Groningen **R**esearch initiative on *h*ealthy **A**ging and **I**mmune **L**ongevity

the answer to a clear medical need

GRAIL

The proportion of elderly in our society steadily increases:

-increased life expectancy
-reduced birth rates
-baby boom generation
(reaches 65 from 2012)

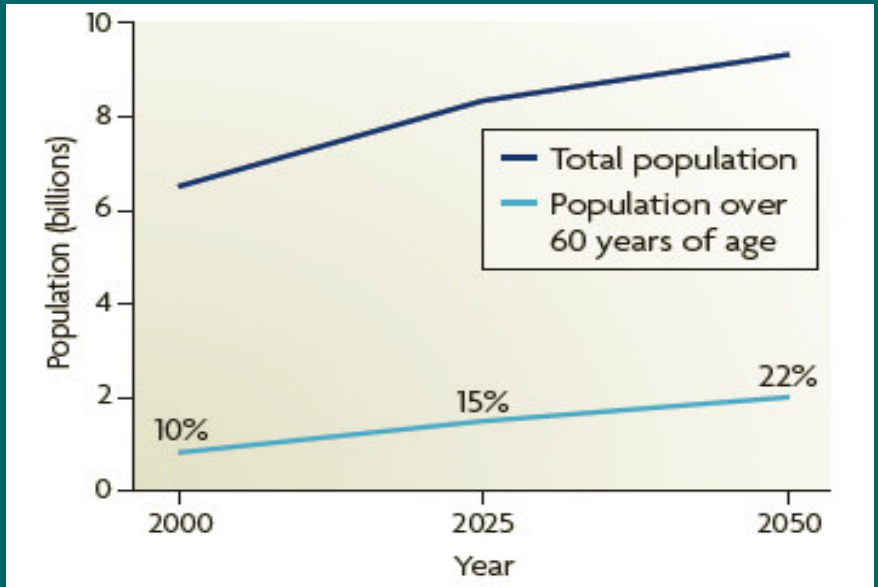

Figure 1 | **The proportion of individuals aged 60 years or older is projected to increase.**

Source: Dorshkind K et al., *Nature Rev Imm 2009*

- Age is a potent risk factor for chronic inflammatory, cardiovascular, neurodegenerative diseases and cancer.

- Vaccine response is compromised in elderly.

humans are evolutionary set to become 40 – 50 yrs

Due to improved conditions of living, we have extended our life expectancy to +/- 80 yrs.

↓

Our immune system has to remain active almost twice as long as it was evolutionary destined to be.

- results in phenotypic changes in the immune system:
  30% of people develop an immune risk phenotype (IRP)

- results in specific immune-related clinical conditions:
  e.g. CVD, Alzheimer, atherosclerosis, RA, diabetis, sarcopenia, cancer

the Immune Risk Phenotype is a collection of immune markers related to diminished immune function (immunosenescence)

- No immune risk phenotype (IRP)
  - Maintained CD4:CD8 ratio
  - Preserved lymphoproliferative response
- Antigen presentation conserved
  - Decreased number of APC
  - Increased functional capacity
- NK cytotoxicity well preserved
  - Increased number of NK cells
  - Decreased per-cell cytotoxicity

HEALTH AND SURVIVAL

- Immune risk phenotype (IRP)
  - Diminished CD4:CD8 ratio
  - High numbers of CD8+CD28null
  - Low lymphoproliferative response
  - Very restricted CD8 T cell repertoire
  - CMV seropositivity
- Antigen presentation decreased
  - Low expression of costimulatory molecules
  - Low production of IL12
- NK-mediated cytotoxicity diminished

MORBIDITY AND MORTALITY

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A concerted action to study the mechanisms underlying age-associated deterioration of immune function and ensuing chronic disease

Aims

- increase our understanding of the physiology of immunity in relation to aging
- increase our understanding of initiation and development of immune-aging related chronic diseases
- define and develop strategies for early detection, treatment and / or prevention of, immune-aging related, chronic diseases:
  - control inflamm-aging
  - control infection risk
  - restore immune competence
  - compress morbidity period in later life

contributors to GRAIL

- *departments involved:* Medical Biology, Rheumatology and Clinical Immunology, Geriatrics

- *people involved*

strategy group: Bart-Jan Kroesen, Mieke Boots, Liesbeth Brouwer

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Groningen Research initiative on healthy Aging and Immune Longevity

GRAIL platform and research focus

platform/edge

technical facilities

fundamental biology and clinical input

Lifelines/patient samples (blood and tissue)

GRAIL critical mass and collaborative spirit

research focus

immune regulation and aging

adaptive immune response

phenotype and function

periphery ⇔ site of pathology

research focus:

- interrelated projects
- common concepts, infrastructure and technology platform
- integration in UMCG *Healthy Aging* program

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