

# INTEGRATED SYSTEM OF AGING BIOMARKERS



Science for Life Extension Foundation

longevity.foundation@gmail.com  
www.scienceagainstaging.com

Savitskaya E.<sup>1</sup>, Chistyakov.D.<sup>3</sup>, Shemyakina N.<sup>4</sup>, Kaleshnyk A.<sup>2</sup>, Konovalenko M.<sup>2</sup>, Batin M.<sup>2</sup>

<sup>1</sup> Institute of Gene Biology RAS ;

<sup>2</sup> Science for Life Extension Foundation;

<sup>3</sup> State Research Institute of Genetics and Selection of Industrial Microorganisms;

<sup>4</sup> Institute of Human Brain RAS.

**AGING** is a multicausal complex genetically determined biological process, that leads to gradual decrease in adaptive capacity of an organism, is accompanied by development of age-related pathologies and inevitably leads to death.

Traditionally evaluation of age-related changes is performed by physiological, functional and psychological tests, by visual examination and some biochemical analyses.

There is a big gap between the molecular data of aging and their implementation in practice mainly because aging data is scarce and it gets lost in the stream of bio-medical knowledge.

As we know only a few databases exist that concern the molecular aspects of aging and none of them describes age-related changes and phenotype context like cell type or tissues.

## THE GOALS OF THE PROJECT:

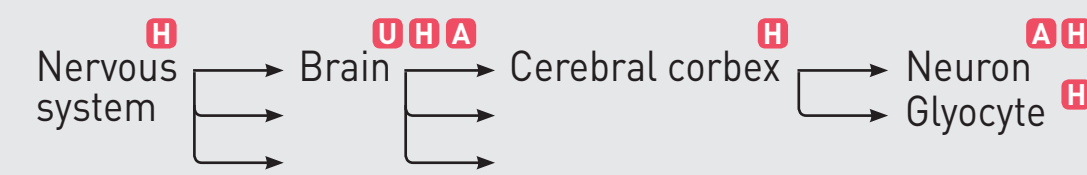
- 1 Systematization of data on age-related changes happening on the molecular level
- 2 Systematization of data on age-related changes happening on the cellular and tissue level
- 3 Identification of interrelations between molecular and cellular and tissue levels
- 4 Identification of associations between age-related changes and age-related processes and diseases

## 1 OBJECT SELECTION

**BIOMARKER OF AGING** is a parameter that changes qualitatively or quantitatively during aging or age-related disease

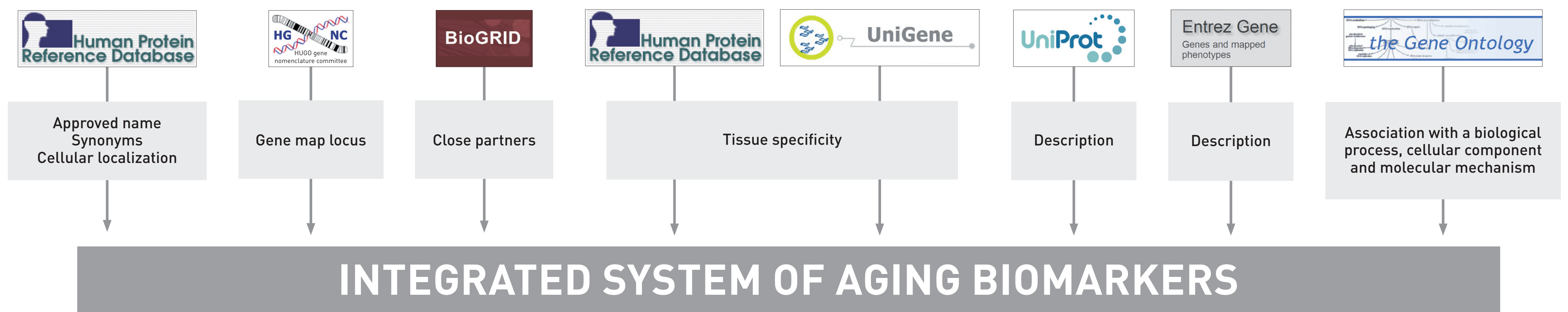
Groups of biomarkers	Selection criterion
<b>Molecular biomarkers:</b> Proteins/genes, miRNA, hormones, mediators, vitamins, metabolites, inorganic compounds, lipids	<ol style="list-style-type: none"> <li>1. Biomarker age-related changes</li> <li>2. Experiments on model organisms reported involvement of the biomarker in life span regulation or aging processes</li> <li>3. Polymorphism association with longevity or premature aging</li> </ol>
<b>Cellular biomarkers:</b> cells and extracellular matrix components	The common hierarchical lists from organs to cells

An example fragment of the hierarchical list



## 2 GENE/PROTEIN CHARACTERIZATION

DATA IMPORT FROM EXTERNAL DATABASES



### DATA FORMALIZATION ACCORDING TO:

- Model organism
- Type of experiment
- Type of intervention
- Type of changes (decrease, increase, posttranslational modification, alternative splicing, etc.)
- Cellular context (Phenotypic context)
- Related diseases, association with longevity
- Age-related biological processes

Age-associated changes in humans and model organisms

Description of polymorphisms related to aging pathologies or longevity

Experimental interventions on model objects associate with aging, longevity or age-related pathologies

Description of existing diagnostics methods

### IMPORT OF CLINICAL DATA FROM DIFFERENT SOURCES



PubMed SEMIAUTOMATIC DATA EXTRACTION FROM FOCUSED RESEARCH ARTICLES AND EXTRACTION OF HIGH THROUGHPUT ASSAY RESULTS

### EXAMPLE OF OBJECT CHARACTERIZATION

Name:  Tissue specificity:  Data type/intervention:

Age-related process:  Age-related alteration:  Model/organism:

Disease/lifespan effect:  Clinical diagnostics:

**Gene: APOE**

Name: APOE Type: gene/protein Reason for selection: longevity association  
 Synonyms: LDLCO5, LPG, MGC1571, AD2 Approved name: apolipoprotein E Gene map locus: 19q13.2  
 Close partner: A2M, LRP2, LRP8, MART, NEFM, PLTP Cellular localization: extracellular

**Clinical diagnostics**  
 Clinical diagnostics: yes method: ELISA/EIA sample: serum  
 External database linksout:  
[Entrez Gene](#) [UCSC Genome browser](#) [Ensemble](#) [HGNC](#) [GeneCards](#)  
[UniProtKB](#) [HPRD](#) [OMIM](#) [KEGG](#) [GenAtlas](#)  
[ORF accession](#) [RefNet](#) [HomoloGene](#) [Pathways Interaction database](#) [CTD](#)

**Short description**  
 GO process: [34 terms](#) GO function: [11 terms](#) GO component: [7 terms](#)  
 HPRD process: transport HPRD function: transport activity HPRD molecular class: transport/cargo protein

**Detailed description**  
**Entrez gene summary:** Chylomicron remnants and very low density lipoprotein (VLDL) remnants are rapidly removed from the circulation by receptor-mediated endocytosis in the liver. Apolipoprotein E, a main apoprotein of the chylomicron, binds to a specific receptor on liver cells and peripheral cells. ApoE is essential for the normal catabolism of triglyceride-rich lipoprotein constituents. The APOE gene is mapped to chromosome 19 in a cluster with APOC1 and APOC2. Defects in apolipoprotein E result in familial dysbetalipoproteinemia, or type III hyperlipoproteinemia (HLP III), in which increased plasma cholesterol and triglycerides are the consequence of impaired clearance of chylomicron and VLDL remnants. [provided by RefSeq]  
**UniProtKB/swissProt function:** Mediates the binding, internalization, and catabolism of lipoprotein particles. It can serve as a ligand for the LDL (apo B/E) receptor and for the specific apo-E receptor (chylomicron remnant) of hepatic tissues.

**Tissue specificity**

**Aging and longevity associated data**

<b>Age-related alterations:</b> <a href="#">increasing - corpus callosum - rat</a> <a href="#">decreasing - hypothalamus, cortex-mouse</a> <a href="#">increasing - hilus of hippocampus - rat</a> <a href="#">decreasing - plasma-human</a>	<b>Age-related processes:</b> <a href="#">Fibrosis</a> <a href="#">lipofuscin accumulation</a> <a href="#">pro-inflammatory cytokine accumulation</a> <a href="#">decreasing of antioxidant enzymes</a> <a href="#">cholesterol accumulation</a>	<b>Age-related diseases:</b> <a href="#">shortening lifespan</a> <a href="#">atherosclerosis</a> <a href="#">Parkinson disease</a> <a href="#">Alzheimer disease</a> <a href="#">Longevity</a> <a href="#">Stroke</a>
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**Citation**

## 3 DATABASE INFORMATION EXTRACTION

### LIST OF TYPICAL QUERIES TO THE KNOWLEDGE DATABASE:

1. What kind of alterations happen to a given object during aging? For what tissues have they been described?
2. What molecular biomarkers of aging are specific for a given tissue?
3. What is known about the object's association with aging processes, age-related diseases or longevity?
4. What kind of experimental data supports association of a given object with an age-related process, disease or longevity?
5. What biomarkers characterize a given disease or process?
6. What polymorphisms are associated with a given disease, process or longevity?
7. Are there any annotated polymorphisms associated with a given biomarker-coding gene?
8. What kind of response can be observed to a given type of intervention?

## FUTURE WORK, DIRECTIONS FOR DEVELOPMENT:

1. The database is meant to be an open source in web with possibility of external additions after expert edition. Free web access and the possibility of external additions after moderation by an expert
2. Broadening object characterization: addition of posttranslational modifications and protein substrates, visualization of signal transduction pathways and homologs, interactions with small molecules, genetic interactions, epigenetic alterations of biomarkers gene loci
3. Inclusion of other types of molecular biomarker (hormones, neuromediators, metabolites, etc.), as well as cellular/tissue level biomarkers
4. Entry of genetic and epigenetic alterations which are not associated with coding genes
5. Aging Biomarkers Network construction
6. Extension by the aging process modeling block

## THE DATABASE CAN BE USEFUL FOR:

1. New clinical aging biomarker development
2. Development of new evaluation methods of aging alterations
3. Personal predictions of longevity and disease susceptibility
4. Modeling of aging processes
5. Search for aging process intervention targets and possible therapeutic agents

Our project is at the initial stage of development. Any suggestions and collaborations are welcome!!!