

Transnational research on the genetics of healthy ageing

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Introduction:

Approximately 25-30% of the variation in adult lifespan is attributable to genetic factors. As yet, however, only a few genetic variants have been found consistently to influence longevity. The first to be discovered was the $\epsilon 4$ allele of the apolipoprotein E (*APOE*) gene, and recently variation in the human forkhead box O3A gene (*FOXO3A*) has been shown to contribute to survival into old age in various populations. **The aim of this German-Danish co-operation is to identify molecular mechanisms that lead to a long life in good mental and physical health.**



Figure 2: Recruiting of long-lived individuals

Sample collection:

Both institutes have already collected a large number of biological samples of long-lived individuals (LLI) and younger controls (Figure 2). The Danish 1905 cohort study is a prospectively designed examination of the birth-cohort of the year 1905. The German case-control study sample consists of ~1600 LLI and 1100 younger controls. The combination of both collections results in one of the largest data- and biobanks of this kind worldwide (> 5000 LLI).

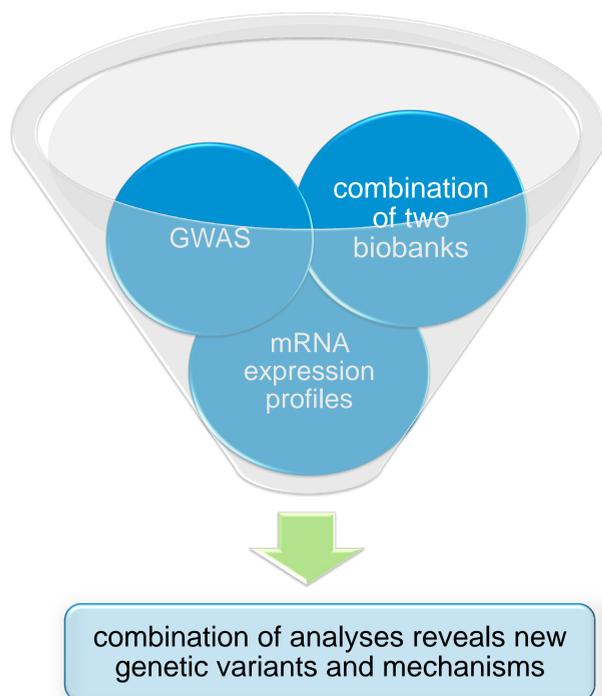


Figure 1: Study layout

Genetics and functional genomics:

The collaboration is based on two parts:

1) analysis of genome-wide SNP Chip data of Affymetrix 6.0 Chip (763 German LLI and 1085 younger controls) and Illumina Omni Express Chips analyzing ~600 Danish individuals (92-93 years) and younger controls, and 2) comparison of mRNA expression profiles using transcriptome sequencing (Figure 3). This data will be obtained from 100 monozygotic and dizygotic Danish twins (83-92 years, controls: 57-59 years, Figure 4) and ~50 German LLI (90+ years) and 50 controls (30-50 years).

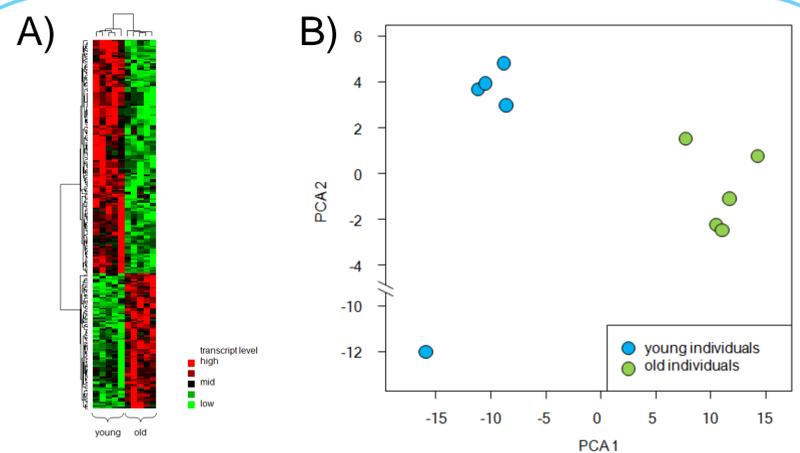


Figure 3: mRNA expression patterns

Initial results:

Initial results indicate that various transcripts are differentially regulated in older and younger individuals (Figure 3). These transcripts represent distinct mRNA expression patterns which are characteristic for each group. A subsequent pathway-analysis revealed that immune as well as developmental processes may be of relevance for molecular mechanisms of ageing.



Figure 4: Six sisters from Denmark; all of them are older than 90 years

The findings of this collaboration may provide new targets for the diagnosis, prevention and pharmacological therapy of age-related diseases.

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