

# Workshop

## Human health: medicine and nanobiotechnology

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**President, Swiss Academy of Medicine and Ethics**

**Safety and Risks of Nanotechnology, Lucerne, April 20-21, 2004**



# Contributors

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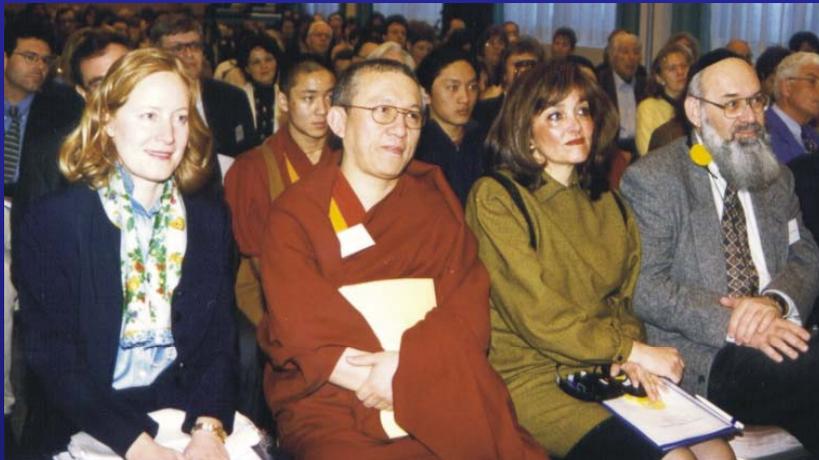
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# Swiss Academy of Medicine and Ethics

[www.medizin-ethik.ch](http://www.medizin-ethik.ch)

- Symposia Medicine and Ethics in Davos  
1998, 1999, 2000, 2003



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# Definition of health

**Resolution WHO Executive Board 1998:  
Health is a dynamic state of complete  
physical, mental, spiritual and social well-  
being and not merely the absence of  
disease and infirmity.**



# Globalisation of medical ethics

- **Buddha as „great doctor“**
- **Moral duty to protect individual health in  
japanese Rhi-Shu code und in Hippocratic  
oath**
- **Christus Medicus**
- **Guidelines of the World Medical Association:  
Declaration of Geneva (1948)  
Declaration of Helsinki (1975)**



# Gro Harlem Brundtland

## Health

The Key to Human Development  
Campus, Frankfurt/New York (2000)

„Environment, personal wellbeing and wealth  
are intimately connected.“

„*Health for All* emphasises a comprehensive  
approach to health.“

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# Franz Kafka

„To prescribe pills is easy, but to reach an understanding in people is very hard.“



# Olivia Newton-John

**...If we only have love**

**We can reach those in pain**

**We can heal all our wounds**

**We can use our own name**

**If we only have love we can melt all the guns**

**And than give them new words**

**To our daughters and our sons...**

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# The Dalai Lama

Having a good heart is more important  
than religion.

# Indira Gandhi

Poverty is the greatest polluter.

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# Aims of the workshop

- **Assess research results concerning toxicology and pathology of nanoparticles, nanotubes and fullerenes**
- **Clarify contradictory published results and develop methods for standardization**



# Key questions to answer

- **Impact of nanoparticles on human health?**
- **Absorbption by the human body – are there any barriers?**
- **Distribution within the organism? Are there organs for preferential accumulation?**
- **Effects on cell structure, function and interaction?**
- **Immunological responses, elimination?**



# Key questions to answer

- **Expected advantages and hopes from nanobiotechnology?**
- **Possible risks? Is it toxicology or is it fear, anxiety or phobic reactions due to negative propaganda?**
- **What are the best methods to answer these questions?**



# Summing up day 1

- **Definition by Eric Drexler, Foresight Institute (1995):**  
**Nanotechnology is a manufacturing technology able to inexpensively fabricate structures consistent with natural law, and to do so with molecular precision.**



# Definition - Statements

- Learning from life
- Molecular model of a hypothetical planetary gear
- Enabling technology
- Ultimate precision to fabricate materials, devices and structures
- Impacts all technology sectors, crosses all disciplines



# Definition - statements

- **Material properties: Mechanical, electrical, optical, thermodynamical features, specific size-dependent properties, abilities for self assembly and recognition**
- **„Nanotechnology has given us the tools to play with the ultimate toy box of nature – atoms and molecules...everything is made from it...The possibility to create new things appears limitless“ (Horst Stormer)**



# Ethical issues

- **Are we interfering with nature on a scale that it can get out of control?**
- **Ability to measure the state of the body by monitoring on a nano-scale**
- **Combination of ubiquitous sensing and ubiquitous information**
- **Intrusion of privacy**
- **Labelling, DNA make up, stratification of society, insurance issues**



# Medical issues – state of the art

- **Nanobiotechnology will have a great impact in medicine within the next 20 years, especially in tumor therapy and anti-virus-strategies**
- **Important are nanoparticles and nano-based technologies, e.g. chip technology, nanorobots**
  - **Fields of interest:**
- **Food industry, wellness (e.g. sunscreen with ZnO, TiO<sub>2</sub>)**
- **Diagnosis (e.g. biomarkers, DNA chips, MRI)**
- **Therapy (e.g. drug delivery systems, virus infections, tumor therapy)**



# Advances in medicine

- **Breakthrough in tumor therapy using super paramagnetic properties: nanoparticles with Fe core < 3 nm are injected into tumor tissue, absorbed 10 mio particles/cell, warmed up with 100,000 Hz to 45 degrees C, phagocytosis (Jordan, Charité Berlin, [www.cc-nanochem.de](http://www.cc-nanochem.de))**

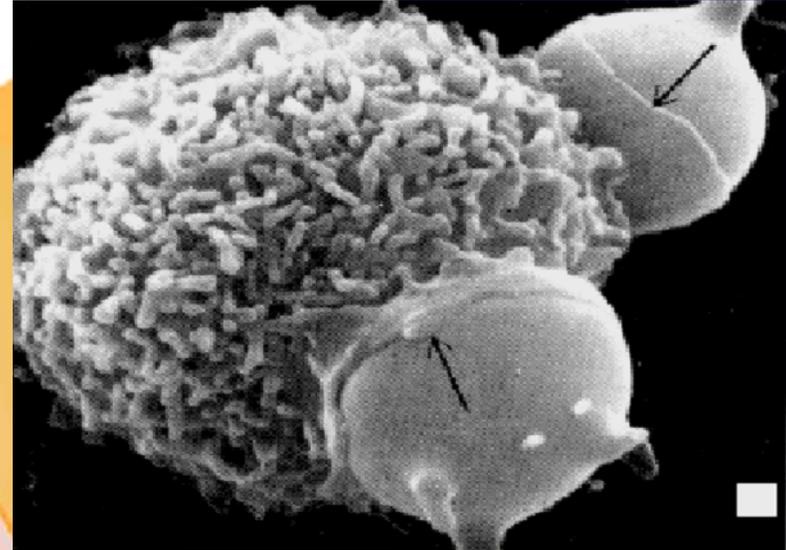
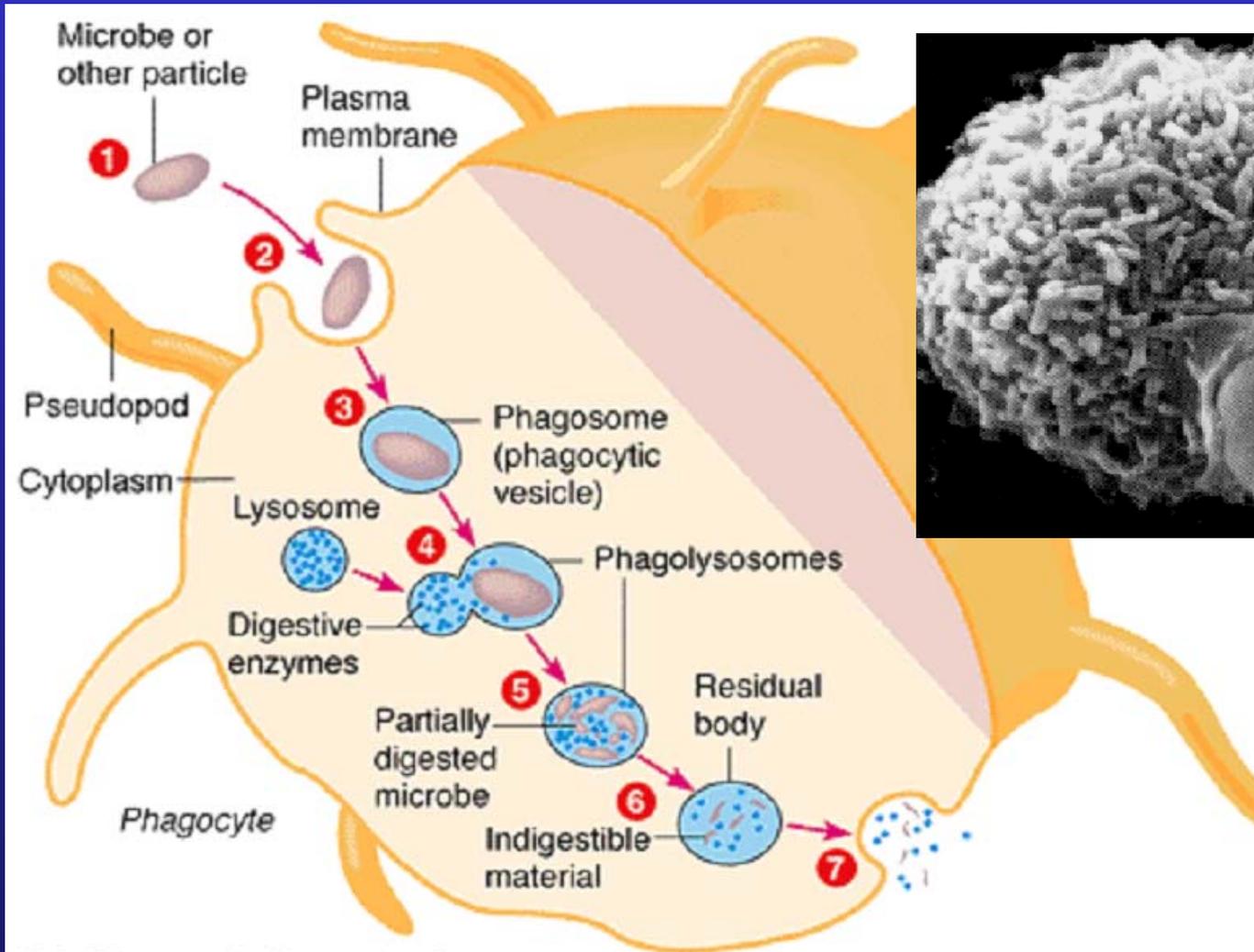


# Possible adverse effects

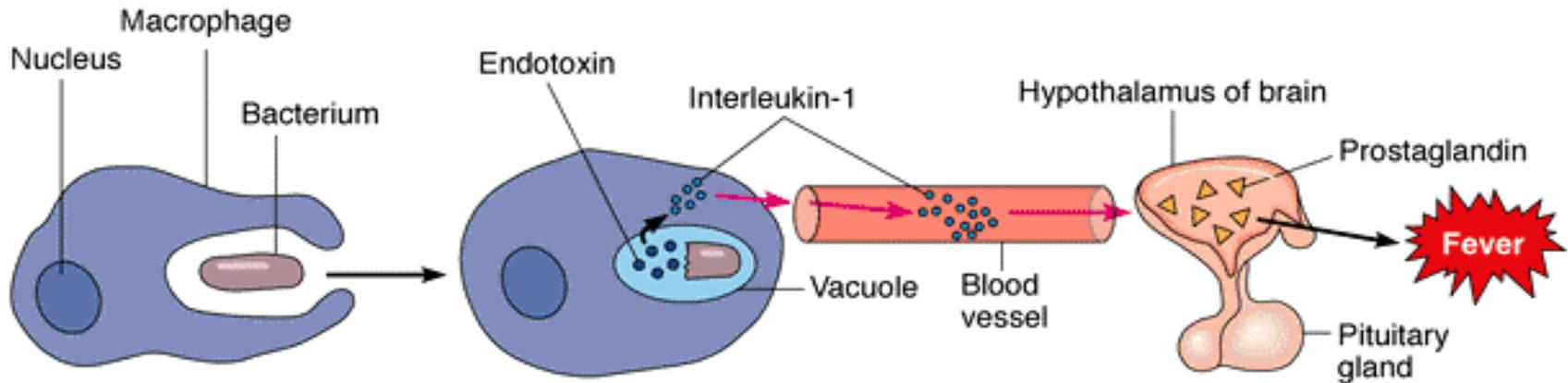
- Nanoparticles migrate through all physiological barriers: skin, mucosa, alveoli-capillaries, blood-brain, olfactory nerve-brain
- Phagocytosis takes place, but cannot stop nanoparticles from passing e.g. alveolar walls
- New antigens, possibly new allergens
- Very limited knowledge so far of toxicity



# Phagocytosis



# Inflammation and fever



**1** A macrophage ingests a gram-negative bacterium

**2** The bacterium is degraded in a vacuole, releasing endotoxins that induce the macrophage to produce interleukin-1 (IL-1)

**3** IL-1 is released by the macrophage into the bloodstream, through which it travels to the hypothalamus of the brain

**4** IL-1 induces the hypothalamus to produce prostaglandins, which reset the body's "thermostat" to a higher temperature, producing fever

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# We are able to detect everything

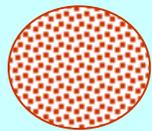


- **Immunosystem detects foreign and auto-antigens**
- **...all proteins and many sugars**
- **about  $3 \times 10^{12}$  structures**
- **Structures outside of our earth?**
- **New nanoparticles!**

# Detectable structures

## Relative seize

- **Antibody 0.01  $\mu\text{m}$** 
  - **Toxin 0.01  $\mu\text{m}$**



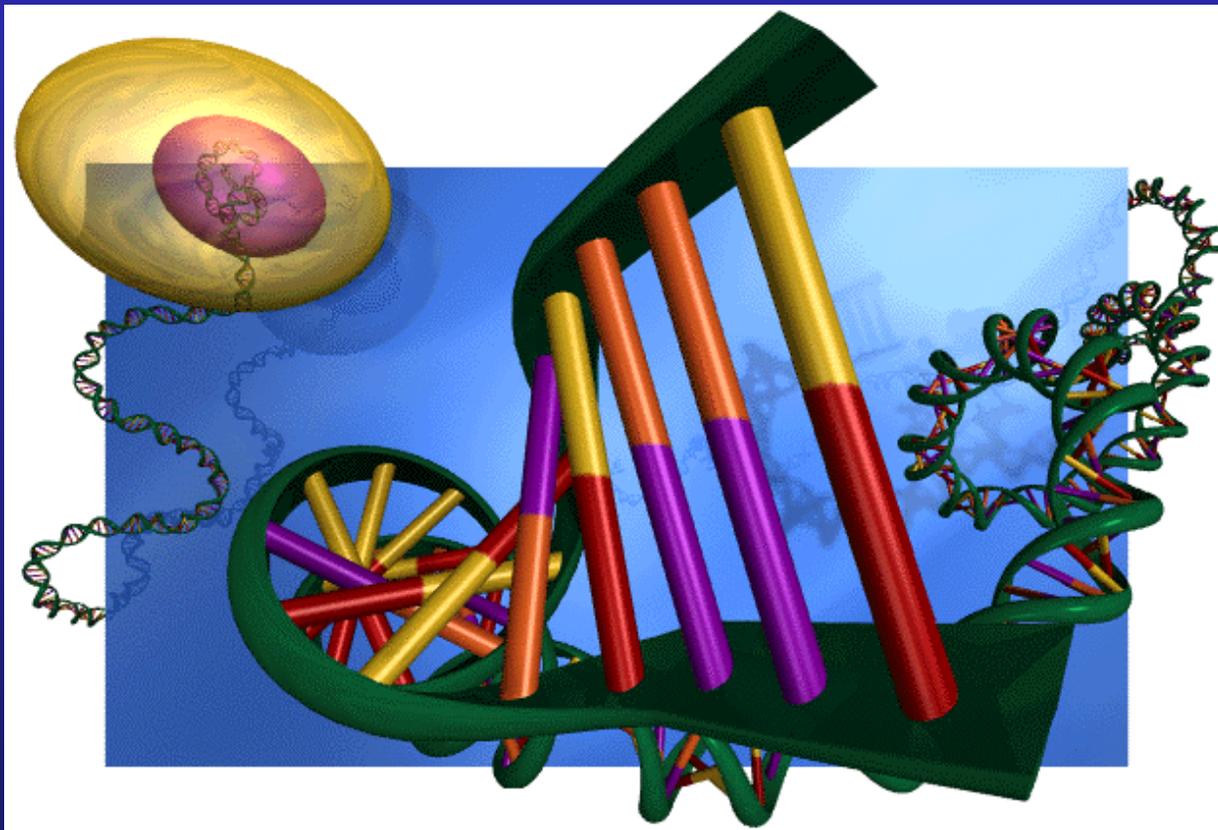
**Virus 0.1  $\mu\text{m}$**

**Bacterium 1  $\mu\text{m}$**

**Cell 10  $\mu\text{m}$**

# Repertoire

Genome	Proteome	Repertoire
$3 \times 10^4$	$5 \times 10^5$	$3 \times 10^{12}$



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# Conclusion

- **Nano-pathologies have to be detected by new diagnostic tools like ESEM, a new electron microscopic technique. Examples are Fe, Ba, Al, Mg, Ti, Ag debris in colon cancer, Ba in thrombus, U, Sb in mesoendothelioma, Silicate particles in granulomatous liver.**



# Conclusion

- **In vitro studies in cell cultures have to determine the effects of nanoparticles on cell structure, function and interaction.**
- **Evidence has to be proven in animal models by different application e.g. skin contact, inhalation, ingestion, injection.**



# International Risk Governance

**Council, [www.irgc.org](http://www.irgc.org)**

**Prof. Dr. Wolfgang Kröger, Founding Rector**

- **Foundation according to Swiss law**
- **Based in Geneva**
- **Independent organization including industry, governments, scientists**
- **Risk analysis – risk assessment**
- **Learning from the past – e.g. asbestosis, very costly: expected 70 billion US\$**



# Risk assessment: priorities

- Research on the physical and chemical properties of nanoparticles and it's biochemical reactions in humans: short-term and long-term toxicity
- Adverse effects from large scale production, exposure and application



# Conclusion

- **Knowledge from case reports and case-control-studies should lead to hypotheses, which have to be proven or rejected in prospective, controlled, clinical studies, following GCP guidelines.**
- **New knowledge about nanobiotechnology should be brought to the public by the scientific community together with the media. Ethical consensus is needed.**

