



# Forschung aus erster Hand

## Healthy Ageing

# 08

### Newly developed Eczema during ageing

Little is known about eczema in the elderly. New insights on this topic were recently published in the Journal of Allergy and Clinical Immunology. They are based on a two-step investigation of researchers from the IUF in Düsseldorf

### Bioactive compound improves memory

The progressive loss of memory severely impairs the quality of life of those affected. So far, no drugs are known to prevent age-related cognitive decline. A new study proves the memory-enhancing effect of a plant ester as an active ingredient from the medicinal plant *Rhodiola rosea*.

### Better understanding cardiovascular diseases

Cardiovascular diseases are the most common cause of death in Germany. They can markedly lower life expectancy and quality of life. Researchers successfully identified a new marker which could be used in future to determine the risk of heart attack, stroke and other adverse cardiovascular events earlier and with more precision.

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### Imprint

Publisher: Leibniz Institute in Aging – Fritz Lipmann Institute (FLI), LFV Healthy Ageing · Beutenbergstr. 11, D - 07745 Jena

Phone: ++49 (0)3641 / 65 63 14, healthyageing@leibniz-fl.de · Editor: Astrid van der Wall (resp.)

Layout: pigurdesign, Potsdam · page layout: Astrid van der Wall · Print: GS Druck GmbH, Potsdam

Corrections: Dr. Anne Seidlein, February 2019, Picture page 1: Adobe Stock

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IUF Leibniz Research Institute for Environmental Medicine

## Newly developed eczema during ageing: What influence do genes and air pollution have?

Little is known about eczema in the elderly. New insights on this topic were recently published in the *Journal of Allergy and Clinical Immunology*. They are based on a two-step investigation of researchers from the IUF in Düsseldorf, Germany.

While risk factors are known for atopic eczema in childhood, there are far less insights into eczema in adulthood. What role do predisposition and environmental factors play? Is this the “atopic eczema of the elderly”?

### Eczema in the elderly is very common

With regards to these questions scientists from the IUF – Leibniz Research Institute for Environmental Medicine have analyzed data from the long-term study SALIA. Results which were published in July 2018 show that the development of eczema in the elderly is very common. Thus, about 8 percent of 834 women have indicated that they developed eczema for the first time at the age of 55+. A correlation between long-term exposition to traffic-related air pollution and the initial development of eczema beyond 55 years was shown. The scientists specifically found a correlation between increased values of fine particles ( $PM_{2.5}$ ,  $PM_{10}$ ) and gaseous environmental pollutants ( $NO_2$ ,  $NO_x$ ) and eczema in elderly women.

### Elderly do seldom suffer from atopic eczema like children do

Next, the scientists from the Leibniz Research Institute for Environmental Medicine together with a colleague from the Monash University in Melbourne, Aus-



*New studies indicate that air pollution such as fine particles or gaseous environmental pollutants may contribute to the development of eczema in the elderly. Source: Adobe Stock*

tralia, asked themselves whether this is a form of atopic eczema. It was found that eczema in the elderly differs from atopic eczema in childhood. Accordingly, the correlation between air pollution and eczema in elderly women was stronger, if they had neither hay fever, nor elevated anti-IgE antibodies in the blood, and if they had no genetic predisposition to develop atopic diseases such as atopic eczema. These in-

vestigations were recently published in the *Journal of Allergy and Clinical Immunology*.

### Chronic exposure to air pollutants correlate with eczema

“Our investigation shows that first time development of eczema at the age of 55+ is more frequent than previously assumed. Additionally, it suggests a correlation with chronic exposure to traffic-related air

### About the SALIA study

The analyses are based on data from the SALIA study which was initiated in 1985 in order to investigate the long-term effects of air pollution on health. Elderly women from the former highly industrialized Ruhr area and the rural, Southern “Münsterland” were considered. Men were excluded as they were occupationally exposed to high air pollution in coal mining and steel industry at this time. The initial examination took place with 54-55 years (1985-1994). The first follow-up of health data was conducted via questionnaire. 834 women with an average of 73.5 years participated in the second examination (2007-2010). The hereby presented analyses are based on the results of this examination. The statistical correlations are calculated with so-called regressions models. In this process, diverse confounding factors e.g. smoking are included and the models adapted thereto. The air pollution strongly decreased in the Ruhr area during the study so that health improvement can already be observed to some extent. The SALIA study is supervised by Dr. Schikowski from the IUF.

pollution”, explains Dr. Tamara Schikowski, environmental epidemiologist and group leader at IUF. Prof. Jean Krutmann, derma-

tologist and director of IUF adds: “Up to now, we know very little about eczema in the elderly. The finding that eczema in the

elderly differs from atopic eczema in children indicates that this is an independent, so far unknown entity.”

**Original publications:** Schnass W, Hüls A, Vierkötter A, Krämer U, Krutmann J, Schikowski T (2018): *Traffic-related air pollution and eczema in the elderly: Findings from the SALIA cohort.* *Int J Hyg Environ Health* 221(6): 861-867, doi: 10.1016/j.ijheh.2018.06.002.

Hüls A, Abramson MJ, Sugiri D, Fuks K, Krämer U, Krutmann J, Schikowski T (2018): *Nonatopic eczema in elderly women: Effect of air pollution and genes.* *J Allergy Clin Immunol* 143(1): 378-385.e9. doi: 10.1016/j.jaci.2018.09.031. **Contact:** info@iuf-duesseldorf.de

## DDZ German Diabetes Center

# Increased blood flow triggers liver regeneration

The liver is one of the most important human organs. It is essential for metabolism, blood detoxification and the functioning of the immune system. Moreover, the liver is the only organ which can fully regenerate its cell mass within a few weeks after more than half of the organ has been removed. The researchers led by Professor Eckhard Lammert have discovered that it is due to increased blood flow and subsequent dilation of the liver vasculature that the liver receives signals for growth.

The signals come from the cells of the blood vessels that react to the mechanical stimulation. The publication is based on the findings published in 2001 that blood vessels affect organs in their function and growth (Lammert et al., *Science* 2001).

„In our study of the liver and its blood vessels, we identified an important trigger for organ growth. For the first time, we were able to show that blood flow and vasodilation release growth-promoting signals from blood vessels,” said Professor Eckhard Lammert, director of the Institute for Beta Cell Biology at the German Diabetes Center (DDZ) and head of the Institute for Metabolic Physiology at Heinrich Heine University Düsseldorf. „In the future, these exciting results could also become important for the understanding and treatment of fatty liver disease in obesity and diabetes,” added Professor Michael Roden, scientific director and board member of the German Diabetes Center and director of the Department of Endocrinology and Diabetology at Düsseldorf University Hospital. “The research results are of great importance for understanding the complex processes involved in liver regeneration and its disorders,” said Professor Dieter Häussinger, director of the Department of Gastroenterology, Hepatology and Infectious Diseases at Düsseldorf University Hospital and spokesperson of the Collaborative Research Center 974.



*An illustration of an artificially stained blood vessel is shown. It is a scanning electron micrograph of a hepatic blood vessel.*

*Source: Dr. Daniel Eberhard (Institute of Metabolic Physiology, HHU) and S. Köhler (Center for Advanced Imaging, HHU).*

## Experimental Procedure

The molecular causes of this organ regeneration are the subject of a study published by Düsseldorf scientists in the journal *Nature* (Lorenz et al., *Nature* 2018). Specifically, the scientists were able to show that

increased blood flow through the liver leads to the release and activation of growth signals from blood vessels. One of these signals is the hepatocyte growth factor (HGF), which is particularly important for the growth and survival of liver cells. The endothelial cells of the blood vessels recognize the increased blood flow through the liver by means of so-called integrins. These are cell surface proteins that connect the extracellular matrix to the cytoskeleton and are able to activate other receptors such as the vascular endothelial growth factor receptor-3 (VEGFR3). The activation of the  $\beta 1$  integrin (a subunit of the integrins) due to the increased blood flow leads in endothelial cells to the activation of VEGFR3 and the activation and release of growth factors such as HGF. The latter induce the growth of the liver. As soon as the liver has grown to its normal size and new blood vessels have formed, a normal amount of blood per endothelial cell flows through the liver again. This normal mechanical stimulation of the endothelial cells could explain why the liver stops growing. The scientists postulate that this molecular mechanism causes the liver to grow as soon as its organ size is reduced and then to stop growing when it is restored.

**Original publication:** Lorenz L, et al. *Mechanosensing by  $\beta 1$  integrin induces angiocrine signals for liver growth and survival.* *Nature.* 2018 Sep 26. doi: 10.1038/s41586-018-0522-3.

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FLI Leibniz Institute on Aging

## Inflammatory processes impair nerve regeneration in old age

The regenerative capacity of the nervous system declines during ageing; the risk to develop nerve pathologies increases. Researchers of the Leibniz Institute on Aging (FLI) in Jena investigated the regeneration of ageing nerves in collaboration with colleagues from the University Hospital Jena and the University Bonn. They found that a disturbed immune response leading to chronic inflammation is significantly involved in this and identified promising ageing markers that are currently being tested as therapeutic targets.

The human body is spanned head to toe by numerous nerves. Together they form the peripheral nervous system, which connects the brain and spinal cord (central nervous system) with the rest of the body, to transmit pain and sensory perceptions and movement signals. Impairments of the peripheral nervous system have a great impact on the quality of life and lead to organ dysfunctions, reduced sensory function and unspecific pain sensation. Therefore, a good regenerative ability is crucial for maintaining nerve functions throughout life and restoring them after injury. This regenerative ability, however, declines during ageing and with it the functionality of the peripheral nervous system.

Although the ageing-associated decrease of regenerative ability has been known for a long time, its causes are still largely unexplored and therapies have been ineffective or impossible so far. Researchers of the Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) in collaboration with colleagues of the University Hospital Jena and the University Bonn were able to gain important insights into the underlying molecular and cellular processes of nerve ageing and identified possible therapeutic targets. The results of the study were published in the journal *Aging Cell* recently.

### Chronic inflammation processes impair regeneration in old age

The researchers investigated the regenerative capacity of the peripheral nervous system in the model organism mouse. Young mice were able to regenerate much faster after an injury than older mice and also showed a faster complete recovery. In contrast, old mice did not achieve a complete

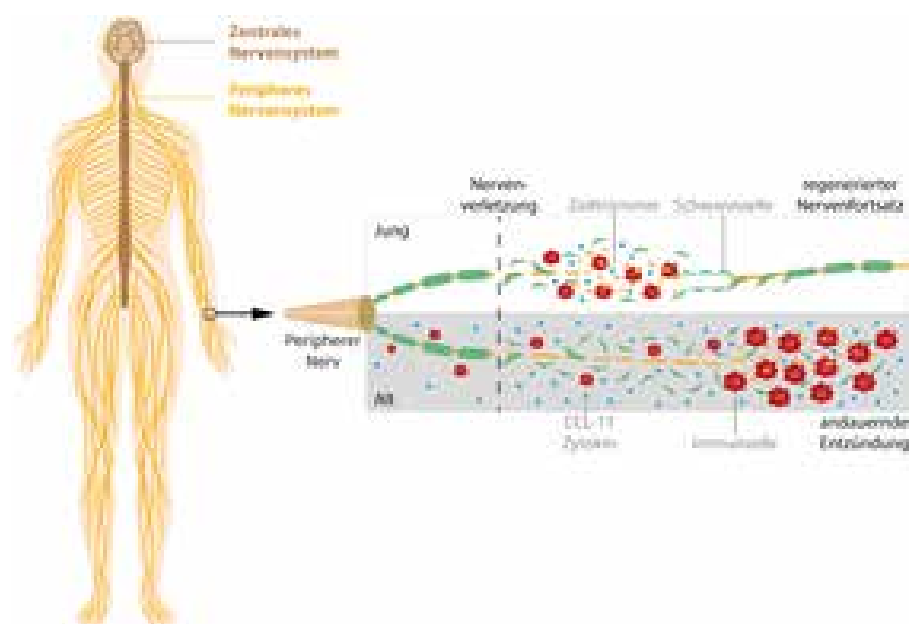
recovery of nerve functions even after longer times of regeneration.

“The peripheral nervous system is a complex system of different cell types, which have to communicate and collaborate closely,” Dr. Helen Morrison, Group Leader at FLI explains. “This is even more important during the regeneration process of nerves, which has to be highly coordinated in time and space to be successful.” Main actors in the regeneration process are neurons, Schwann cells, and immune cells – especially macrophages – that help to remove the injured nerve and debris to provide space for regenerating nerves.

Prior studies have shown that particularly the functions of Schwann- and immune

cells are impaired in the ageing process. Researchers previously assumed that the aged immune system was not sufficiently activated in response to injury or that its cellular function was reduced. Thus, an impaired immune response – unable to clear the area for the regenerating nerves after an injury – was suspected to be the cause of the reduced regeneration capacity.

However, this appears to be only one part of „the story”, tells Robert Büttner, who was working on this project for his doctoral thesis at FLI and is first author of the study. “We do see that the immune response after nerve injury is initially reduced, but upon closer observation it merely is delayed”, explains Büttner. “In fact, old injured nerves show an overshooting immune response



The immune system plays an important role in the regeneration of peripheral nerves. In old age, the immune response is disturbed, leading to a persistent inflammation that impairs regeneration. Graphic: Lars Björn Riecken / FLI, Source: <http://de.freepik.com> and others

leading to a persistent inflammatory state impairing regeneration." Consequently, the researchers found that an anti-inflammatory treatment with acetylsalicylic acid (ASA, known as Aspirin®) effectively prevented this development and significantly increased nerve regeneration in old mice.

#### Identification of inflammatory markers as new therapeutic targets

The team then investigated how the overshooting immune response influences regeneration. They analyzed signal molecules that transmit information between the involved cells. "Cytokine CCL-11 was the most interesting one", Dr. Michael Reuter, Postdoc in the Morrison Research

Group, sums up. This cytokine is mainly known from allergies and parasite defense; additionally a role in declining cognitive function during ageing has been described. "However, its function in nerve regeneration was completely new", Dr. Reuter emphasizes the results.

The researchers were able to show that CCL-11 interfered with Schwann cell differentiation, preventing them to optimally support regeneration. This altered Schwann cell behavior likely evokes an increased infiltration of immune cells, leading to a persistent hyper-inflammatory state, accompanied by a diminished regenerative capacity; a vicious circle.

"The identification of individual signaling molecules involved in the nerve ageing process opens up completely new targets for promising therapies", says Dr. Morrison. "In contrast to the non-specific inflammation inhibitor ASA with its known side effects, this opens up the possibility to very precisely intervene in the regeneration process." In this context, it is particularly interesting that both mice and humans show chronically elevated CCL-11 levels in their blood during ageing. Thus, CCL-11 could be a specific ageing marker. Currently, the team around Dr. Morrison is investigating, whether the cytokine CCL-11 indeed is suitable as a therapeutic target aiming to improve nerve regeneration in old age.

**Original publication:** Büttner R, Schulz A, Reuter M, Akula AK, Mindos T, Carlstedt A, Riecken LB, Baader SL, Bauer R, Morrison H. (2018): *Inflammaging impairs peripheral nerve maintenance and regeneration*. *Aging Cell*, e12833. doi: 10.1111/accel.12833. **Contact:** presse@leibniz-fli.de

LIN Leibniz Institute for Neurobiology

## Bioactive compound from the *Rhodiola* plant improves memory

In an ageing society, more and more people suffer from memory disorders. The progressive loss of memory severely impairs the quality of life of those affected. So far, no drugs are known to prevent age-related cognitive decline. For the first time, a study conducted by scientists from the Leibniz Institutes for Neurobiology (LIN) and for Plant Biochemistry (IPB) and published in the journal *Science Advances* now proves the memory-enhancing effect of a plant ester as an active ingredient from the medicinal plant *Rhodiola rosea*.



*Rhodiola rosea*, the rosewort plant, is a traditional medicinal plant. Source: Pixabay

In order to prevent age-related memory loss, there are so far – apart from physical exercise – no effective strategies. In traditional medicine, plant preparations are widely used to enhance memory performance. However, due to fluctuating drug concentrations, these can be inactive or lead to incorrect dosages – especially if the bioactive drug is not known. In such cases, neither the effects nor the side effects are predictable for the patient or the doctor.

*Rhodiola rosea*, the rosewort plant, has been known for a long time to exert a beneficial effect on mental performance. However, as the first author of the study, Dr. Birgit Michels from the LIN, explains: „In order to make this knowledge useful for medicine, we wanted to find out which specific substances from *Rhodiola* improve

memory. After all, without an identified active ingredient no targeted dosage and plant breeding, no quality control and therefore no drug development are possible.“

Scientists at the IPB in Halle combined extensive bio tests at the LIN in Magdeburg, initially on fly larvae, with phytochemical analyses. This made it possible to isolate the substance ferulic acid eicosyl ester (FAE-20), which promotes memory performance, and to unambiguously determine its memory-enhancing effect. „Although it is a chemically simple molecule, identifying it as an effective component of the plant extract was not trivial. It is more complicated to relate cognitive performance, such as the ability to learn, to the hundreds of natural substances in the plant than it is, for

example, to search for new antibiotics," explains Prof. Dr. Ludger Wessjohann from the IPB. Importantly, the pure substance synthesized in his laboratory also provided clear proof of the effect of FAE-20.

„Next, we were interested in finding out whether it was possible to improve the memory of ageing flies," says Prof. Dr. Berttram Gerber from the LIN. The researchers from Magdeburg were able to show that the addition of FAE-20 to fly food improved the memory of aged fruit flies by a third compared to their non-treated counterparts. These learning experiments were based on so-called classical conditioning. This means that the animals learn to asso-

ciate a scent with a reward, for example sugar. In a subsequent test, it is then possible to see whether they have remembered this association and now find the scent more attractive than before.

The scientists were also able to show that FAE-20 prevents the age-related excessive accumulation of proteins at synapses, the connections among nerve cells in the brain of the fly. As Michels explains: „In flies, 'old' means only about 14 days. Therefore, it was particularly encouraging for us, together with colleagues from the Otto-von-Guericke University in Magdeburg and the German Center for Neurodegenerative Diseases, also to be able to confirm the po-

sitive effects on memory performance in mice even over 2 years old." Initially based on the positive effect of the *Rhodiola* plant in humans, the researchers were thus able to identify FAE-20 as a concrete natural substance that improves memory performance in old age – at least in animal models. They now hope that the circle can be closed and that their discovery can be used for medical dementia research: „We are quite optimistic about this. After all, the plant is already being used by humans. Our results with FAE-20 in animals are therefore likely to be transferable back to humans," says Gerber. A patent application for the newly found application of FAE-20 has already been filed.

**Original publication:** Birgit Michels et al. (2018): *Memory enhancement by ferulic acid ester across species*. *Science Advances* 24 Oct 2018: Vol. 4, no. 10, eaat6994, DOI: 10.1126/sciadv.aat6994. **Contact:** sophie.ehrenberg@lin-magdeburg.de

IfADo Leibniz Research Centre for Working Environment and Human Factors

## How breast cancer cells use fat to protect themselves

**Breast cancer is the most frequent type of cancer in women in Germany. Why cancer cells are so viable is a central research question. Dr. Cristina Cadenas, a researcher at the Leibniz Research Centre for Working Environment and Human Factors (IfADo), and her team have discovered a mechanism by which breast cancer cells use fat to improve their survival. The stronger this survival mechanism, the higher the risk of a negative patient outcome.**

Every cell requires nutrients such as carbohydrates, proteins and fats to function properly and to divide. The same is true for cancer cells, which are capable of producing fatty acids on their own to enable cell division and tumor growth. Cancer cells are much less adept at doing this under stressful conditions and consequently must ensure their supply of fat in another way, as now determined by Dr. Cristina Cadenas and her team of researchers at the Leibniz Research Centre for Working Environment and Human Factors (IfADo).

### Fat protects cells against free radicals

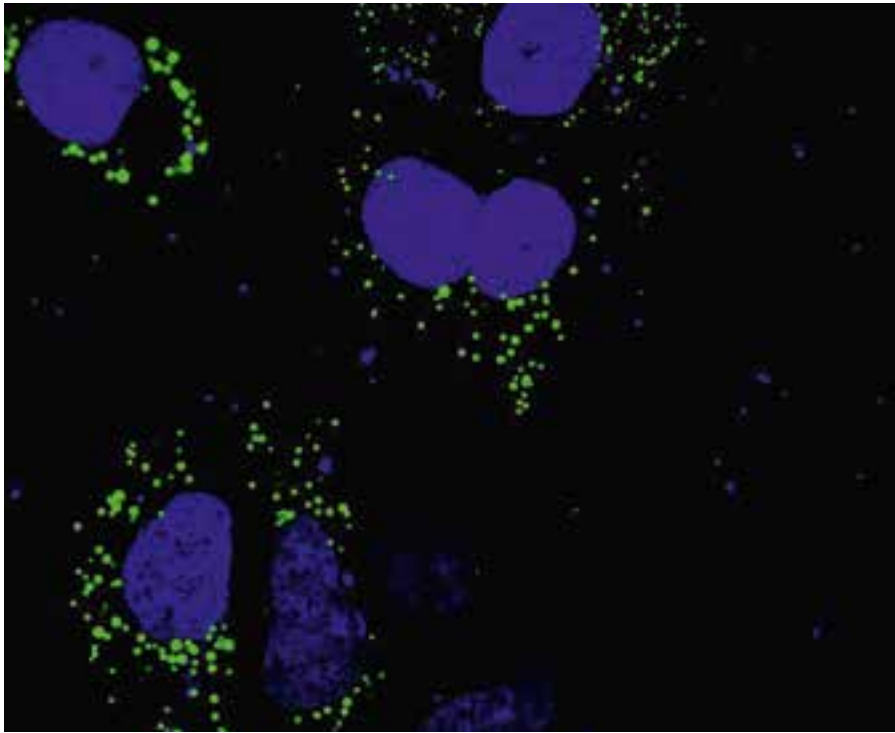
Under oxidative stress some breast cancer cells make use of the enzyme endothelial lipase G (LIPG) to supply themselves with fat. These cancer cells produce LIPG and send it to the outer cell membrane where it binds and metabolizes complex fats from the blood stream. Thus, LIPG feeds breast cancer cells with "bite-sized" fatty acids.



Breast cancer in mammography. Source: Adobe Stock

Simultaneously, LIPG helps protect the breast cancer cells against damage by oxidative stress. Oxidative stress develops after accumulation of oxygen radicals that result from metabolic processes or by external factors when environmental toxins

enter the body. This can damage cells or even kill them. Cadenas and her team have been able to account for this protective mechanism against cell death by deactivating the LIPG gene so that the breast cancer cells were no longer able to produce LIPG.



Breast cancer cells that express the enzyme LIPG show lipid droplets (green). These lipid droplets protect the cells against stress-related cell death. The cell nuclei are stained blue. Source: IfADo

Without LIPG many of the cells died in response to oxidative stress.

#### The more LIPG, the higher the risk for further metastases

The researchers were also able to show a significant association between a very high level of LIPG in the tumor and the metastasis-free period of time for the patients. The more fat-splitting enzyme that is produced, the higher the risk of additional metastases, explained IfADo molecular biologist Cristina Cadenas. She proposes that this could be because LIPG protects breast cancer cells from oxidative stress thus aiding cell survival. This connection was observed in patient data in which the primary tumor was surgically removed and there were no metastases present in the lymph nodes. The scientists state that more research is still needed to find out if LIPG deactivation or blocking the fat supply can be used to treat breast cancer.

**Original publication:** Cadenas, C et al. (2019): *LIPG-promoted lipid storage mediates adaptation to oxidative stress in breast cancer*. *International Journal of Cancer*. doi:10.1002/ijc.32138. **Contact:** [pressereferat@ifado.de](mailto:pressereferat@ifado.de)

DIfE German Institute of Human Nutrition Potsdam-Rehbruecke

## Better understanding and recognizing cardiovascular diseases

Cardiovascular diseases are the most common cause of death in Germany. Primarily older people are affected. Cardiovascular diseases can markedly lower life expectancy and quality of life. Researchers at DIfE successfully identified the protein chemerin as a new marker which provides insights into partially still unknown mechanisms of the disease onset and could be used in future to determine the risk of heart attack, stroke and other adverse cardiovascular events even earlier and with more precision.

Chemerin is a messenger substance (adipokine) that is primarily produced in fatty tissue, the liver, kidneys and pancreas. It plays a role in helping the initially undifferentiated cells in fatty tissue special-

ize in form and function for specific tasks. Chemerin also attracts immune cells to sites of tissue damage where they immediately cause inflammation to defend against infection. This signalling protein is thus

part of the body's finely regulated alarm system.

"If the system is no longer under control, then arteriosclerosis, heart attack and

#### EPIC-Potsdam Study

The European Prospective Investigation into Cancer and Nutrition (EPIC) Potsdam Study is a prospective cohort study. Between 1994 and 1998, 27,548 men and women between the ages of 35 and 65 years were recruited. Study participants filled out questionnaires on their eating habits, lifestyle and health status. This survey was repeated about every three years. The EPIC-Potsdam Study is part of one of the largest longitudinal studies worldwide with a total of approximately 521,000 study participants from ten European countries. The aim is to investigate the effect of diet on the development of cancer and other chronic diseases.



stroke become threats,” explained Dr. Krasimira Aleksandrova, a scientist at the German Institute for Human Nutrition Potsdam-Rehbruecke (Dife) who is studying how the interplay between diet, body composition and the immune system influences age-related diseases.

### Missing Link

The precise connections between inflammatory reactions and cardiovascular diseases are not yet fully understood. To shed more light on this, Aleksandrova’s team analysed blood samples from a total of 2,500 men and women. The basis for these analyses came from the data of the EPIC-Potsdam Study with over 27,500 study participants. Scientists observed for the first time that the concentration of chemerin in the blood is already elevated before a heart attack or stroke occurs. Chemerin could therefore be used in the future as an indicator to more precisely predict the risk of cardiovascular disease. “Our results confirm that the signalling protein chemerin

plays an important role not only in inflammatory processes, but also in the development of cardiovascular diseases. This line of inquiry should definitely be pursued

further. Understanding chemerin’s exact functions could improve efforts to find new preventive therapies and medications,” stated Aleksandrova.



Cardiovascular diseases are the most common cause of death in Germany. Primarily older people are affected. Source: Adobe Stock

**Original publication:** Eichelmann F, Schulze MB, Wittenbecher C, Menzel J, Weikert C, Di Giuseppe R, Biemann R, Isermann B, Fritsche A, Boeing H, Aleksandrova K (2019): *Chemerin as a Biomarker Linking Inflammation and Cardiovascular Diseases*. *Journal of the American College of Cardiology* Jan 73 (3) 378-379; DOI: 10.1016/j.jacc.2018.10.058. **Contact:** presse@dife.de

## Focus Groups and Projects

### ISAS Biomarkers of Ageing associated dysfunctions and diseases

## Sports and alzheimer – diabetes and arteriosclerosis increase the risk of alzheimer’s disease

Earlier or later approximately 6 percent of the population will develop Alzheimer’s disease. About one percent of Alzheimer cases involve a genetic mutation that is the inevitable and direct cause of the disease. For the remaining cases, the risk of disease varies. But what are the risk factors? Is it possible to determine the probability of future onset even before the disease emerges? These questions are being investigated by the collaborative partners of the project group studying biomarkers of ageing-associated dysfunctions and diseases led by Professor Dr. Helmut E. Meyer at ISAS in Dortmund. This group is

searching for biomarkers to predict not only the risk of developing Alzheimer’s dementia, but also type-2 diabetes and cardiovascular disease.

Among the known risk factors for Alzheimer’s disease are various genetic variants of apolipoprotein E (ApoE) and the amyloid precursor protein (APP). As an example, these different isoforms of ApoE are referred to as ApoE2, ApoE3 and ApoE4. It is already known that about 50% of those who have the pure ApoE4 gene variant develop the disease. For the ApoE2 gene type, the risk of Alzheimer’s disease is distinctly

lower compared to that for the total population. The probability of developing Alzheimer’s disease increases sharply if type-2 diabetes is simultaneously present.

### The interplay between ApoE4, type-2 diabetes and cardiovascular diseases

How can an individual’s risk of developing Alzheimer’s disease be predicted if disease onset has not yet occurred? The project group studying biomarkers of ageing-associated dysfunctions and diseases is looking into this question by searching for biomarkers in extracellular vesicles found in the blood. These vesicles contain proteins,



Prof. Dr. Helmut E. Meyer (left) and Dr. Fouzi El Magraoui (right) are researching on Alzheimer's disease within the LRA Healthy Ageing at the Leibniz-Institut für Analytische Wissenschaften – ISAS – e. V. in Dortmund. Source: Astrid van der Wall/LRA Healthy Ageing

lipids and miniscule particles of NA, called micro-RNA, that indicate early on the risks of Alzheimer's disease, type-2 diabetes and cardiovascular disease. The researchers'

aim is to give a reliable prognosis many years before the first symptoms of disease appear to influence the risk of disease. The researchers are looking at lifestyle with

particular scrutiny, since a healthy diet and regular exercise not only reduce the risk of type-2 diabetes and heart attack, but also dementia via the mechanisms described. In Sweden, for instance, adolescents who wish to seriously engage in boxing are already being tested for the ApoE gene variants. Since boxing is also linked to the development of Alzheimer's disease, those with the pure ApoE4 gene variant are discouraged from practicing this type of sport. The current diagnostic procedures for determining the risk of dementia are very complex and expensive. The classification of biomarkers present in the blood can change this. Furthermore, the progression and treatment of these diseases can be better monitored through such biomarkers. At the end of development, the researchers want to offer medicine a prognostic test that enables the measurement of individual biomarkers in the blood for dementia, type-2 diabetes and cardiovascular disease.



The probability of developing Alzheimer's disease increases sharply if type-2 diabetes is simultaneously present. The interplay between ApoE4, type-2 diabetes and cardiovascular disease is similar. Source: Astrid van der Wall/LRA Healthy Ageing

**Cooperation partners:** Leibniz-Institut für Analytische Wissenschaften – ISAS – e. V., German Diabetes Center (DDZ) Düsseldorf, German Institute of Human Nutrition Potsdam-Rehbrücke (DIfE), German Primate Center (DPZ), Göttingen, Deutsches Zentrum für Neurodegenerative Erkrankungen (DZNE), Leibniz Institute for Farm Animal Biology (FBN) Dummerstorf, Leibniz Institute on Aging - Fritz Lipmann Institute (FLI) Jena, Friedrich Schiller Universität (FSU) Jena, University Hospital Regensburg, University Göttingen, University Hospital Lübeck

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**Publications of the Focus group:** Wolfsgruber S et al. (2017): *Cerebrospinal Fluid Biomarkers and Clinical Progression in Patients with Subjective Cognitive Decline and Mild Cognitive Impairment*. J Alzheimers Dis. 58(3):939-950. doi: 10.3233

Schrötter A et al. (2017): *LMD proteomics provides evidence for hippocampus field-specific motor protein abundance changes with relevance to Alzheimer's disease*. Biochim Biophys Acta. 1865(6):703-714. doi: 10.1016

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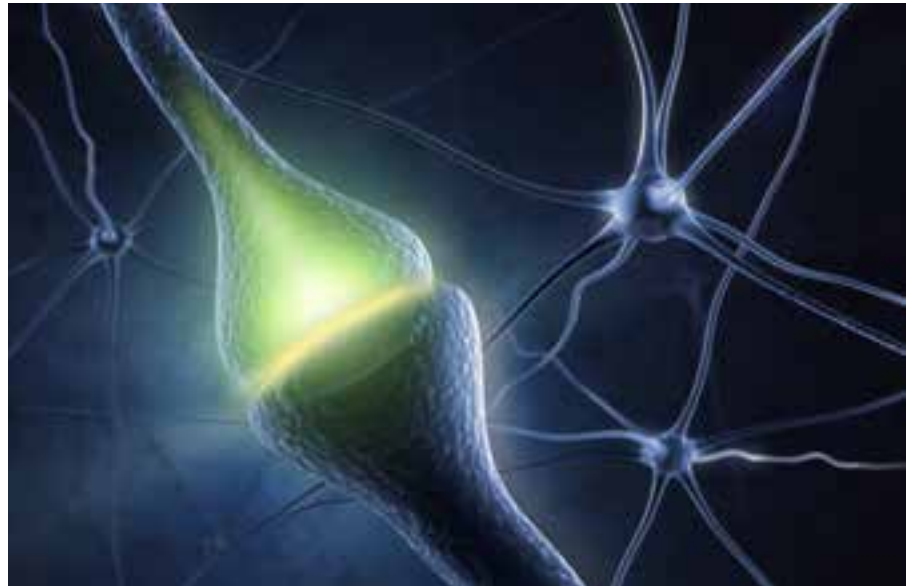
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## LIN Synaptic Ageing

## Junior scientists researching on ageing synapses

The focus group synaptic ageing brings together researchers from different Leibniz-Institutes but also partners from Universities and the German Center of Degenerative Diseases. Members of the group incorporate expertise from very different areas. The group is currently applying for funding of a German Research Foundation (DFG) research unit dealing with the synaptic role of autophagy. Several members of the focus group were also involved in establishing a novel graduate programme. The Otto-von-Guericke University, the Leibniz Institute for Neurobiology (LIN) and the German Center for Neurodegenerative Diseases (DZNE) in Magdeburg are involved in a new Research Training Group funded by the DFG, which focuses on the molecular, cellular, systemic and behavioral biology of cognitive decline. The DFG is providing 4.2 million euros for the first four-and-a-half year funding period.

The research and qualification programme enables 13 junior scientists from all over the world to do their doctorate at a high professional level in Magdeburg. Daniela C. Dieterich, Director of the Institute of Pharmacology and Toxicology at the Faculty of Medicine serves as spokesperson and Prof. Dr. med. Oliver Stork from the Department of Genetics and Molecular Neurobiology at the Institute of Biology as co-speaker.



Ageing drives memory impairment in the synapses. Source: Adobe Stock.

With age, a cognitive decline in performance is observed even in otherwise healthy people. The reasons for these restrictions have only scarcely been investigated, although they result in significant sacrifices in the quality of life for both directly affected and as well as their families and also cause considerable costs for the social security systems. This is the motivation for the topic of the Research Training Group, hence, RTG2413 SynAGE will focus on the ageing synapse as a focal point of cognitive decline and explore the complex causes on four different levels.

### Consequences of synaptic ageing will be explored

Within the framework of the Research Training Group the molecular, cellular, systemic and behavioral consequences of synaptic ageing will be explored. The RTG has a total of 13 projects, in which 13 scientific as well as 13 medical doctoral students will explore the basics of altered protein homeostasis, aberrant functionality of the multiparticulate synapse, dysfunctional immune system, and altered neuromodulation: RTG SynAGE concentrates on synaptic dysbalances involving these four core principles:

- altered synaptic proteostasis (Dieterich Lab, Stork Lab, Kreutz Lab),
- dysfunctions of the immune system (Kreutz Lab, Dunay Lab),
- altered functionality of the multiparticulate synapse (Dityatev Lab, Schreiber Lab, Gundelfinger Lab, Seidenbecher Lab, Dieterich Lab) and
- changes in neuromodulation (Leßmann Lab, Stork Lab, Düzel Lab, Ullsperger Lab)

SynAGE addresses these four transversal themes in a joint effort by a team of molecular/cellular and systems neurobiologists



Speakers of the Research Training Group SynAGE: Daniela Dieterich und Oliver Stork.  
Source: Regina Nitschke.

to eventually break ground for innovative intervention strategies.

This interdisciplinarity and, above all, the joint research of natural scientists as well as aspiring physicians has the clear goal in mind to develop a translational potential in order to jointly create interventions in the future.

#### Research training group

The Research Training Group is training doctoral students in the life and natural sciences and at a high international level. In

addition to direct scientific support in the research groups involved, SynAGE also includes a structured supervision and qualification concept. The teaching programme consists of interdisciplinary lectures, seminars and workshops with complementary retreats, summer and winter schools, symposia and national and international internships, all of which convey and train relevant contents and methods, key skills and soft skills. Personal mentoring and coaching as well as network building within and outside the academic research landscape round off the programme, with the aim of

optimizing the personal development and career opportunities of the young junior researchers. The Magdeburg consortium pays special attention to the diversity in education. It deliberately focuses on an interdisciplinary event programme, cooperatively supervised doctoral programmes and intensive networking measures for junior scientists. The overarching goal is to train generalists for various occupational fields in research within as well as outside the universities, institutions and clinics, in order to advance research and application as quickly as possible for our society.

**Cooperation partners:** Leibniz Institute for Neurobiology (LIN) Magdeburg, Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP) Berlin-Buch, German Center for Neurodegenerative Diseases (DZNE) Magdeburg, Otto von Guericke University Magdeburg

**Contact:** Michael R. Kreutz kreutz@lin-magdeburg.de

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## Symposia and Workshops

### 3rd International Symposium Healthy Ageing: 20 - 22 February 2019 at the FMP in Berlin-Buch

The next international Symposium of the LRA Healthy Ageing will take place at the Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP) in Berlin-Buch from 20 until 22 February 2019. The LRA Healthy Ageing expects about 120 participants from the cooperating Leibniz Institutes and from international and national partners. The first two days, the participants will discuss biomedical aspects of ageing, environmental factors and self-determined ageing. This year the symposium could be prolonged for one day thanks to the financial support of the Joachim Herz Stiftung. The third day will be dedicated to the junior researchers of the LRA Healthy Ageing, PhD students and Postdocs will discuss aspects of interdisciplinary research.

On Monday evening, the symposium will present a special event: Prof. Dr. Konrad Beyreuther, director of the Network Aging Research at the University Heidelberg, will give a public talk about Alzheimer and its therapies. Afterwards, the audience is invited to a reception with the STEGREIF.Orchestra Berlin.



**3. International Symposium  
Healthy Ageing**

**20 - 22 February 2019**  
At the Leibniz-Forschungsinstitut für  
Molekulare Pharmakologie (FMP)  
in Berlin-Buch / Germany

**Chairs:** Dr. Helen Morrison  
Leibniz Institute on Aging (FLI)  
Prof. Dr. Jean Krucman  
Leibniz Research Institute for  
Environmental Medicine (IHE)

**Organizer:** LRA Healthy Ageing

[www.leibniz-healthy-ageing.de](http://www.leibniz-healthy-ageing.de)

## 1st Jena Aging Meeting (JAM) from 6-8 September 2018



*Big rush during the 1 Jena Aging Meeting. Source: Magdalena Voll/FLI.*

From 6-8 September 2018 the first international conference in Jena on the issue of ageing took place; the “Jena Aging Meeting (JAM)”. About 200 participants from 16 countries met to discuss the latest research results, methods and developments in the field of ageing research. Topics included the gene- and protein-related mechanisms in ageing, DNA damage response in cancer and ageing, metabolism in health, disease and ageing, genomic instability and senescence in ageing, stem cells in tissue homeostasis, regeneration and ageing.

The Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) together with the Leibniz Research Alliance “Healthy Ageing”, the “Aging Research Center Jena”, and the “Jena Centre for Healthy Aging” were organizers of the first “Jena Aging Meeting”, which took place in the lecture halls of the Friedrich Schiller University Jena (FSU) on the Ernst Abbe Campus. To foster scientific exchange at every level, the three-day conference offered much space to socialize in addition to numerous lectures and poster sessions. More than 20 internationally renowned speakers gave insights into their field of expertise in ageing research. Together with its partners including the FSU and the Jena University Hospital, research on ageing has a special significance for the city: The

common goal is to bolster ageing research in Jena with a combined basic and translational research approach in order to understand the mechanisms that contribute to ageing and ageing-related diseases.

Keynote speakers at the JAM were the stem cell researcher Prof. Dr. Emmanuelle Passegué from Columbia University, New York, USA and the molecular biologist Prof. Dr. Jan Hoeijmakers from the Erasmus Medical Center in Rotterdam, Netherlands.

Emmanuelle Passegué investigates how hematopoietic stem cells regulate blood production in a constantly changing organism during its lifetime. Emmanuelle’s question is of central importance for tissue development, maintenance and tissue regeneration and has implications for e.g. response to stress, development of diseases and the ageing process. Jan Hoeijmakers’ investigates the mechanisms of DNA repair and the consequences of the defects in repair mechanism on gene stability during ageing and cancer as well as various hereditary diseases. His current goal is to elucidate how DNA damage, senescence, apoptosis and stress induction affect the stem cell niche and contribute to the process of skin ageing.

## Workshop Healthy Ageing 2020 at the IfADo in Dortmund

The Workshop 2020 of the Leibniz Research Alliance Healthy Ageing will take place on 17-18 March 2020 at the Leibniz Research Centre for Working Environment and Human Factors (IfADo) in Dortmund. Again, all focus groups of the LRA Healthy Ageing are invited to meet for one- or two-day workshops and to discuss their research with other scientists and disciplines.



*Source: IfADo*

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## Ageing without Alzheimer's - Will our grandchildren still know the disease?

Prof. Dr. Dr. h.c. Konrad Beyreuther will speak on hereditary factors and environmental influences of Alzheimer's dementia on **20th February 2019, 18:00 h - 19:30 h** at the **Max Delbrück Communication Center MDC.C, Room Axon, Campus Berlin-Buch, Robert-Roessle-Str. 10, 13125 Berlin**

Avoiding dementia through sport, healthy nutrition and mental fitness? The probability of developing Alzheimer's is only about one percent dependent on the genes. However, the transmission of ageing processes and dementias from one generation to the next is not only determined by genes, but also by environmental influences and social factors such as financial possibilities, place of residence, education, lifestyle or professional reputation. Prof. Dr. Konrad Beyreuther from the University of Heidelberg will present these processes in his public lecture. During human ageing, this type of inheritance, known as epigenetics, drastically alters cellular metabolism. In Alzheimer's disease, lifestyle, in particular physical and mental activity, plays a decisive role. Together with the development of drugs to slow down Alzheimer's dementia, this makes long-term ageing without Alzheimer's possible.



*Prof. Dr. Dr. h.c. Konrad Beyreuther,  
Source: NAR University Heidelberg*

Professor Dr. Dr. h.c. Konrad Beyreuther is founding director of the Network Ageing Research (NAR) at the University of Heidelberg. His research interests focus on human brain function, Alzheimer's disease and the genetics of ageing. As a former Professor of Molecular Biology, Director of the Centre for Molecular Biology (ZMBH) and Dean of the Faculty of Biology, he has held a senior professorship at the University of Heidelberg since 2009. Beyreuther's current research interests focus on plaque formation in Alzheimer's dementia and the development of rational therapies.

## Volker Haucke receives Feldberg Prize

Prof. Volker Haucke, Director at the Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP) receives the Feldberg Prize 2020, which is awarded annually by the Feldberg Foundation for anglo-german scientific exchange. The aim is to promote scientific exchange between British and German researchers in the field of experimental medicine, in particular in the disciplines of physiology and pharmacology. The biochemist Volker Haucke studies together with his team the molecular mechanisms of endocytosis and endolysosomal membrane dynamics and its role in cell signaling and neurotransmission. The overarching goal of his work is to provide a mechanistic understanding of exo-endocytosis and endolysosomal function and its regulation by proteins and lipids and to use this know-how to develop novel strategies for acute chemical and pharmacological interference. Volker Haucke's contributions to science have been recognized by his election as a Member of Leopoldina, the German National Academy of Science (Halle) and of the Berlin-Brandenburg Academy of Science. Since 2014 he is an EMBO member. In 2017 he received the Avanti Award of the American Society for Biochemistry and Molecular Biology (ASBMB).



*Prof. Dr. Volker Haucke, Source: FMP*

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## The better half - What we can look forward to in the middle of life



The second half of life is better than its reputation! In the middle of life you can run out of breath. Everything is stressing at the same time: job, children, parents and the first physical quirks that won't go away. Does it feel like it's only going downhill from the age of 40? No, say Eckart von Hirschhausen and Tobias Esch. On the contrary. For most people, satisfaction increases in the second half of life! In an inspiring dialogue, the two doctors search for happiness that grows through experience, wisdom and maturity. They find personal role models, discuss scientific research and build on their own experiences. This is how the two happiness experts succeed in the little miracle: you really feel the desire to get older! The event is part of the lecture series Science & Society. It will take place in the Abbe-Zentrum at the Beutenberg in Jena on 26 September 2019, 16:00 h. It is free of charge and open for the public.

*In an entertaining dialogue, the two physicians Eckart von Hirschhausen and Tobias Esch develop ideas why we can look forward to old age. Source: Camillo Wiz*



[www.leibniz-healthy-ageing.de](http://www.leibniz-healthy-ageing.de)