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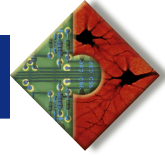
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Combinatorial Biomarkers for Aging Research

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Risk Factor Age

The biology of aging has been recognized as our biggest risk factor in developing a range of chronic and costly diseases like cancer, diabetes or Alzheimer's. An increasingly aging population demands investigation of mid-life decline and development of individualized treatment strategies. Key in this view is to identify biomarkers reflecting biological age.

Table 4. Age-related percentages (with standard errors) of cancer among persons 18 years of age and over, by selected characteristics - United States, 2004

Selected characteristic	Age	Male	Female	Total	Relative risk
18-24 years	1.2	1.2	1.2	1.2	1.0
25-34 years	2.2	2.2	2.2	2.2	1.8
35-44 years	4.2	4.2	4.2	4.2	3.5
45-54 years	8.2	8.2	8.2	8.2	6.8
55-64 years	15.2	15.2	15.2	15.2	12.5
65-74 years	28.2	28.2	28.2	28.2	23.5
75-84 years	48.2	48.2	48.2	48.2	40.0
85+ years	78.2	78.2	78.2	78.2	65.0

Source: CDC

Problems Finding Biomarkers

1. Chronological age as a primary classification parameter does not well reflect biological age
2. Heterogeneity in age groups
3. Classical bioinformatics approaches for expression analysis are "gene-centric", and can not dissect heterogeneity
4. Sensitivity of any analysis is limited .

Related Patent Applications

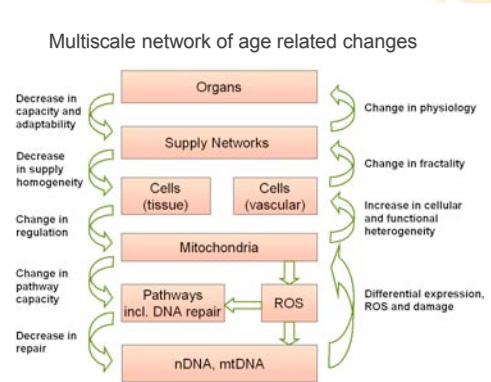
Use of genes differentially expressed during aging of liver for treatment and diagnosis. Kopchick JJ, Coschigano KT, Boyce K, Kriete A (US) CA2527957 - 2005-01-06 4

Diagnosis of Hyperinsulinemia and Type II Diabetes and protection against same. Boyce K, Kriete A, Kelder B, Kopchick JJ (US) CA2521757 - 2004-10-28 5

Diagnosis and treatment methods related to aging, especially in muscle. Kopchick JJ, Coschigano KT, Boyce K, Kriete A (US) CA2521757 - 2004-10-28

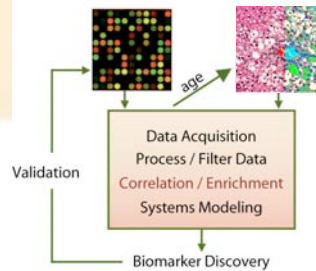
System and method of generating and storing correlated hyperquantified tissue structure and biomolecular expression datasets. Johnson P, Kriete A, Boyce K, Stone R, Lesniak R (US) US20040086873 - 2004-05-06 C.

An Approach Inspired by a Systems View of the Aging Process



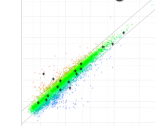
Transfers into Novel Analysis Method

Systemwide data acquisition

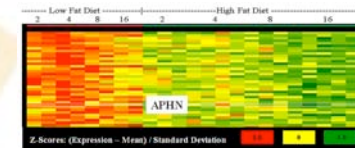


Results in

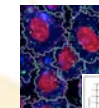
Correlated genes



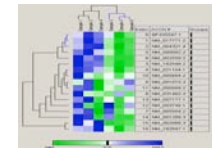
Applications



Diabetes and aging drug target identification: Tissue data (like APHN) indicate relevant gene expression profiles



Fibroblasts Cell Lines: Enriched detection of age related gene expression changes, involvement in impaired wound healing



Alzheimer's disease: Sample stratification by tissue phenotype and improvement of clustering

Summary

Inspired by a systems biology view, we have developed a novel method to define correlative biomarkers. We use a bioimaging based hyperquantification of cells and tissues to enrich the data mining process of related gene expression profiles. Dissection of data heterogeneity and consideration of individual responses is likely relevant to identify early onset markers of age related diseases.

References

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Boyce K, Kriete A, Nagatomi S, Kelder B, Coschigano K, Kopchick JJ. (2005) Phenotypical enrichment strategies for microarray data analysis applied in a type II diabetes study. OMICS. 2005 Fall;9(3):251-65.

Kriete A, Boyce K (2004) Automated tissue analysis - a bioinformatics perspective. Methods Inf Med. 2005;44(1):32-7.

Kriete A, Anderson M, Love B, Caffrey J, Young B, Sendera T, Magnuson S, Braughler M. (2003) Combined histomorphometric and gene expression profiling applied to toxicology. Genome Biology 2003; 4:R32

