

*His work has significantly affected today's understanding of telome-res and their role in the emergence of cancer.* 

Prof. Matthias Doppelstein in his laudation during the ceremony for the award of the Deutscher Krebspreis to Prof. K. Lenhard Rudolph.

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Leibniz Institute on Aging – Fritz Lipmann Institute



# Cancer Research at FLI



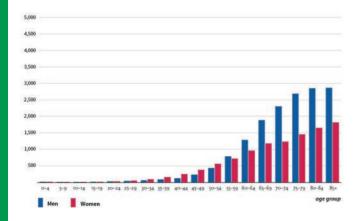
# Cancer is an Age-Associated Disease

Causes for the age-associated emergence of cancer are manifold and complex. And research is still far away from 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 accumulate 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.

# Cancer Research at Leibniz Institute on Aging (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

#### 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

#### 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

## **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

#### 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.

## 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

Growth

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

In various cooperation projects and funded by several foundations and assocations, cancer research has established as one of the key research foci at FLI.





