Cancer in Old Age

Cancer Research at Leibniz Institute on Aging – Fritz Lipmann Institute (FLI)

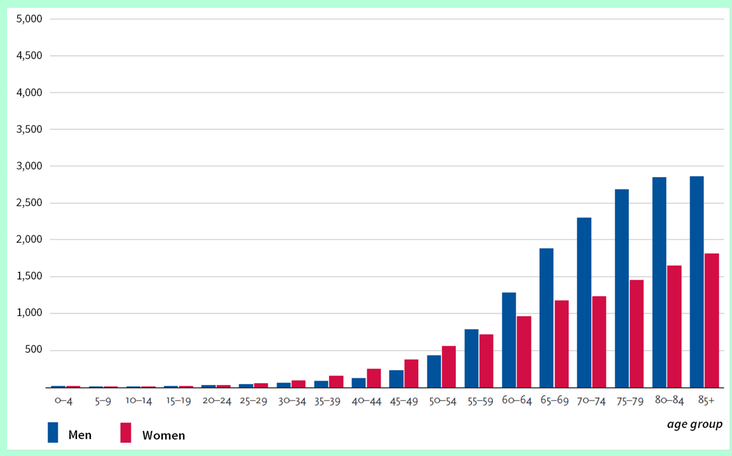
Cancer is an age-associated disease

Causes for the age-associated emergence of cancer are manifold and complex. And research is by far not knowing and understanding the underlying processes in detail.

However, it is known, that aging is linked to a diminishing capability of the human body to regenerate, to changes in the endocrine system (hormone system) and a weakening immune system – all this contributing to the emergence and growth of tumors.

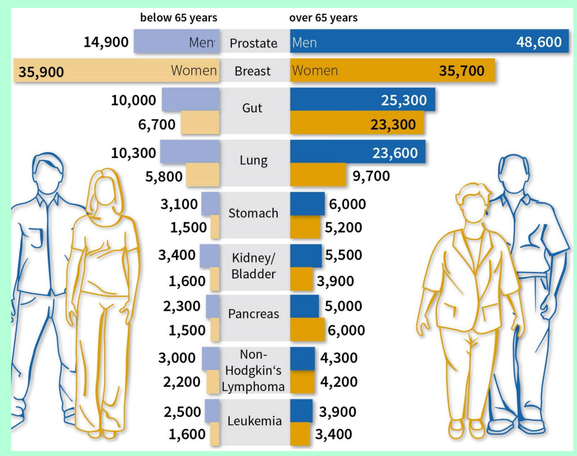
Furthermore, aging cells are characterized by an accumulation of cellular damages caused by a myriad of defective processes, as e.g. inaccurate DNA damage repair, defective cell division, or faults in cell senescence and cell death. If defective cells gain a growth advantage over healthy cells (clonal dominance), the emergence of tumors may be a severe result.

Number of new cancer cases in Germany by age and sex (every 100.000 inhabitants)



Source: Krebs in Deutschland 2009-2010, 9th edition, Robert Koch Institute [ed.] 2013.

Frequency of cancer cases by type and sex



Source: Krebs in Deutschland 2007-2008, 8th edition, Robert Koch Institute [ed.] 2012. Graph: Roche

Cancer Research at FLI – At a Glance

CD44 and Metastasis of Cancer Cells

Herrlich Emeritus Research Group

Tumor stem cells and tumor cells which are capable to build metastases are characterized by a certain form of the surface protein CD44. If CD44 is missing, tumor emergence and metastasis decrease. However, CD44 is also needed in healthy cells for the regulation of cellular processes – hence, a complete "knock-out" would have severe side-effects.

Objective: Inhibition of metastasis and growth of cancer cells

Telomere Shortening

Rudolph Research Group

During life, stem cell telomeres shorten with every cell division. If these „protective caps" are gone, cell division may result in an imbalance in the division of the chromosomes in daughter cells, leading to a chromosomal instability and carcinogenesis.

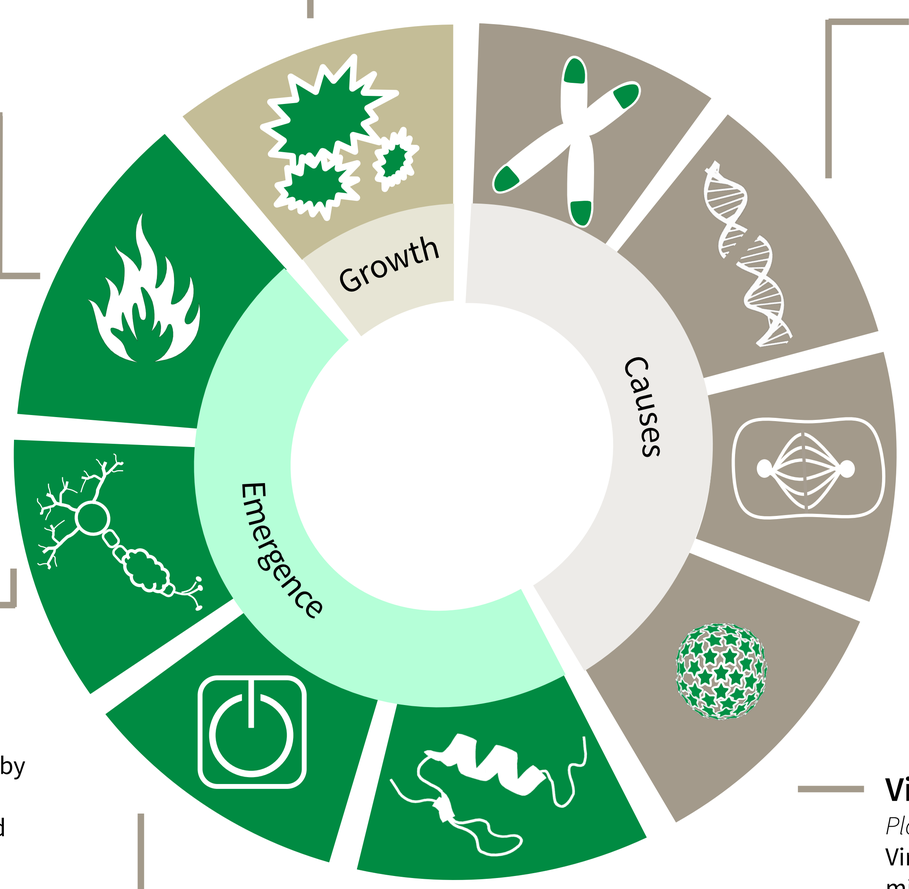
Objective: Avoidance of chromosomal instability to prevent carcinogenesis

Aging Immune System

Rudolph, Ermolaeva and Weih/Hänold Research Groups

In old age, hematopoietic stem cells loose their capability to produce immune cells. As a consequence, defective body cells are no longer reliably eliminated. Thus, they may survive longer, limit the functionality of tissues and organs and may contribute to carcinogenesis during aging.

Objective: Improvement of immune functions in old age and reduction of tumor emergence



Inaccurate DNA Damage Response

Wang und Kaether Research Groups

DNA damages that are caused by external or internal factors lead to a DNA damage response impacting stem cell functionality and tissue homeostasis. An inaccurate damage response leads to lasting DNA damages which may result in carcinogenesis.

Objective: Avoidance of DNA damages in aging cells to reduce carcinogenesis in older age

Defective Cell Division

Große Research Group

If the cell division of a mother cell (DNA doubling) is defective, daughter cells with an anomalous number of chromosomes may occur. Usually, they are inoperable or may degenerate into cancer cells.

Objective: Clarification of cell division mechanisms to avoid defective divisions.

Oncogene Signaling

Morrison Research Group

RAS proteins are molecular switches turning cellular signaling pathways on or off. More than 30% of cancer types are caused by RAS mutations. These mutations lead to a permanent RAS activation, that results in an uncontrolled cell proliferation and the emergence of cancer. The tumor suppressor protein neurofibromin 2 (merlin) and the putative tumor promoters ezrin, radixin and moesin (ERM) act as counter players in RAS activation. Mutations in the gene encoding Merlin are the reason for the hereditary disease Neurofibromatosis Type 2 (NF2), which is characterized by tumorigenesis in the peripheral nervous system.

Objective: Investigation of tumor-induces RAS signaling pathways to prevent cancer in older age and develop possible treatments of NF 2

Virus-Induced Oncogenesis

Ploubidou Associated Research Group

Viral infections may lead to a defective formation of microtubules necessary for a correct cell division. This results in an inactivation of the centrosome and possibly in a defective cell division.

Objective: Understanding of the viral causes of carcinogenesis to develop future therapies

Wilms Tumor Suppressor WT1

Englert Research Group

Wilms Tumor (WT) is a kidney tumor in children, that is caused by the inactivation of certain genes. One of these genes encodes transcription factor WT1 – a molecular switch regulating the activation of other genes.

Objective: Identification of target genes of transcription factor WT1 by means of genetically modified mice

Selected cooperation and funding partners of cancer research at FLI