Protein-Biomarker und Systembiologie

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Protein biomarkers and "systems biology"

- **Complexity of biological reaction to toxic intervention**
- **This biological complexity to a large extent takes place on the level of posttranslational modifications of proteins**
- **Time as a crucial biological dimension: necessity of kinetic control and synchronization, examples from ageing research**
- **Requirements for surrogate biomarkers and modeling: adequate data acquisition and storage solutions, interfaces**
- **Setting up models of high potential regions of metabolic/signalling networks for validating promising surrogate protein biomarkers**
- **Signatures of neuroprotection, cancer progression and embryotoxicity**

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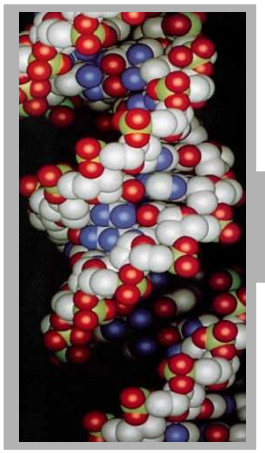
Complexity of proteomes – proteins are first targets of external stimuli: Numbers of molecules, time scales and dynamic range

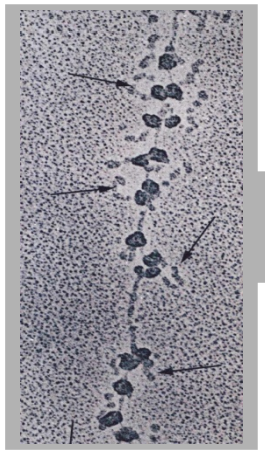
Minutes, hours, years → Seconds (?) minutes, hours, → µ-m-seconds (!) minutes, hours, years (!)

Genes (DNA)



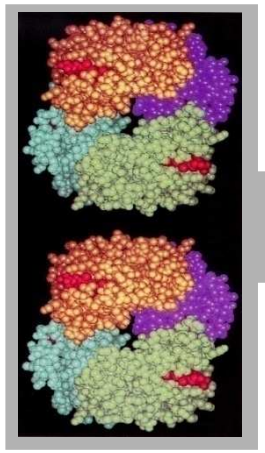
<23,000 in homo s.?

RNA



1 Mio. ?

Proteins



10 Mio. ?

- Dynamic protein modification patterns
- Small molecule and protein/protein interactions

?

Posttranslational modifications!

Schrattenholz & Soskic (2008) CMC 15, 1520
Schrattenholz et al., (2010) Meth.Mol. Biol, 662, 19

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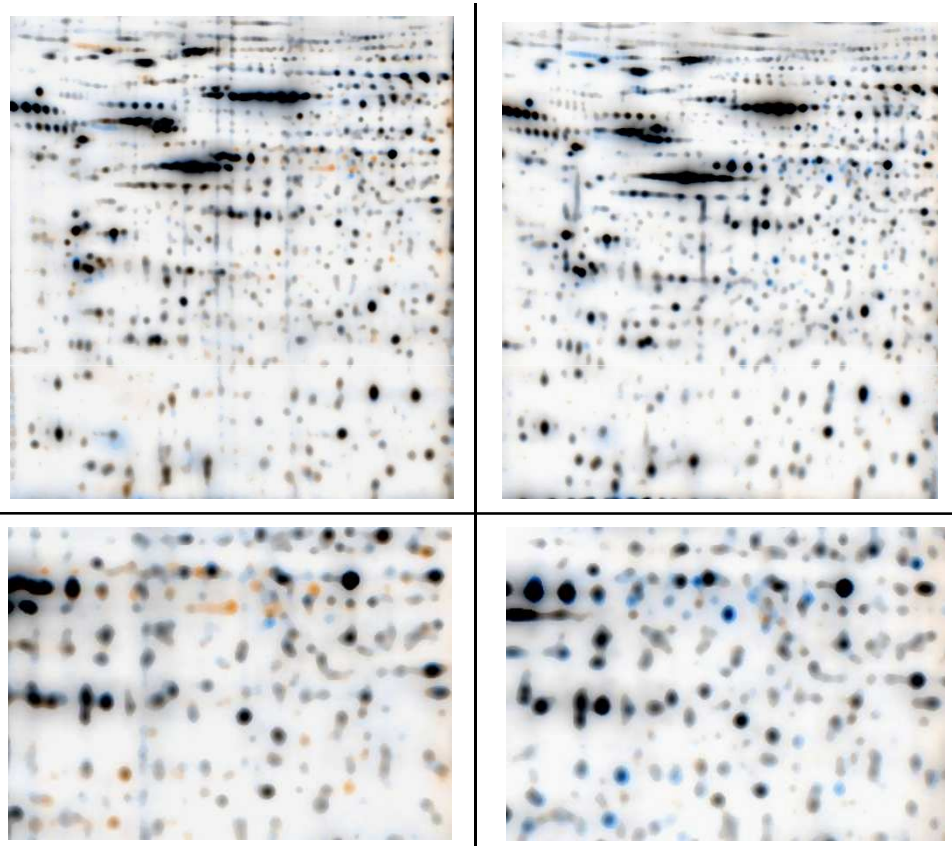
Differential protein pattern control – Reduction of complexity and precise quantitative information



Gel 1
^{131}I=Cancer vs ^{125}I=Control

Gel 2
^{131}I=Control vs ^{125}I=Cancer

Two samples are inversely labeled with different isotopes (or fluorescent dyes) and then investigated in two independently quantified series of experiments.

In false color images all orange/blue spots indicate different intensities in both samples and thus represent differential protein abundances between the samples.

THIS APPROACH ENABLES STATISTICAL TREATMENT OF NORMALIZED DATA OVER AN ADEQUATE DYNAMIC RANGE

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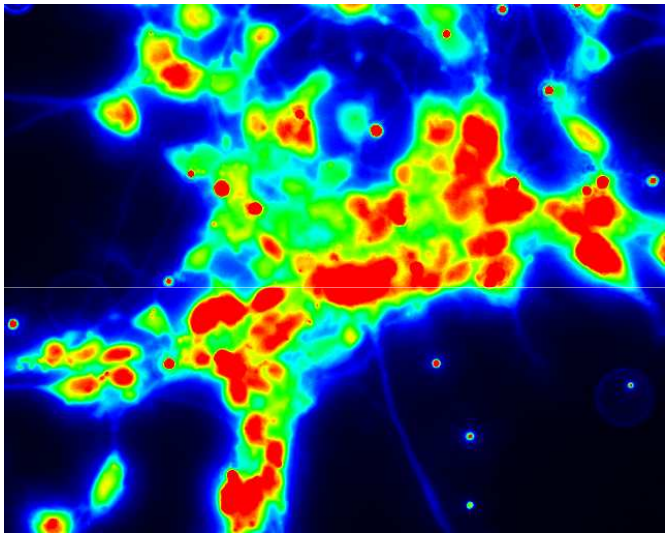
Recent peer-reviewed publications of ProteoSys: Toxicology, ageing and cancer research, neurobiology

Groebe et al (2010) Journal of Proteome Research, in press
Groebe et al. (2010) Reproductive Toxicology 30, 121
Groebe et al. (2010) Exp. Gerontology 45, 632
Šoškić et al.(2008) Journal of Proteome Research 7(6), 2262
Bunk et al. (2008) Journal of Immunology 180(8), 5490
Šoškić et al., (2008) Exp. Gerontology, 43(4), 247
Köllermann et al. (2008) Eur. Urol. 54, 1314
Schostak et al. (2008) J.Urol.181, 343
Reineke et al.(2007) Nature, 446, 415-419.
Groebe et al., (2007) Exp. Gerontology, 42, 887
Schrattenholz & Groebe (2007) Electrophoresis, 28(12), 1970
Wozny et al. (2007) Proteomics 7, 313

More at: www.proteosys.com

Dimension time:
Synchronization of protein patterns with functional cellular parameters –



www.reprotect.eu

www.mimage.org

www.neurocypres.eu

www.esnats.eu

FP7: Detective, Fight-MG

www.proteosys.com

Schrattenholz et al., (2010) Annals NY Acad. Sci. 1197, 118
Šoškić et al.(2008) Journal of Proteome Research 7(6), 2262
Schrattenholz and Klemm (2007) ALTEX, 24(1), 9-15
Schrattenholz and Klemm (2006) Drug testing in vitro (Marx U, Sandig V, eds.) Wiley-VCH, Weinheim, 205-228

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Summary

- **ProteoSys has discovered a novel biomarker for early detection of prostate cancer (Annexin A3); outlicensed and in development**
- **ProteoSys has concluded a drug reprofiling program; one substance out-licenced and in clinical phase II for Alzheimer‘s disease**
- **ProteoSys has discovered a novel therapeutic principle for the treatment of Parkinson’s disease; outlicensed and in preclinical development**
- **Portfolio in devleopmental toxicology**