

Cancer, the immune system, differentiation, and the sensitivity of children: how supportive are the laboratory studies?

i.lagroye@enscpb.fr

PIOM Laboratory - Bioelectromagnetics group
Bordeaux, France



Laboratory studies

- Considering the title topics,
- Considering the available literature in bioelectromagnetics

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Only a few protocols have been designed to specifically answer the question of a potential higher sensitivity of children

Laboratory studies and cancer

Relevance of bioassays for the question of children's sensitivity - 1

- Standard NTP assays begin when rodents are sexually mature
some relevance for young adults
- Protocols that include *in utero* exposure (i.e. developing toxicology-like)
some relevance for children

Laboratory studies and cancer

Relevance of bioassays for the question of children's sensitivity - 2

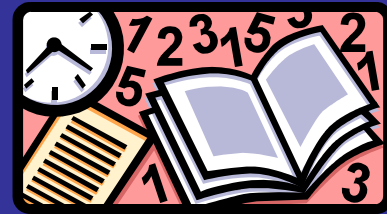
- Children's cancers are different from adults' cancers
- Models of lymphoma (acute lymphoblastoma) and neuroblastoma would be most relevant



Laboratory studies & cancer - ELF

The facts:

IARC classified power-line magnetic fields as 2B carcinogens for childhood leukaemia only




Classification based on:

- association found in pooled-analyses
- insufficient support from laboratory studies

Laboratory studies & cancer - ELF



What has been done?

- Mostly negative outcomes in bioassays
- Controversy on mammary cancer (rat genetic background important?) 
- No effect on spontaneous leukaemia (Mandeville, 97) and lymphomas in transgenic mice (Harris, 98)
- No alteration in clinical progression of:
 - induced lymphocytic leukaemia (Sasser, 96)
 - induced acute myeloid leukaemia (Devevey, 00)

Laboratory studies & cancer - ELF

What is being done?



No model of acute lymphoblastic leukaemia available until recently:

- chemically-induced acute lymphoblastic leukaemia model:
 - ongoing study using 50 Hz magnetic fields + harmonics (N. Bernard, BEMS 03, 04)

Laboratory studies and cancer - RFR

The facts:

- RFR source close to the head,
- different absorption of microwaves in children' heads,



Laboratory studies & cancer - RFR

What has been done?

- Laboratory studies: no evidence of effects at low levels

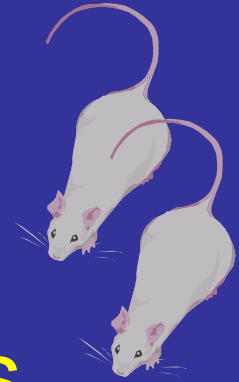
Bioassays : negative so far

Controversy on lymphoma in transgenic mice (Repacholi 97, Utteridge 02, ongoing PerformA)

Laboratory studies & cancer - RFR

What has been done?

R. Adey et al., (1999, 2000)



Developing toxicology-type studies

- *In utero* exposure to american signal for mobile telephony at 836.55 MHz:
- Pregnant rats injected with ENU
- Exposure to RFR at day 19 until weaning (D21), then local exposure from D35 for 25 months
- No effect in CNS tumours

Laboratory studies & cancer

What should be done?



- **Transgenic models**
 - Caution is needed: the $E\mu$ pim-1 mice story...
 - Useful to study acute lymphoblastic leukaemia for which different transgenic models now exist (TEL-JAK2 for instance)
 - Useful to study brain cancer?
- **Follow-up of Adey's and Bernard's works**

Laboratory studies & immune system

Relevance of immunological tests for the question of children's sensitivity

- The immune system is not fully developed at birth, thus unsafe environments may interfere with its normal development

- Agents that are immunotoxic to neonates are usually immunotoxic for adults



Lab studies & immune system -ELF

What has been done?

- A number of published results (ICNIRP blue book)
- The vast majority of studies investigated hematopoiesis and the functionality of the immune system of adult rats/mice
- The general consensus: “there is little consistent evidence” that ELF-exposure can affect the functions of the immune system (cell phenotyping, proliferation, cytokine production, etc)

Lab. studies & immune system -RFR

What has been done?

- Many results published with RFR with reported effects at high levels only (Black, 03)
 - Studies on blood cells & functionality
 - Russian studies showing erythrocytes breakdown not replicated
- Only a few data available with mobile phones' signals



Lab. studies & immune system -RFR

What has been done?

- **Russian experiments**

- usually only russian version available
- immunological functions largely investigated
- studies on autoimmunity seem to be the more significant input

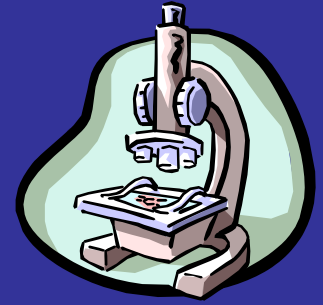


What is being done?

Attempt to set a multicenter programme for re-evaluation of autoimmunity

Lab. studies & immune system -RFR

What has been done?



- **Gatta et al, 2003**

- C57Bl/6 mice (2 months-old) exposed to 900 MHz GSM, 1 or 2 W/kg, 2 hr /day for 1, 2 or 4 weeks
- spleen cells : cell count, phenotyping of sub-populations, activation (proliferation, early activation markers, cytokine production)

- **No effect overall**

- **Transient increase in IFN- γ production (1 week): adaptation?**

Laboratory studies & immune system

What is being done?



Investigation of toxic effects GSM or UMTS signals at 0.4 W/kg over three successive generations of rats (Bornhausen, ICNIRP/URSI/WHO 04)

What should be done?

Testing the developing immune system (different development stages) with EMF

Laboratory studies & differentiation

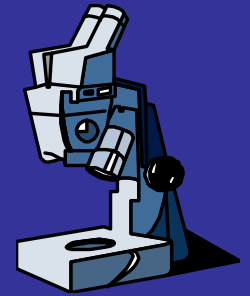
Relevance of differentiation tests for the question of children's sensitivity

- Differentiation is a major process during development
- Availability of stem cells makes investigations easier

Lab studies & differentiation

ELF

ELF magnetic fields (0.8 mT) enhanced the differentiation of mouse stem cells into cardiomyocytes (Reflex programme)



RFR

RFR (1.5 W/kg) upregulated the neuronal genes' expression in p53-deficient neuronal precursor cells (not in wild-type cells, Czyz 03)

Laboratory studies - Conclusions ELF

To be informative and helpful for risk assessment, additional well-designed experiments (statistical power, dosimetry, etc) are needed using:

- *in utero* and post-natal exposures to ELF magnetic fields
- animal (transgenic) models of ALL

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Laboratory studies - Conclusions RFR

- more post-natal exposures to RFR for the investigation
- the investigation of autoimmunity and inflammation in the brain



... should be encouraged

Laboratory studies - Conclusions

- There may be nothing special with EMF and children's sensitivity



- However, there is a global need to gain information on the potential children's higher sensitivity to environmental agents

- The investigation of EMF at different development stages and the use of differentiation assays using stem cells should be encouraged