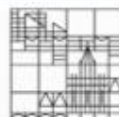
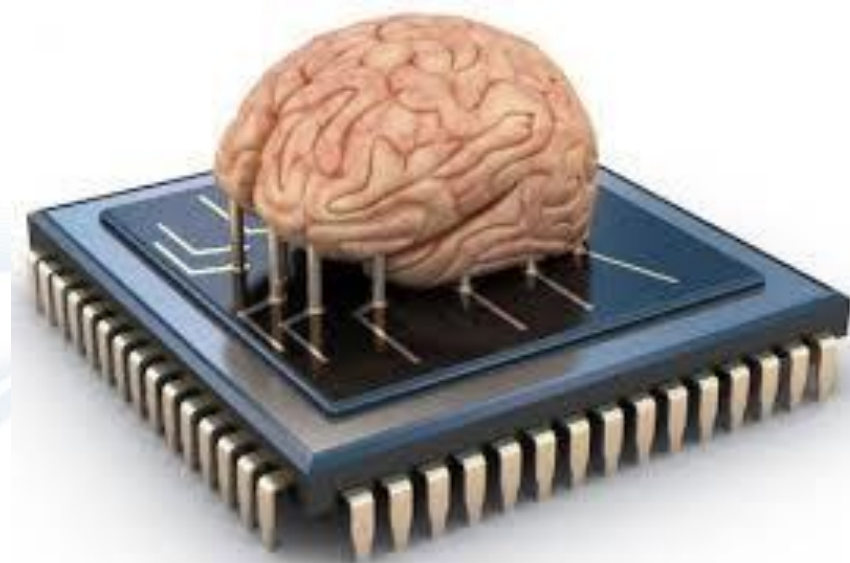
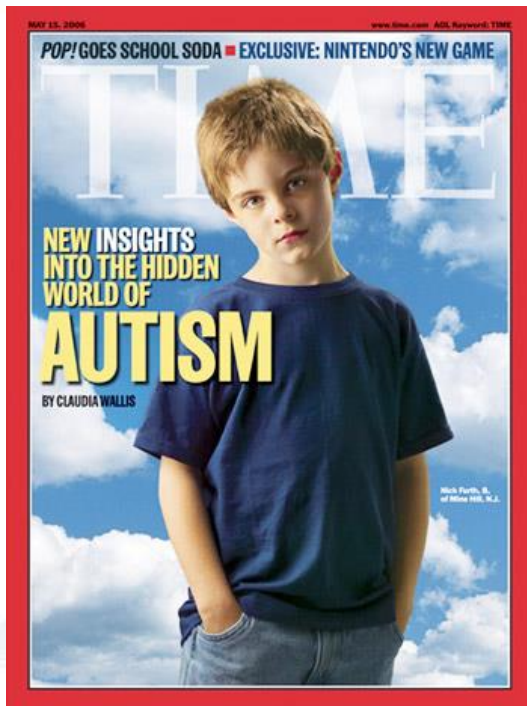


Tackling the autism epidemic

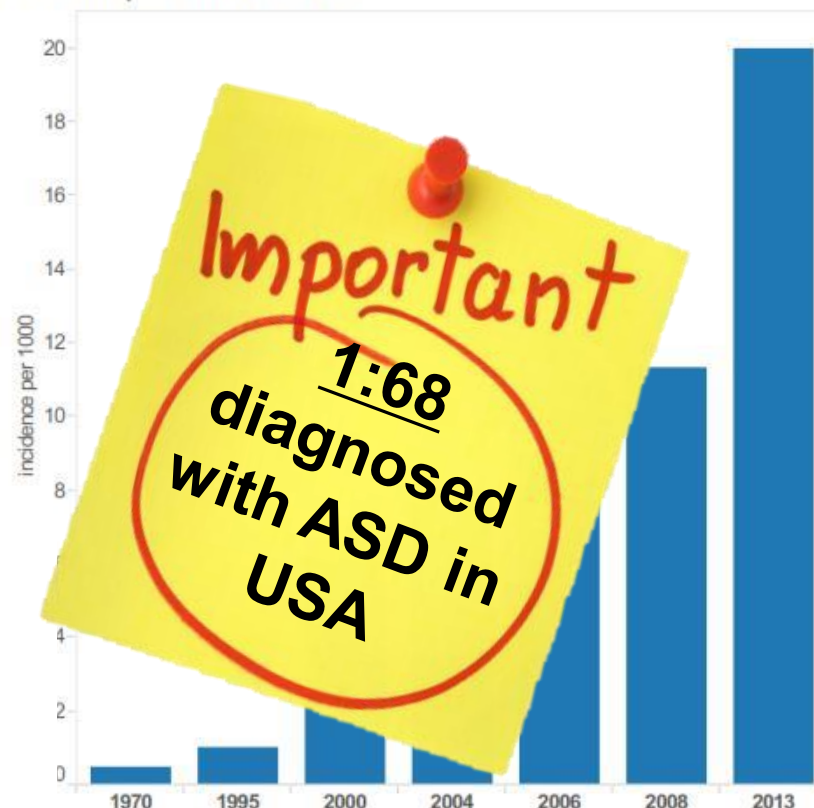
Thomas Hartung





The autism pandemic

Autism Spectrum Disorders

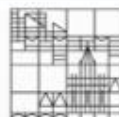


from Studies completed by the CDC on Autism Spectrum Disorder incidence

au·tism [aw-tiz-uhm]

noun

1. Psychiatry . a pervasive developmental disorder of children, characterized by impaired communication, excessive rigidity, and emotional detachment.
2. A tendency to view life in terms of one's own needs and desires.





The lack of toxicological knowledge

Known neurotoxic to humans during development, $N > 10$

Neurotoxic to humans

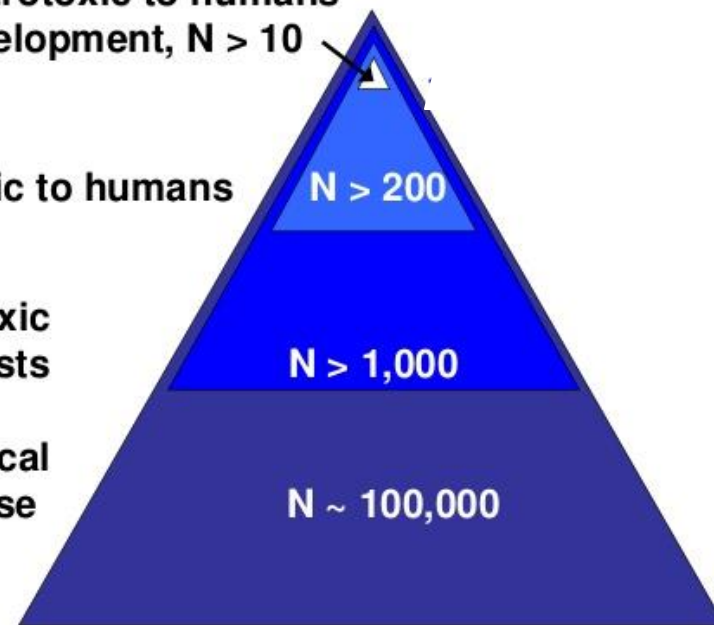
$N > 200$

Neurotoxic in lab tests

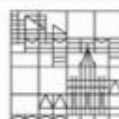
$N > 1,000$

Chemical universe

$N \sim 100,000$

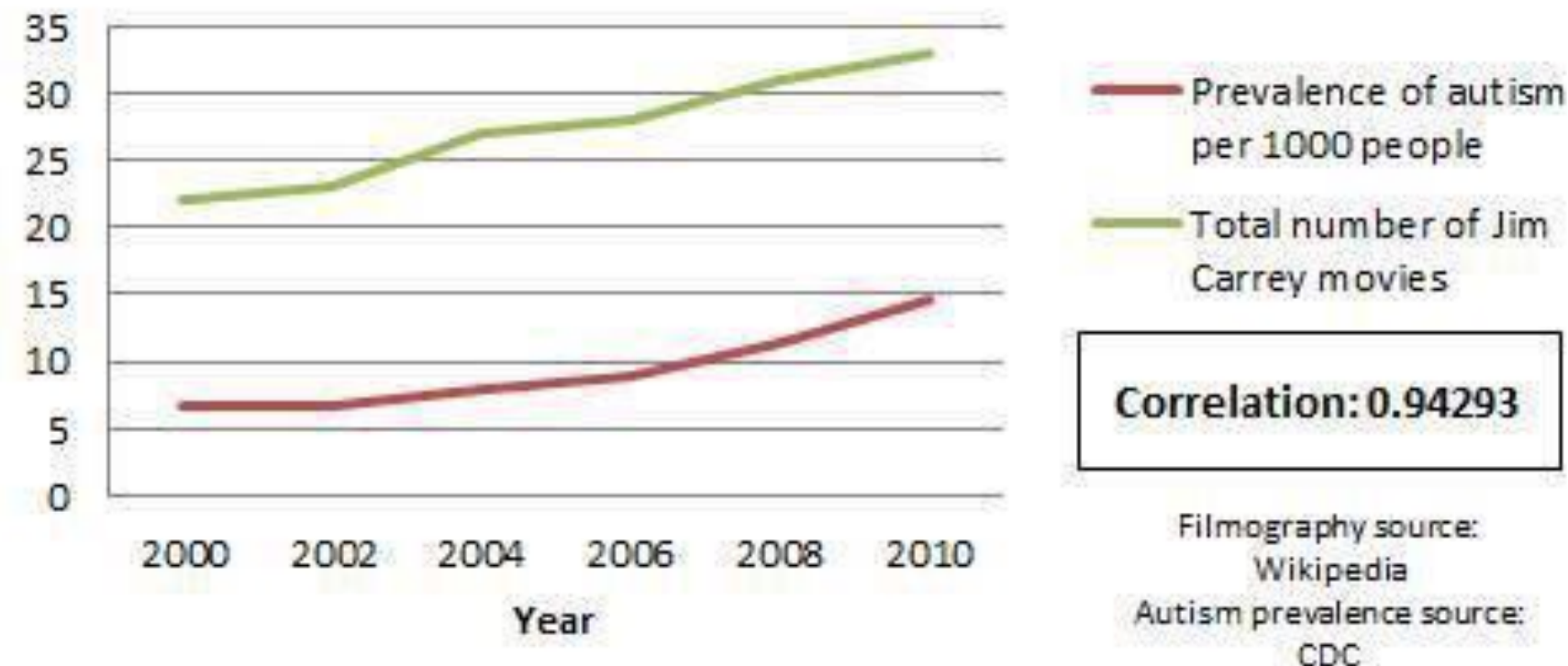


(Updated from Grandjean and Landrigan, *The Lancet*, 2006)



Correlation of chemical use and autism

Definitive Proof that Jim Carrey Causes Autism



The contribution of chemical exposure to autism is not clear - we have to test !!!



100,000 mostly
untested chemicals

Chemophobia

EU: REACH

- **Some chemicals produce developmental neurotoxicity**
- **Exposure often minor**

- **Other factors:**

- **genetics**
- **infections**
- **maternal obesity and age**



- **vaccines**



Scientific American 2005

PROTECTING MORE THAN ANIMALS

Reducing animal suffering often has the unexpected benefit of yielding more **RIGOROUS SAFETY TESTS**

By Alan M. Goldberg and Thomas Hartung



84 SCIENTIFIC AMERICAN

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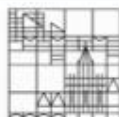
Animal testing for developmental neurotoxicity

- 1,400 rats
- \$1,4 million
- Little human predictive



Johns Hopkins University
Center for Alternatives
to Animal Testing

- Information, Grants
- Think tank
- EU branch, policy program
- Stakeholder consensus



TESTSMART
DNT
DEVELOPMENTAL
NEUROTOXICITY **4**

Four International Conferences
jointly with European Center for
the Validation of Alternative
Methods (ECVAM)

Our mini-brain project



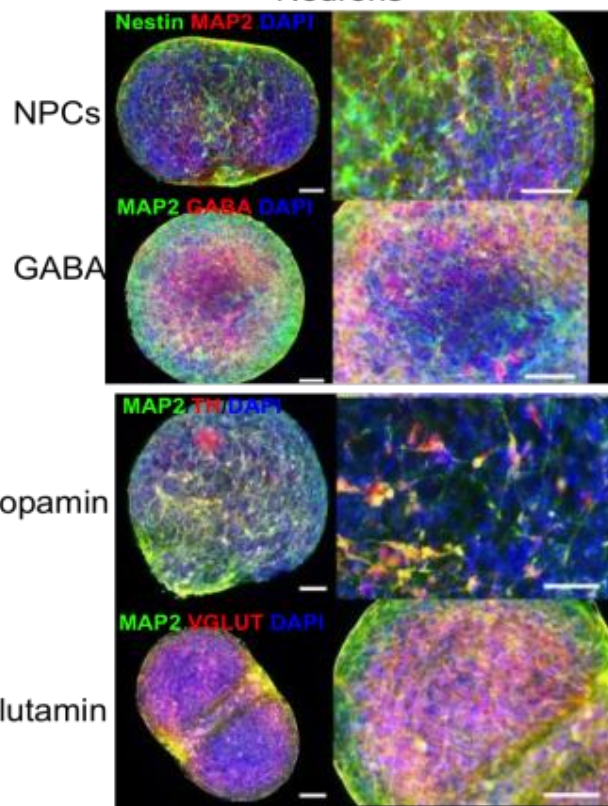


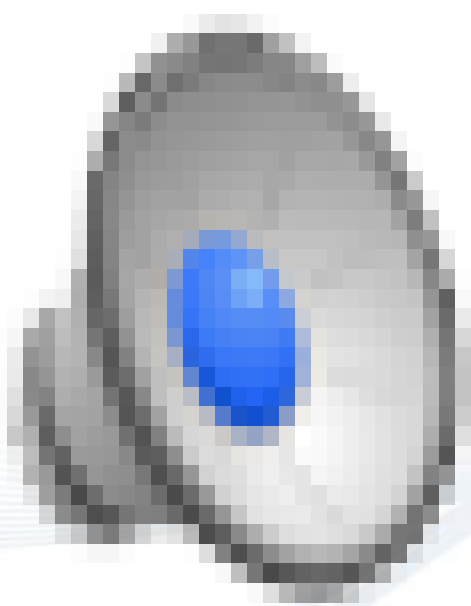
Summary

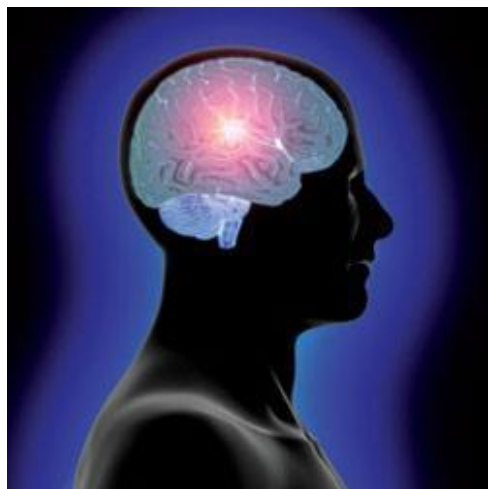
Human “mini-brain” developing from iPSC

- All cell types but micro-glia
- 350um diameter
- 800 per batch
- Reproducible
- Electrophysiological active
- From patient cells:
gene/environment
interactions

Neurons

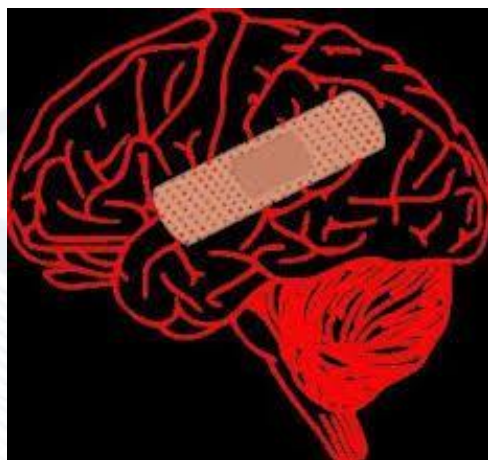






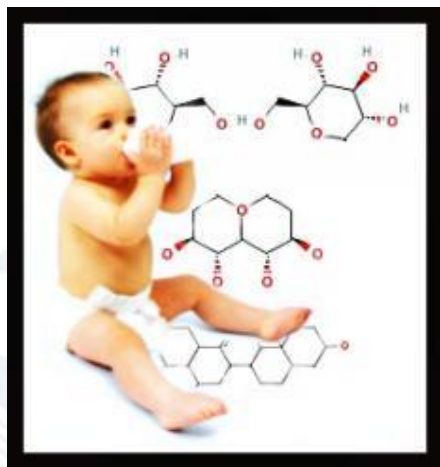
Opportunities for human mini-brain research

- Map the neurotoxic chemical universe
- Characterization of medical countermeasures
- Neurotoxic and DNToxic side effects
- Brain trauma, infectious disease and neurodegenerative disease research
- Individual susceptibility using patient iPSC – genetic risk factors
- Long-term culture and co-culture with other organs





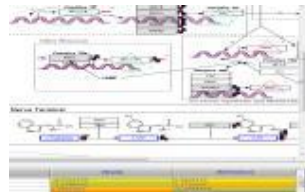
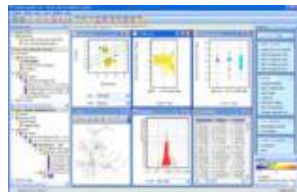
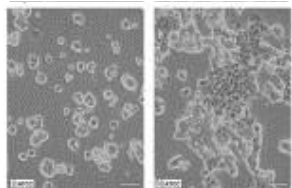
Diseases like autism cannot be explained by genetics or exposure alone



Disposition to DNToxicants?

Test on a genetic background that allows DNT





**In vitro
model**

**omics data
generation**

**Software
tools**

**Pathways
of Toxicity**

**Validation
tools**

**Human
Toxome
Database**

Mapping the Human Toxome by Systems Toxicology



International expansion?

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ChemicalWatch

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EUToxRisk21 to start this autumn

Project aims to put mechanistic-based alternative toxicity testing in a regulatory context

17 June 2015 / Europe, Risk assessment, Test/non test methods

François Busquet, Johns Hopkins University, Center for Alternatives to Animal Testing, CAAT Europe Policy Coordinator, Brussels

François Busquet: Why Europe needs the Human Toxome Project

30.05.2012 - What is the Human Toxome Project? It's a wide-reaching programme aimed at helping us to reconsider how hazard/risk assessment has been performed over the last 50 years on marketed substances like chemicals, cosmetic products, pharmaceuticals, pesticides, biocides and feedstuffs.

It's necessary because most of the scientific community now accepts that animal models for testing the safety of these products have more limitations than advantages. In basic terms, the loose genetic homology to humans is no match for modern cell-culture technology, which promises to be much more apt to correctly predict toxic effects in humans. These cell cultures can

| | | |
|--------------------------|----------|---------|
| CO.DON (D) | 2.80 EUR | 5.26% |
| FLOP | | |
| ANTISOMA (UK) | 1.32 GBP | -14.84% |
| XENETIC BIOSCIENCES (UK) | 6.00 GBP | -14.29% |
| PAION (D) | 3.18 EUR | -7.29% |

NO LIABILITY ASSUMED, DATE: 22.06.2014

Toxicology for the 21st century

- ***Starts with 21st century cell culture***
- ***Big data from good models***
- ***New tests fit for purpose for regulation***



**Mechanistic
& evidence-
based toxicology**

