

Press release

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Cancer or degenerative diseases?

One out of the two is likely to be our cause of death when we get older

Above the age of 50, the most likely causes of death are cancer and degenerative diseases such as heart failure, dementia or diabetes. Since life expectancy has been considerably growing over the last 150 years, the frequency of age-specific diseases has also been on the rise. While death due to cancer is most prevalent among the 60 year olds, its contribution to total mortality declines at more advanced ages, while degenerative diseases are on the rise up to the oldest age groups. Why does this occur and can this shift in cause of death be at least partially explained by studying the molecular alterations that occur as we get older and compare them to the molecular signatures of each of these diseases? To address this question, a large-scale international collaborative effort involving research teams from Kiel and Jena, Germany, and from Maryland, USA, led by Professor Christoph Kaleta investigated to which extent conserved age-related changes in the activity of genes are connected to changes observed in aging diseases. Results from their study have now been published in the scientific journal *Nature Communications*.

To better understand the interaction between the process of aging and the diseases of aging, researchers from the Jena Centre for Systems Biology of Ageing (JenAge) performed the most comprehensive comparison of aging across species and tissues that has been undertaken to date. “Comparative systems-wide approaches are powerful tools to dissect complex biomedical processes like aging,” says JenAge coordinator Dr Jürgen Sühnel from the Leibniz Institute on Aging – Fritz Lipmann Institute, Jena. The present analysis was coordinated by Professor Christoph Kaleta, now a member of the Cluster of Excellence “Inflammation at Interfaces”, from Kiel University in Germany and Professor Eytan Ruppin, University of Maryland, USA. The scientists compared changes in the activity of genes during aging from humans, mice, the zebrafish *Danio rerio* and the short-lived killifish *Nothobranchius furzeri* across several organs. “We found many similarities in the molecular signatures of age-associated changes in the investigated species. Our results clearly indicate that the core of aging is highly similar among very different vertebrates, whose natural lifespans range from a few months to almost a century,” says Professor Kaleta, the corresponding author of the study.

Subsequently, the researchers compared the changes in gene activity with the signatures of age-specific diseases. Age-related changes in gene activity were accompanied by changes observed in degenerative diseases. Surprisingly, those changes showed a reverse development compared to cancer. “Our results indicate that aging does not necessarily promote all age-related diseases, but might have very disease-specific effects,” elaborates Professor Kaleta. Indeed, the different influence of aging on diseases might provide an explanation as to why, at an advanced age, the likelihood of dying of cancer is decreasing compared to degenerative diseases. Intriguingly, the researchers found this difference between cancer and degenerative diseases is also visible on the genomic level: many risk genes that increase the chance of getting a degenerative disease actually protect against cancer and vice versa.

While the researchers can only speculate about the cause for the opposite direction of changes in gene activity between cancer and degenerative diseases, they point out that it might be related to the continuous accumulation of damaged DNA (deoxyribonucleic acid) in cells when humans get older. This raises the risk of getting cancer. As a consequence, the immune system is activated to destroy or keep the damaged cells in check to prevent cancer from developing. A chronic low grade inflammation, which is often observed in the elderly, might be a consequence of the latter, facilitating further degenerative tissue damage. “As the molecular signatures of cancer and degenerative disorders oppose each other in key cellular processes, it logically follows that the molecular alterations occurring late in life may thus not be able to drive away both,

cancer and degenerative disorders, at the same time,” says Professor Ruppin from the University of Maryland. “Indeed, our results show that they are aligned to counteract the increased risk of cancer but, probably inevitably, the price might be an increased risk of a degenerative disease.”

The new data clearly indicates a strong connection between degenerative diseases and cancer. These results are also of particular importance regarding the current search for treatments that reverse age-associated changes. In light of the new results such approaches might have to be carefully evaluated with regard to their effect on cancer development.

Original publication:

Aramillo Irizar, P, Schäuble, S, Esser, D, Groth, M, Frahm, C, Priebe, S, Baumgart, M, Hartmann, N, Marthandan, S, Menzel, U, Müller, J, Schmidt, S, Ast, V, Caliebe, A, König, R, Krawczak, M, Ristow, M, Schuster, S, Cellerino, A, Diekmann, S, Englert, C, Hemmerich, P, Sühnel, J, Guthke, R, Witte, OW, Platzer, M, Ruppin, E and Kaleta, C (2018): Transcriptomic alterations during ageing reflect the shift from cancer to degenerative diseases in the elderly. *Nature Communications*, <http://dx.doi.org/10.1038/s41467-017-02395-2>

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Photos are available to download:

<http://inflammation-at-interfaces.de/de/newsroom/aktuelles/abbildung-sterblichkeit>

Epidemiology of age-associated diseases: the risk of dying from cancer is highest between the ages of 50 and 75 years. The risk of dying of degenerative diseases rises strongly up to the oldest age groups.

Data source: Center for Disease Control and Prevention (CDC, <https://www.cdc.gov/>)

<http://inflammation-at-interfaces.de/de/newsroom/aktuelles/n-furzeri-kurzlebiges-paar>

The short-lived killifish *Nothobranchius furzeri* is frequently used as a vertebrate model to study developmental and aging processes.

Photo: Nadine Grimm, Fritz Lippmann Institute

<http://inflammation-at-interfaces.de/de/newsroom/aktuelles/prof-kaleta>

Professor Christoph Kaleta, Cluster of Excellence “Inflammation at Interfaces” from Kiel University, Germany.

Photo: Dr Tebke Bösch, Kiel University

<http://inflammation-at-interfaces.de/de/newsroom/aktuelles/prof-ruppin>

Professor Eytan Ruppin from the University of Maryland, USA.

Photo: Tom Ventsias, University of Maryland Institute for Advanced Computer Studies

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The Cluster of Excellence "Inflammation at Interfaces" has been funded since 2007 by the Excellence Initiative of the German Government and the federal states with a total budget of 68 million Euros. It is currently in its second phase of funding. Around 300 cluster members are spread across the four locations: Kiel (Kiel University, University Medical Center Schleswig-Holstein (UKSH)), Lübeck (University of Lübeck, UKSH), Plön (Max Planck Institute for Evolutionary Biology) and Borstel (Research Center Borstel (FZB) – Center for Medicine and

Biosciences) and are researching an innovative, systematic approach to the phenomenon of inflammation, which can affect all barrier organs such as the intestines, lungs and skin.

The Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) is the first German research organization dedicated to biomedical aging research since 2004. More than 330 members from over 30 nations explore the molecular mechanisms underlying aging processes and age-associated diseases. For more information, please visit www.leibniz-flj.de.

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