thereof 11.9 FTE Research and scientific services, 3.4 FTE Doctoral candidates, and 5.9 FTE Service staff (including student assistants)]

Subarea 2 focusses on investigating the mechanisms that cause fundamental ageing-related deterioration of organ maintenance. In 2018, one SRG was discontinued when the group leader, who was also head of the subarea, retired. The subarea now comprises the new head’s SRG, a JRG and two ARGs.

SRG Morrison successfully investigates ageing-related signalling disturbances in the nervous system. The experienced head has actively engaged in the various processes of restructuring activities at FLI. Moreover, she is in charge of the institute’s national and international networking. The group’s research work was delayed by the absence of licences to conduct animal experiments. Nevertheless, it managed to produce convincing research outcomes. The plans put forward by FLI and FSU to appoint the head of the group and the entire subarea to a professorship (*ad personam*) are welcomed.

JRG von Eyss was established in 2016 and studies the key molecules involved in stem cell ageing. The group fits well into the subarea and has already produced some very interesting results. The work on haematopoiesis, in particular, is very promising. It has the potential to generate internationally highly regarded results.

ARG Ploubidou (guest status at FLI) successfully pursues cancer research. From 2005 to 2015, the head had a JRG at FLI and was also head of the Functional Genomics Core Facility. Since 2016, she has headed an ARG funded by the EU. ARG Herrlich (emeritus) focuses on cancer research. In themselves, both ARGs produce convincing outcomes but the thematic links to other activities in the subarea are not very strong.

The subarea's third-party funding income is good. All in all, research results are good, in some cases, very good. FLI's plans to anchor the new research field of Microbiota and Aging in Subarea 2 with one SRG and two JRGs are coherent (see Chapter 3). It offers an opportunity to continue honing the subarea's research profile and to promote translation into clinical applications.

Subarea 2 is rated as "good to very good".

Subarea 3: Genetics and Epigenetics of Aging

[Average 2016-2018: 22.9 FTE, thereof 12.5 FTE Research and scientific services, 3.6 FTE Doctoral candidates, and 6.8 FTE Service staff (including student assistants)]

This subarea conducts research on the genetic and epigenetic determinants of ageing. It comprises a SRG, a JRG and three ARGs.

SRG Englert was established at FLI in 2004 and has very successfully addressed the molecular functioning of the influence of gene regulation on the development of organs in fish models. The group played a decisive role in FLI's internationally highly acclaimed work on the short-lived fish *Nothobranchius furzeri* which led to the sequencing of the complete genome of this fish as well as the establishment of *N. furzeri* as a new vertebrate ageing model. The group must, however, now decide to what extent this model organism can really be utilised for novel research on elucidating causative mechanisms of organismal ageing. In this context, the planned use of CRISPR/Cas9 technology opens up promising opportunities.

ARG Cellerino (Scuola Normale Superiore, Pisa, Italy) is also crucially involved in FLI's work on *N. furzeri*. The fish was introduced to the scientific community by the group leader (then University of Pisa, Italy) in 2004. From 2007 to 2010, he headed a Junior Research Group at FLI and has since held a professorship at Pisa with an ARG at FLI. This collaboration is productive and has generated many excellent outcomes.

JRG Neri was established at FLI in 2016 and investigates the influence of ageing and environmental impacts on organs at molecular level. Despite considerable delays to research caused by the absence of licences for animal experiments, the JRG is set on a very good course and pursues very promising projects.

ARG Marz (Friedrich Schiller University Jena) complements the subarea's research activities by contributing important expertise in bioinformatics. Collaboration is very productive and has led to various very good results.

ARG Bierhoff (Friedrich Schiller University Jena) was set up in 2017 and is the third group to be funded by the *Land* Thüringen under the ProExzellenz Programm (see Subarea 1 for the other two). The group focusses on epigenetics and has adopted a coherent approach. The reinforcement it enjoys from cooperation with the university is welcomed.

When the former head retired, the subarea lost a significant portion of its third-party income which is, however, still high. Research findings continue to be produced at a very high level, as evidenced by the corresponding high-ranking publications.

Subarea 3 is rated as “very good”.

Subarea 4: Cell Dynamics and Molecular Damages in Aging

[Average 2016-2018: 29.4 FTE, thereof 15.4 FTE Research and scientific services, 5.6 FTE Doctoral candidates, and 8.3 FTE Service staff (including student assistants)]

The focus of this subarea is research into the ageing-related accumulation of molecular damage. In 2018, one SRG was discontinued when the group leader retired. The subarea now comprises two SRGs and one JRG.

SRG Wang conducts successful research on premature ageing and age-related pathogenesis, such as cancer and neurodegeneration. The group’s expertise in molecular mechanisms is recognised internationally. Furthermore, it boasts important expertise in conducting experiments on mice. Its research results are very good, although work is only tenuously linked to other groups at FLI.

SRG Kaether carries out interesting work on quality control in the endoplasmic reticulum and the secretory pathway in ageing processes. The approach used has great potential which, however, has not yet been fully realised. Just like the Wang group, the work is only tenuously linked to other groups at FLI.

Since 2015, JRG Ermolaeva has successfully been investigating ageing-related metabolic changes and stress reactions. The work is extremely innovative and promising. It has the potential to open up novel perspectives on ageing research.

The level of the subarea’s third-party income is just as good as it was at the last evaluation. Overall, its research outcomes are good, in some cases, very good. It is welcomed that, after the retirement of the head of an SRG, FLI plans to refill his position again as a joint appointment with Friedrich Schiller University Jena, entitled Biochemistry of Aging (see Chapter 6). This will give FLI a good basis for focussing activities in this subarea more precisely on issues which have a clear connection with ageing processes, as had been recommended at the last evaluation.

Subarea 4 is rated as “good to very good”.

Subarea 5: Computational and Systems Biology of Aging

[Average 2016-2018: 5.9 FTE, thereof 2.8 FTE Research and scientific services, 1.7 FTE Doctoral candidates, and 1.4 FTE Service staff (including student assistants)]

This subarea provides indispensable services for FLI’s other subareas whilst conducting very good research of its own. It focusses on the development of methods to analyse and

understand complex biological systems. This includes the design of computer algorithms and biostatistical approaches as well as the development of novel “omic”-strategies to study ageing and ageing-related diseases. The subarea is responsible for two core facilities (Life Science Computing, Proteomics, see below) and provides consulting services in statistics. Furthermore, it organises courses on data analysis and statistics. Due to its extreme importance, the subarea is closely integrated in many of FLI’s activities.

The position of head of the subarea, which was only established in 2014, was initially filled with a very successful researcher from Ulm University as a joint appointment with FSU Jena. However, in 2016, the head accepted a call to return to Ulm University. A very good replacement was then found in 2017. It is welcomed that the expertise of the previous head still flows into the subarea’s work via an ARG (see below). The institute should, however, ensure that in addition to continuing the former head’s very successful work, further new fields of activity are opened up, as well. The subarea currently comprises the new head’s SRG, one JRG and one ARG.

SRG Hoffmann, which was established in 2017, very successfully develops methods for analysing large biological datasets with the aim of modelling and elucidating the influence of the epigenome on ageing. Various valuable research findings have already been produced and appropriately published.

JRG Ori, which was established shortly before the last evaluation, focusses very successfully on the question of how environmental and ageing factors affect ageing processes at molecular level. The group particularly concentrates on developing state-of-the-art proteomics tools. Internationally well-received research results have been achieved and appropriately published. The quality of the group’s activities is also evidenced by the fact that it collaborates with research groups that are amongst the best in the world in their field.

ARG Kestler (Ulm University) adopts a unique approach to modelling data and contributes valuable expertise to FLI. The head of the group is an extremely successful scientist with an international reputation.

Both the research results and the services in FLI’s youngest subarea are very good, in parts even excellent. Third-party income is still low and should be increased in the coming years. It makes sense that FLI plans to expand this subarea to meet the increasing demand for research data management.

Subarea 5 is rated as “very good”.

Core Facilities and Core Services

[Average 2016-2018: 33.3 FTE, thereof 13.3 FTE Research and scientific services, 0.6 FTE Doctoral candidates, and 19.5 FTE Service staff (including student assistants)]

FLI’s extensive Core Facilities and Core Services are a unique feature and an indispensable basis for the highly successful work of the entire institute. They comprise seven facilities, including DNA sequencing, proteomics and life science computing as well as a service unit to provide general laboratory support. The entire staff have outstanding expertise in their

respective fields and provide technologies of the highest quality. It is highly welcomed that the core facilities are also accessible to external partners.

Animal Facilities and Animal Welfare

[Average 2016-2018: 43.3 FTE Service staff (including student assistants)]

FLI has three central animal facilities. The Mouse Facility houses 12,500 mice and the Fish Facility almost 30,000 fish. The Animal Transgenesis Facility generates new mouse lines using CRISPR-based technologies.

In 2016, an Animal Welfare unit was established which oversees all three animal facilities. It is run by the head animal welfare officer who is a veterinarian (see Chapter 4 for details).

8. Handling of recommendations from the last external evaluation

FLI has successfully addressed the recommendations made by the Leibniz Association Senate in 2016. The recommendations on increasing third party funding, the average length of doctoral studies and holding a comprehensive audit of the entire institute by the Scientific Advisory Board between two evaluations are still relevant.

Appendix

1. Review Board

Chair (Member of the Leibniz Senate Evaluation Committee)

Annette G. **Beck-Sickinger** Institute for Biochemistry, University of Leipzig

Deputy Chair (Member of the Leibniz Senate Evaluation Committee)

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

Reviewers

Ilaria **Bellantuono** Professor in Musculoskeletal Ageing, University of Sheffield (UK)

Gerald **de Haan** European Institute for the Biology of Ageing, Groningen (NL)

Wolfgang **Driever** Institute for Biology, Freiburg University

Christopher **Heeschen** School of Medical Sciences, University of New South Wales, Sydney (Australia)

Carien M. **Niessen** Department of cell biology of the skin and CECAD, University of Cologne

Heinz D. **Osiewacz** Institute for Molecular Biosciences, Goethe University Frankfurt a. M.

Nicole **Radde** Systems Theory in Systems Biology, University of Stuttgart

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

Representative of the Federal Government

Anja **Niedworok** Federal Ministry of Education and Research, Bonn

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

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

12 May 2020

Annex C: Statement of the Institution on the Evaluation Report

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

We are most grateful to all reviewers of the Review Committee for their thorough evaluation of our Institute and their highly insightful recommendations. We feel reassured by the reviewers' overall conclusion that the FLI has successfully overcome the institutional turbulences spanning the years 2016 and 2017. We are comforted by the Review Committee perceiving the stringent measures taken by the FLI since 2016 to safeguard the welfare of our experimental animals and to ensure the standards of Good Scientific Practice (GSP) as highly satisfactory, and in some regards even as exemplary. The positive evaluation report gives a strong impetus to all of us at the FLI while we strive for compliance in safeguarding animal welfare and GSP on an even higher level in the future.

The Review Committee appreciated the constructive role of the interim Scientific Director, Prof. Alfred Nordheim, in guiding the FLI in developing and implementing its new Compliance Management System (CMS). In this context, we wish to emphasize that the Administrative Director, Dr. Daniele Barthel, supported by Group Leaders of the FLI, immediately initiated and implemented major steps to secure animal welfare and GSP when such requirements became apparent during the years 2016/2017 (see letter to the Leibniz President Prof. M. Kleiner, dated Oct. 27, 2017).

The Review Committee attested the FLI to engage in scientific work that "is of major relevance to society" and that our researchers "regularly publish in very high - ranking journals". This positive judgement will strengthen effort and motivation by all FLI researchers to aspire towards scientific productivity on very high levels.

In the following we wish to comment on particular insights offered by the Evaluation Committee:

1) Main Recommendation 1 ("filling the position of the new scientific director"). The task to identify the next Scientific Director is pursued with utmost efforts and top priority. Upon search by an international Selection Committee, the currently identified colleague for the position of Scientific Director is negotiating in a very constructive and forward-looking manner with all institutions involved.

2) Main Recommendation 2 ("establish the new field Microbiota and Aging"). Several current group leaders of the FLI have already initiated productive research projects toward studying 'Microbiota and Aging'. The search for a new colleague leading this new field at the FLI, a Senior Group Leader endowed with a W3 professorship of Friedrich Schiller University Jena, has been completed and a call is expected to be issued by the President of the Friedrich Schiller University (FSU) in June 2020. Subsequent to this appointment, two new Junior Group Leaders will be selected to further strengthen and broaden this topic at the FLI.

3) Main Recommendation 3 ("increase income from third-party grants"). FLI will mount further efforts to increase success rates in acquiring external financial support. The existing incentive system to promote applications has been intensified and further improvements are under consideration. New, so-far untapped sources of external financial support shall be targeted increasingly. New research consortia are currently being conceived to apply for joint funding.

4) Main Recommendation 4 (“cost-benefit analysis of the Core and Animal Facilities”). The Institute will initiate an in-depth evaluation process to judge both necessity and productivity of our Core Facilities. Upon initiative of the new Scientific Director, a budgetary overhaul of our facilities will consider the adjustment of service charges to both analysis support and animal husbandry. This, however, must not discourage the use of technology services by internal and external users.

5) Main Recommendation 5 (“intensify cooperations within the Jena area”). The ‘Leibniz ScienceCampus Jena – Regenerative Aging’, ever since its initiation in the year 2015, has proven a highly suitable instrument to catalyze scientific cooperations, enable joint recruitments and conceive new research consortia. A steadily increasing number of joint publications, co-authored by FLI scientists and Jena colleagues, attests to the value of the ScienceCampus. It will be an important effort to perpetuate this excellent structure beyond the year 2020. FLI will invest strong efforts to help prolong the existence of the ScienceCampus and through this and other measures promote the interactive aging research platforms in Jena. New recruitments at the professorial and group leader levels are already under negotiation and will greatly foster this aim.

6) General comment regarding Quality Management (“FLI’s Compliance Management System (CMS) is exemplary and similar structures are already being introduced at other institutions. ... It is welcomed that FLI is implementing strategies to help researchers handle the new CMS regulations. Many researchers who do not speak German are employed at the FLI; particularly for this group, the Institute should communicate the support measures more effectively”).

The FLI will invest every effort to stabilize and further improve upon each component of the compliance management system established recently at the Institute. In both a self-learning and a professionally guided process, we will optimize the system at all levels. We will communicate these efforts widely among all FLI staff. We will also communicate these efforts to colleagues in other institutions and to the public at large. Regarding any training of our international staff, the FLI communicates in a fully bi-lingual manner. All recommendations, guidelines, instructions, etc. are always provided in both German and English. Training courses pertaining to various aspects of compliance (animal welfare, Good Scientific Practice, etc.) are always held in English. The FLI will enhance its training program to teach various aspects of compliance with scientific work ethics. Such courses will be offered to technical staff, PhD candidates, postdocs, and both Junior and Senior Group Leaders.

Specifically, and exemplarily, our comprehensive assessments of research manuscripts and dissertations at pre-publication stages (ABS, assessment before submission) stimulated the introduction of intensified training in the use of statistical assessments of experimental data.

7) General comment regarding Quality Management by the Scientific Advisory Board (“to hold an audit, as is usual at Leibniz institutions, evaluating both the institute as a whole and the individual groups between two evaluations”).

The FLI is visited once every year by its 12-membered international Scientific Advisory Board (SAB). During each such visit the FLI evaluates the scientific productivity of all research groups and of the Core Facilities. The SAB also interviews with representatives of the PhD candidates and of postdocs. In addition, the SAB scrutinizes the budgetary planning in the frame of the annual "Programmbudget". Furthermore, the SAB evaluates in depth the performances of individual research groups. These evaluations take place every fifth year for tenured heads of Senior Research Groups and within the fourth year of a Junior Research Group's existence. To follow the above-cited recommendation by the Review Committee, we will ask the SAB to apply an 'audit' format to every seventh of its annual FLI site-visits (i.e. the site-visit halve-way between two major Institute evaluations).

Once more, we would like to thank all members of the Review Committee for providing us with invaluable insights, vital suggestions and important recommendations.

We gratefully acknowledge the members of the Leibniz Senatsausschuss Evaluation (SAE) for their continuous support.