Mater Health Services Brisbane

# Briefing notes to Parliamentary Committee Hearing on research into Mitochondrial proteins in DeSeal/ReSeal personnel

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# Mitochondria in a cell

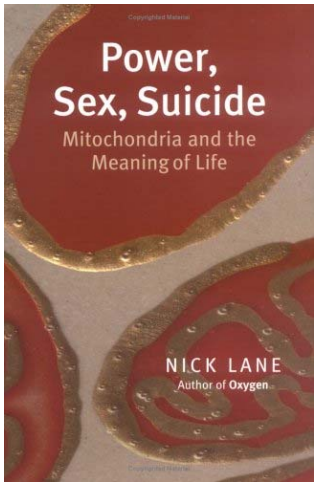
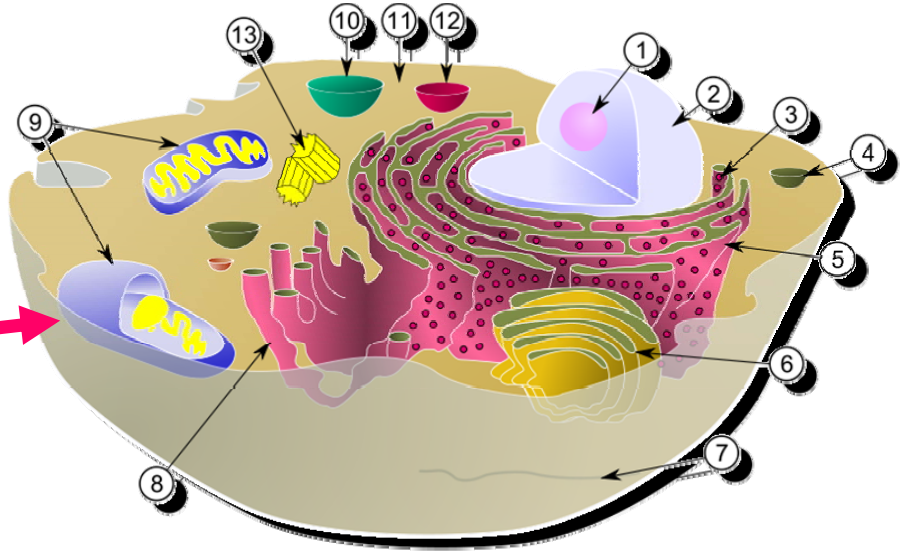
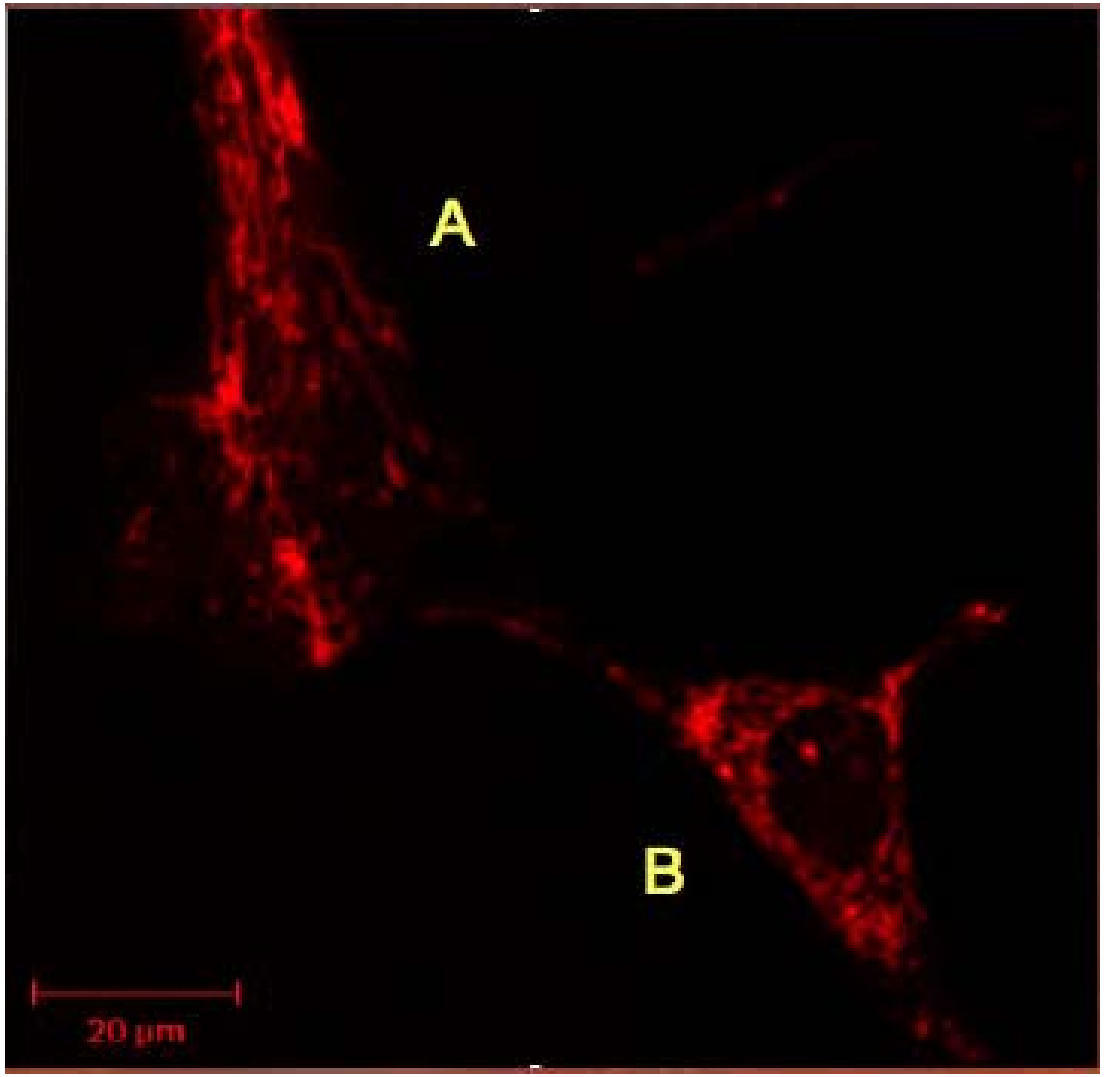



**Diagram of a typical animal cell. Organelles are labelled as follows:**

1. Nucleolus
2. Nucleus
3. Ribosome
4. Vesicle
5. Rough endoplasmic reticulum
6. Golgi apparatus (or "Golgi body")
7. Cytoskeleton
8. Smooth endoplasmic reticulum
9. Mitochondrion
10. Vacuole
11. Cytosol
12. Lysosome
13. Centriole



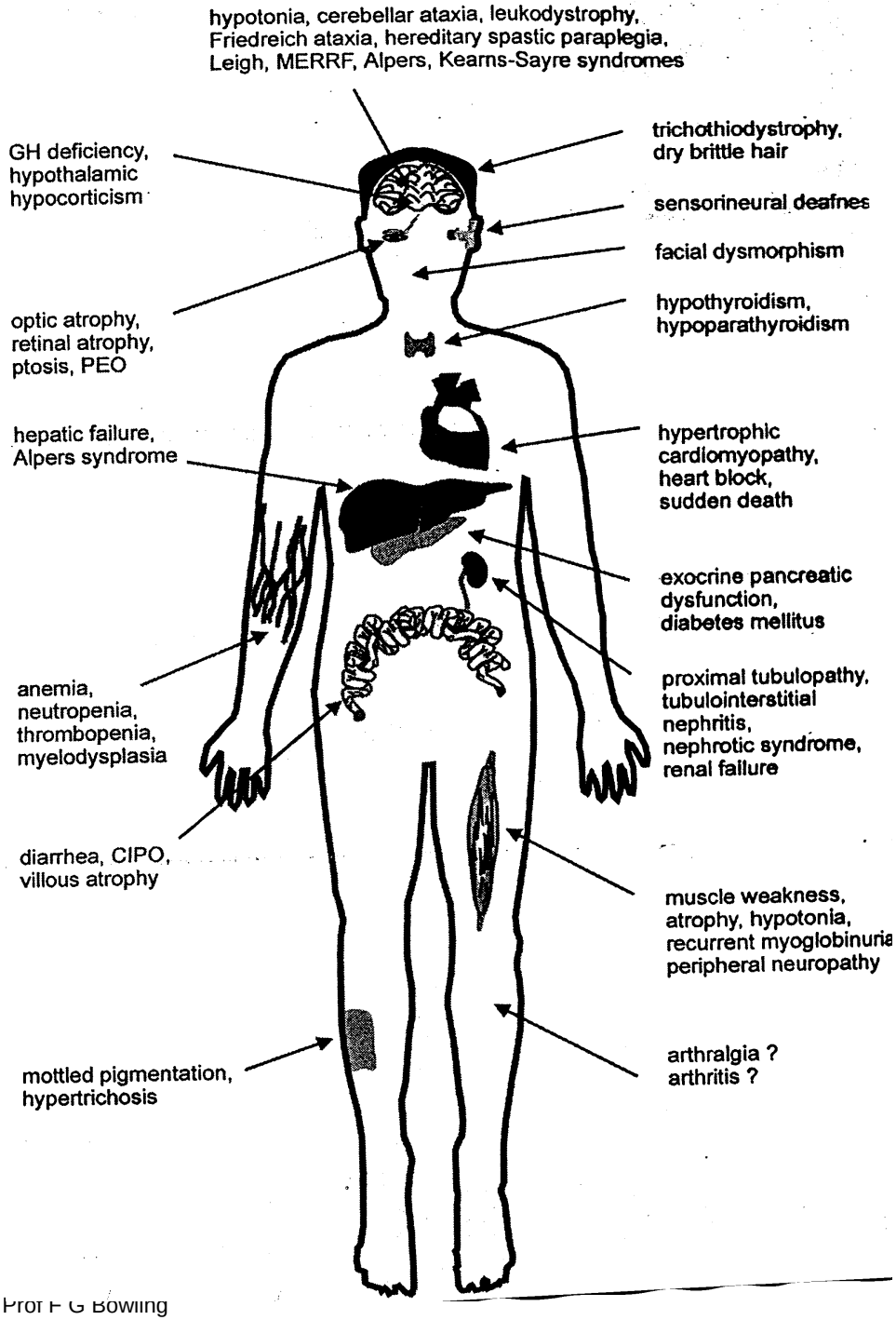
# Mitochondria from stem cells




Intact mitochondria migrate in membrane tubular network connections formed between human stem cells.
Attila Csordas[1], Attila Cselenyák[1], Ferenc Uher[2], Marianna Murányi[1], Simone Hennerbichler[3], Heinz Redl[3], Márk Kollai[4], & Zsombor Lacza[4]

# Symptoms seen in exposed personnel

- Myopathy
- Fatigue
- Parkinsonism
- Dementia
- Psychoses
- Night blindness
- Peripheral neuropathy
- Skin pigmentation

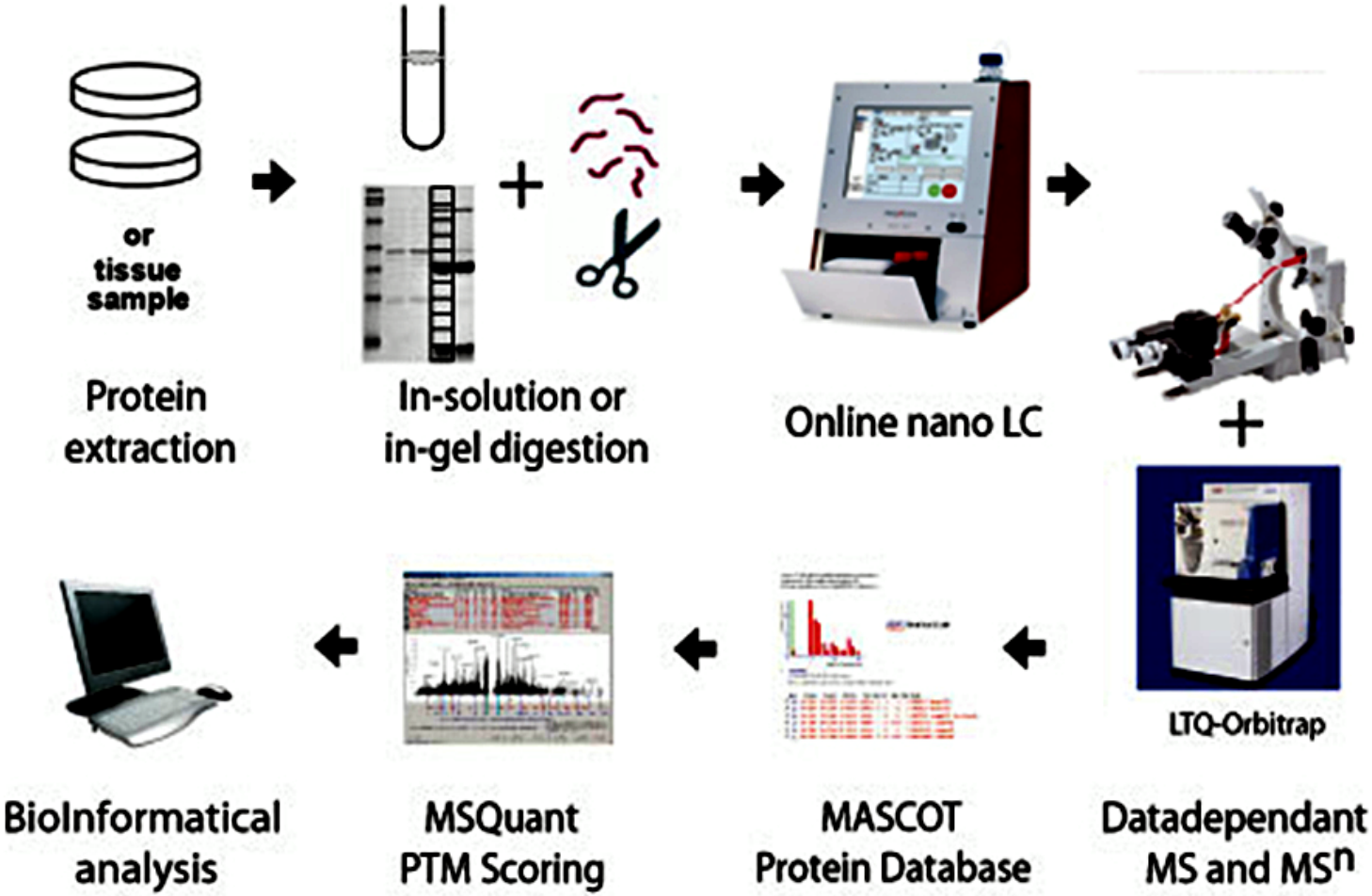


# Substances toxic to Mitochondria

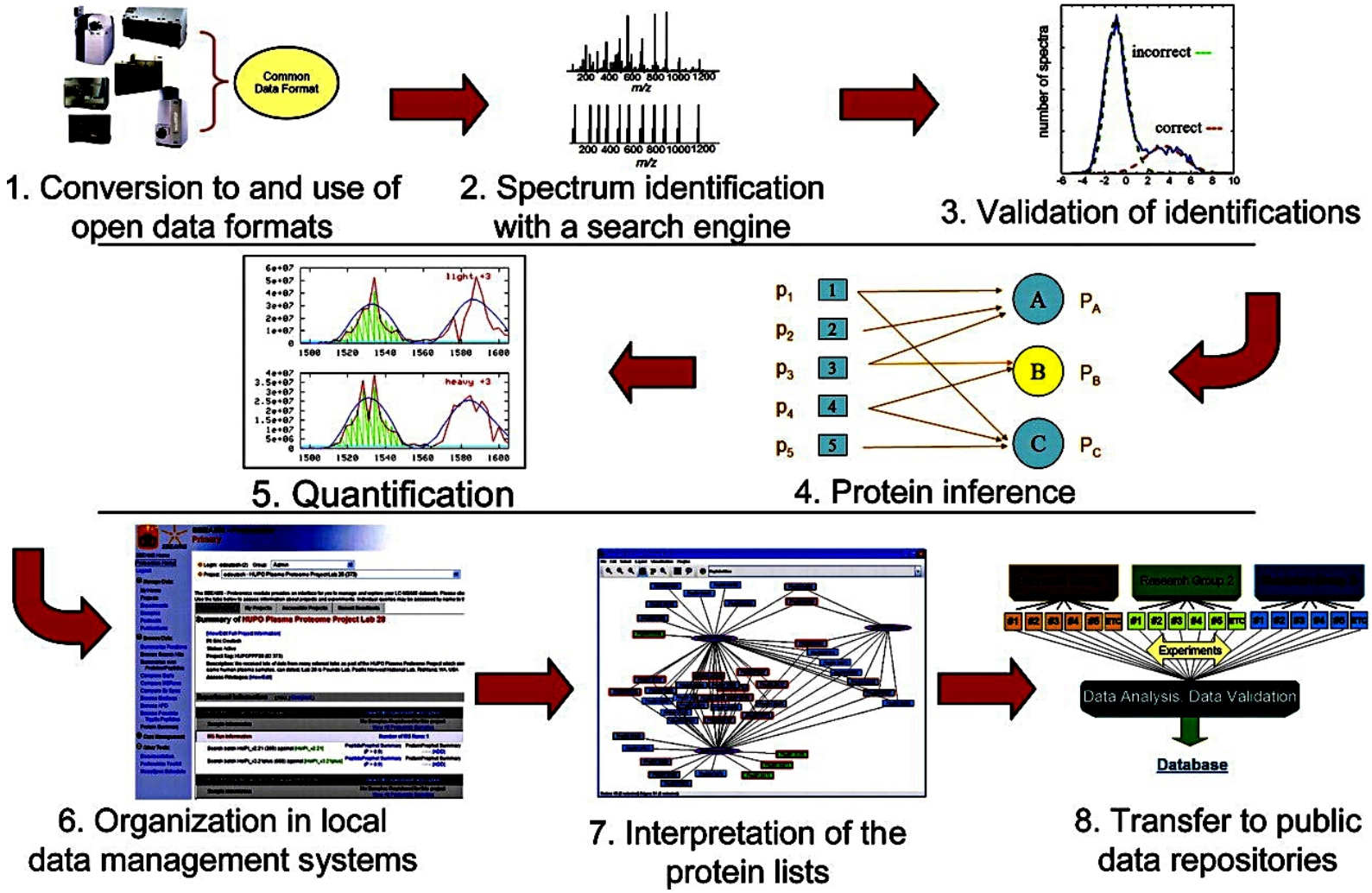
- Approximately sixty (60) hazardous substances involved in all aspects of the Deseal/Reseal Programs. Of these, the major risk chemicals are considered to be:
  - a. Methyl ethyl ketone (also methyl isobutyl ketone);
  - b. Aromatic hydrocarbons:
  - c. Toluene, and
  - d. Xylenes;
  - e. Naphtha;
  - f. n-butyl acetate;
  - g. Ethyl acetate;
  - h. Isopropanol;
  - i. Glycol ethers;
  - j. Thiophenol;
  - k. Isocyanates (HMDI Monomer); and
  - l. Chromium VI compounds, particularly strontium chromate
  - m. Jet Fuel Anti-fungal compound.

- Fuel
- De-Seal/Re-Seal solvent

# Protein Mass Spectrometry



# Schematic overview of the typical workflow of the proteomics informatics processing of a data set

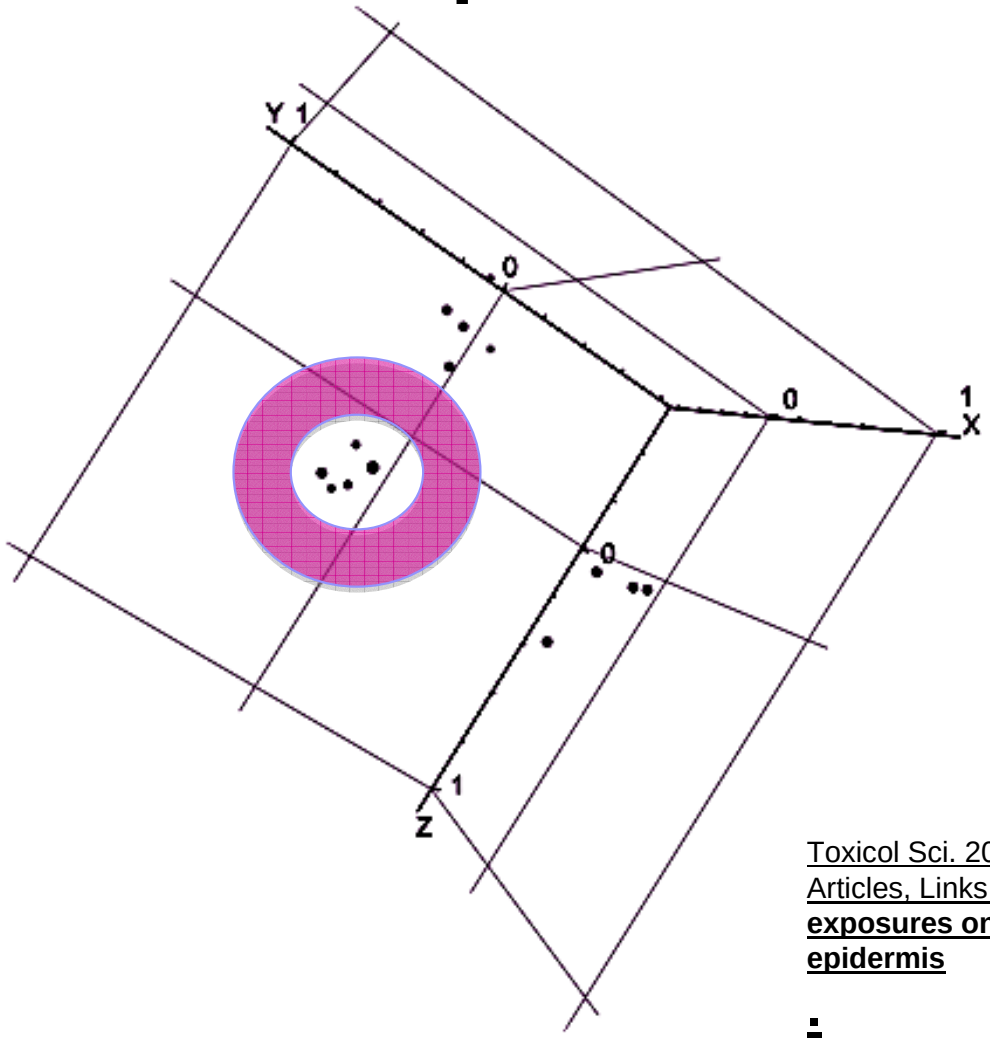



**Deutsch, E. W. et al. Physiol. Genomics 33: 18-25 2008; doi:10.1152/physiolgenomics.00298.2007**



Physiological Genomics

# Principal component analysis to select proteins affected




Toxicol Sci. 2007 Feb;95(2):495-510. Epub 2006 Nov 3.Related Articles, Links **Effects of brief cutaneous JP-8 jet fuel exposures on time course of gene expression in the epidermis**

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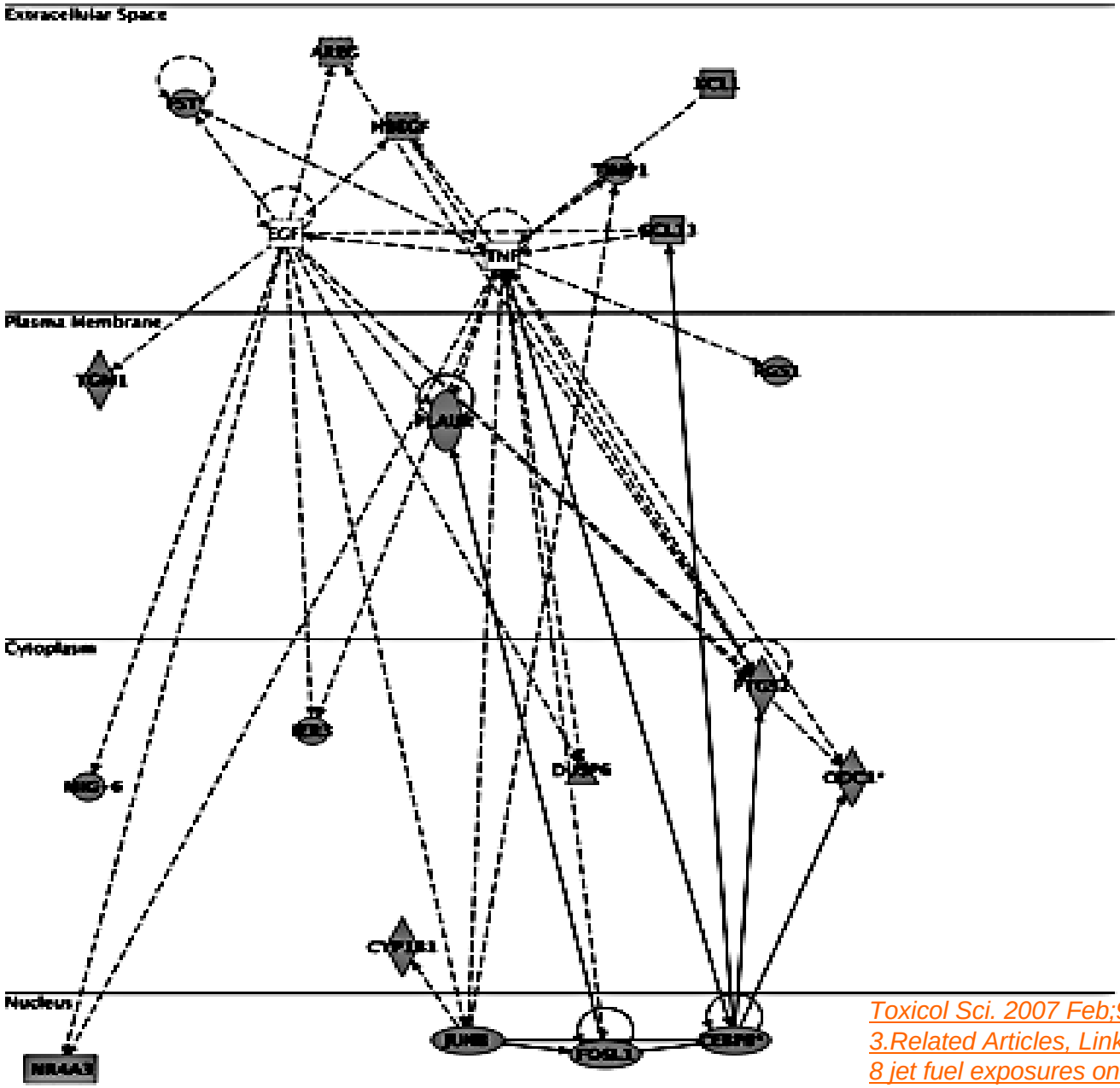
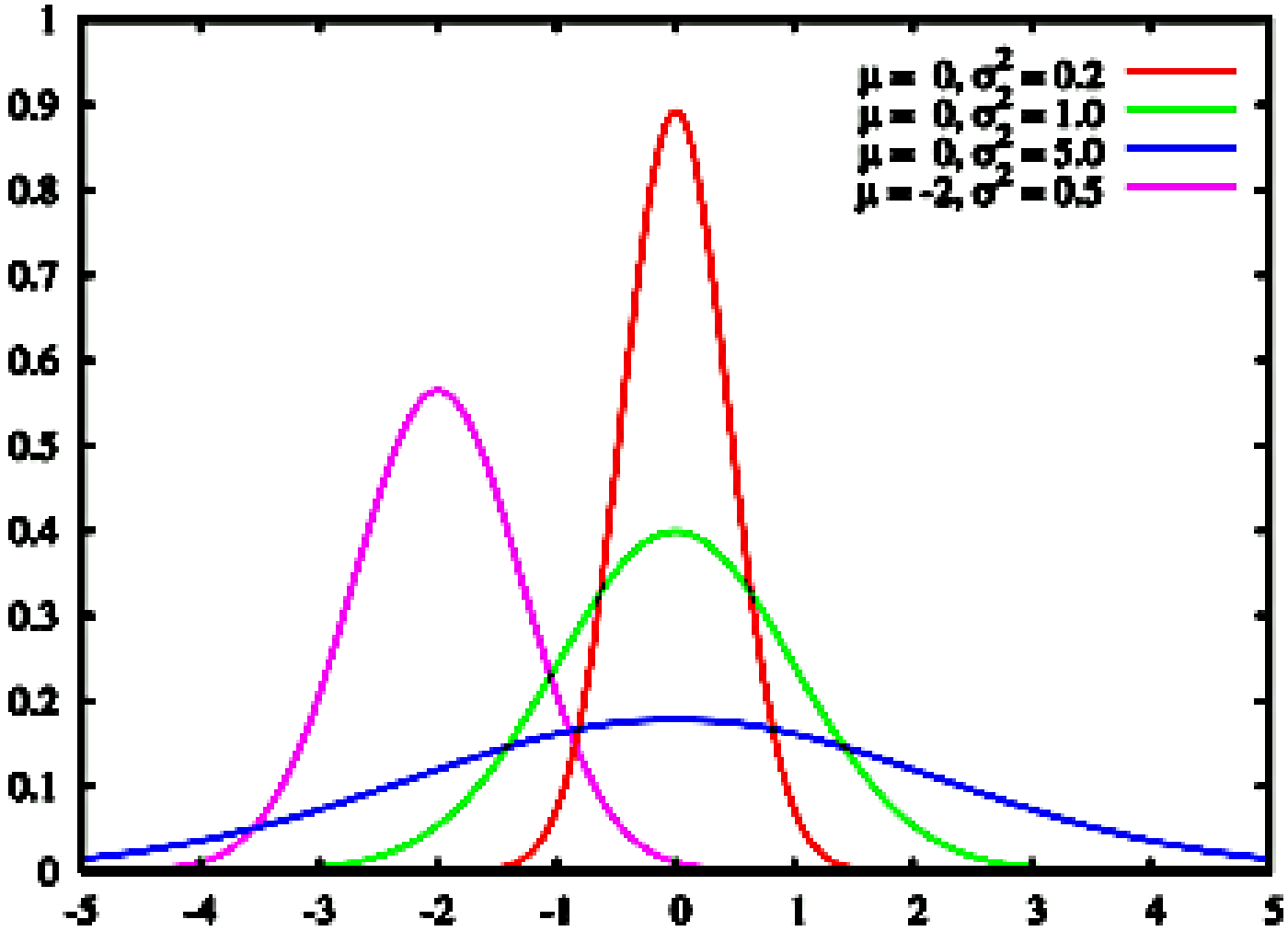
# Pathway analysis of identified proteins




*Toxicol Sci. 2007 Feb;95(2):495-510. Epub 2006 Nov 3.Related Articles, Links Effects of brief cutaneous JP-8 jet fuel exposures on time course of gene expression in the epidermis*

# Basis of a screening test



# Executive Summary

- The results of these studies implicate changes in mitochondrial proteins in peripheral blood samples in individuals exposed to fuel solvents.
- The finding of changes persisting in peripheral blood several years after the exposure suggests that the cells responsible for generation of peripheral blood cells (stem cells) in the bone marrow have been affected.
- The cohort of individuals involved in fuel exposure are likely to vary considerably in their response to the cellular injury. The variation would be due to :-
  - differences in exposure,
  - individual genetically determined susceptibilities,
  - individual genetically determined repair abilities, and
  - other lifestyle factors.
- the protein profile could be used as a test for injury following exposure
- A mechanism to discriminate (injured from non-injured) would be improved by the combination of indices including:-
  - History of Exposure
  - Presence of medical (including psychiatric) symptoms not **fully** explained by other disease causing aetiologies.
  - Abnormal protein profile.