

Workshop

Human health: medicine and nanobiotechnology

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



Contributors

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Swiss Academy of Medicine and Ethics

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, TiO₂)**
- **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)**

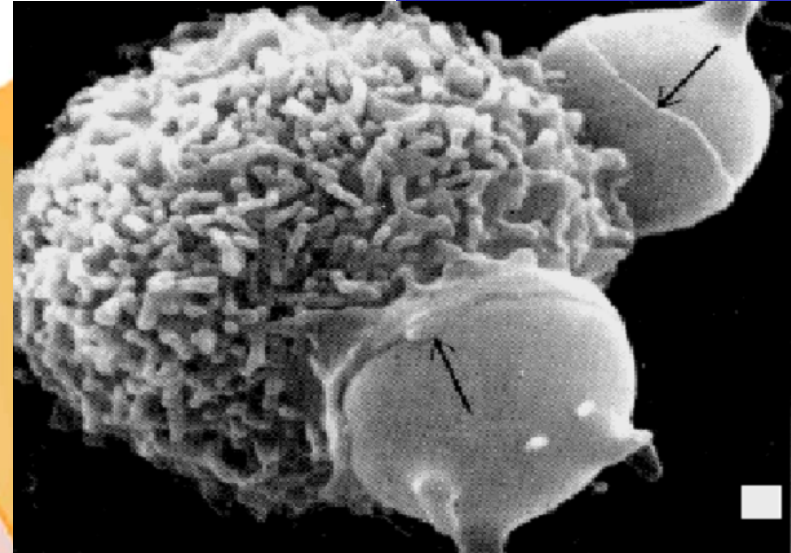
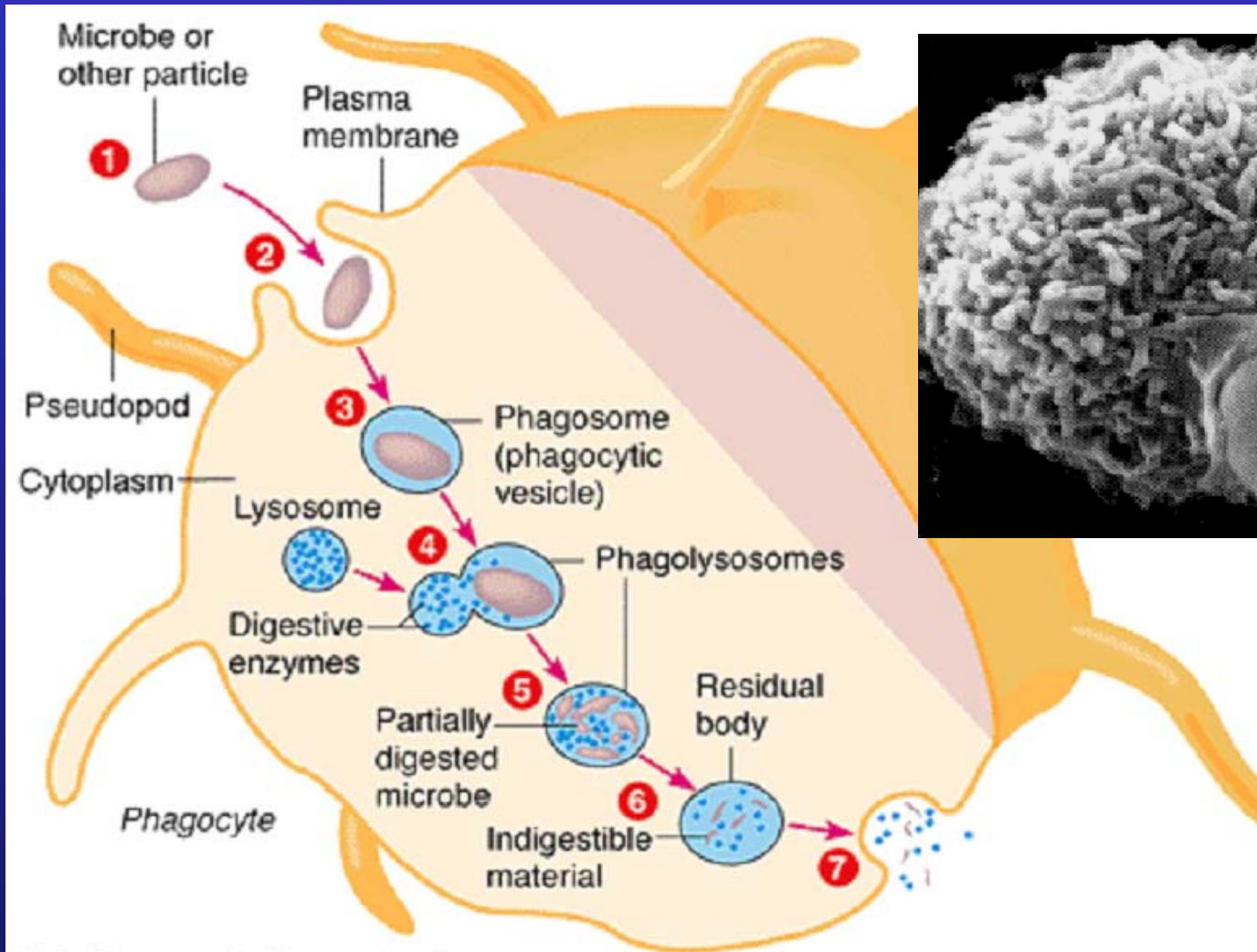


Possible adverse effects

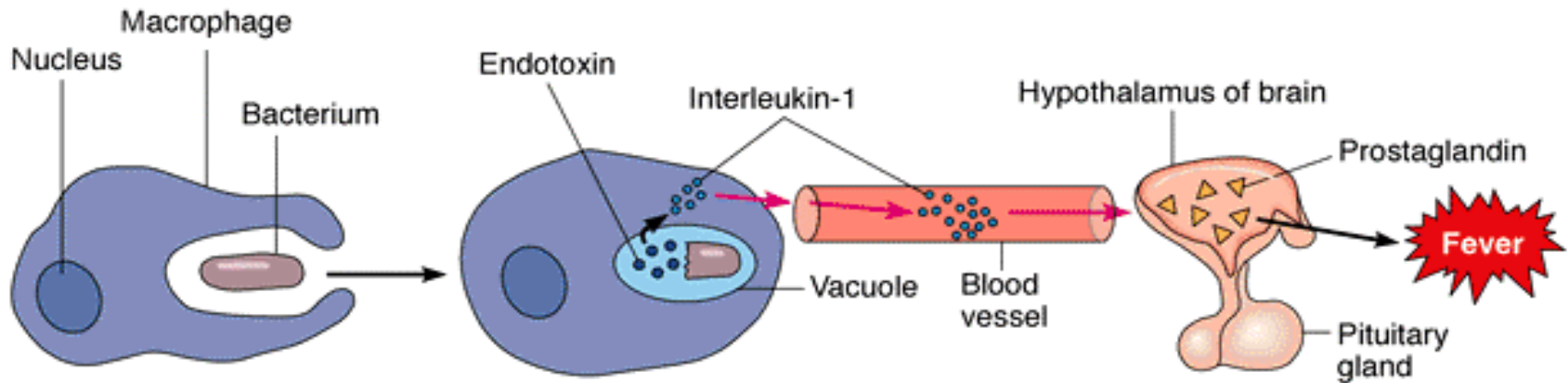
- Nanoparticles migrate through all physiological barriers: skin, mucosa, alveoli-capillaries, blood-brain, olfactory nerve-brain
- Phagocytosis takes place, but cannot stop nanoparticles from passing e.g. alveolar walls
- New antigens, possibly new allergens
- Very limited knowledge so far of toxicity



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

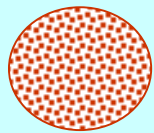


- **Immunosystem detects foreign and auto-antigens**
- **...all proteins and many sugars**
- **about 3×10^{12} structures**
- **Structures outside of our earth?**
- **New nanoparticles!**

Detectable structures

Relative seize

- **Antibody 0.01 μm**
 - **Toxin 0.01 μm**



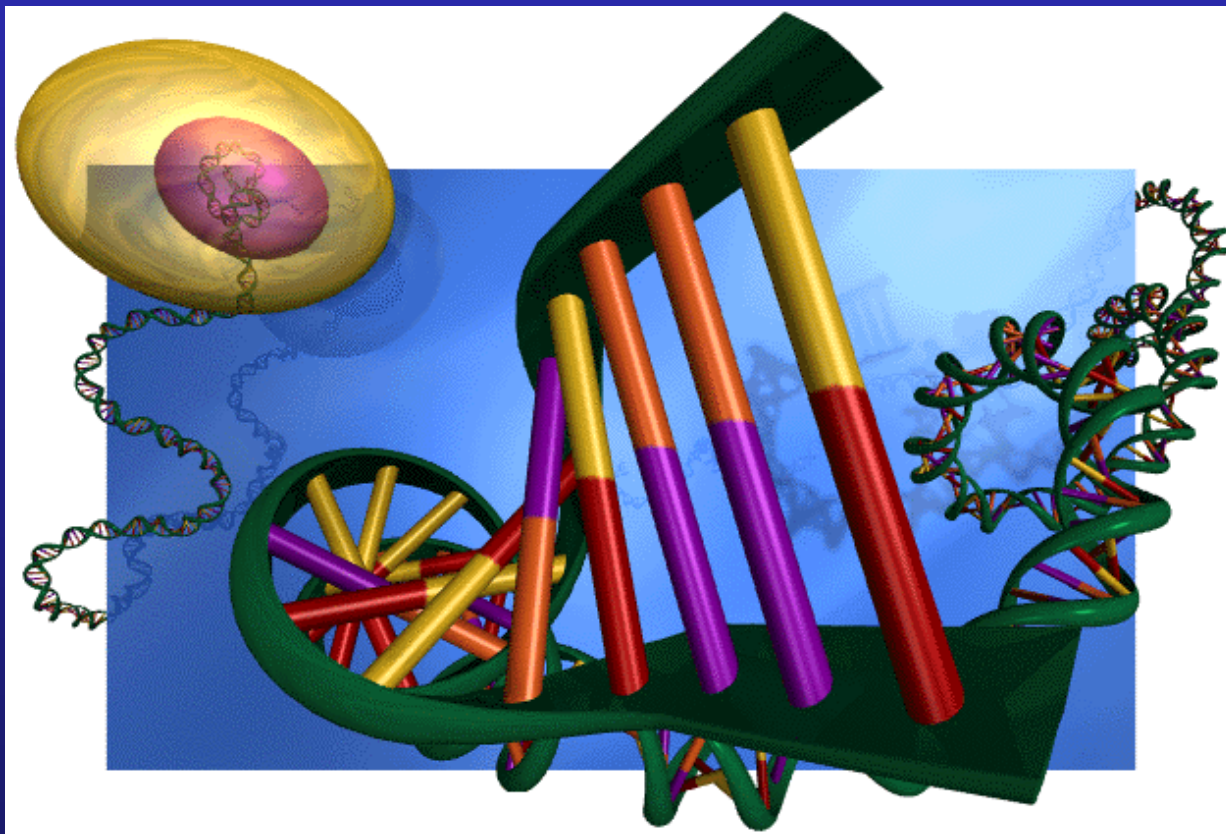
Virus 0.1 μm

Bacterium 1 μm

Cell 10 μm

Repertoire

Genome	Proteome	Repertoire
3×10^4	5×10^5	3×10^{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

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.**

