Childhood leukaemia risks:
Towards a better understanding of unexplained results

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Context

- Several recently published epidemiological studies on childhood leukaemia (CL) near nuclear installations (and after exposures to 50 Hz fields) raised questions which could not be answered by current knowledge on the effects of ionising (and non-ionizing) radiation
- Several committees were asked to provide advice on this issue (Germany, France, Sweden, UK)
- At the end of 2011, BfS and IRSN decided to organize a focussed workshop on this topic, under the auspices of the MELODI European research platform

Workshop

Workshop objectives
- To learn from past studies and to develop a best possible study design for answering questions on CL incidence close to point sources
- To identify and define promising directions for future research into the causes and pathogenesis of CL at European level and world-wide

Workshop organization
- 5 days (18-22 June 2012), in conclave in Bombon (France)
- Participation upon invitation
- 42 participants from 14 countries
- Different disciplines: epidemiology, biology, haematology and genetics, extending widely outside of the radiation protection field

Workshop content
Part 1: Studies of CL risk near nuclear installations
- Review of recent / ongoing studies (UK, FR, BE, CH)
- Methodological issues (study design, bias, power, exposure indicators…)

Part 2: Aetiology and mechanisms of CL induction and development
- State-of-the art regarding CL and B-cell development, haematopoietic stem cells, environmental risk factors, genetic analyses, role of infection, animal models
- Ongoing projects: CLIC, I4C, Arimmora, pilot studies
- Gaps in knowledge, further research recommendations

Results

Points of consensus
Part 1
- Existence of a few well documented clusters near specific nuclear sites
- No excess of childhood leukaemia in general near nuclear installations, but consistent elevated risk in the 0-4y age range less than 5km
- Need for a continuation of the surveillance of childhood leukaemia incidence

Part 2
- Our knowledge on risk factors is still limited, new ways/methods are needed
- Gene variants affect susceptibility to ALL, although they are individually modest in their effects
- Relationship between leukemia and immune status remains important and worth to follow up
- Engineering of animal models is crucial for experimental study designs

Perspectives
- Publication of the conclusions of the workshop
- Basis for developing funding schemes on national and European levels, with appropriate links to other internationally run projects

Recommendations
Part 1
- Need for a better description of the local population (demography, sociology, life habits and exposures)
- Use of improved indicators of radiation exposure in addition to distance
- Creation of collaborative working groups to allow a better coherence of future analyses in Europe, in parallel with the reflexion currently ongoing in the US

Part 2
- Risk factors (RF) under consideration should be analysed in relation to CL subtypes, e.g. include tumour characterization (epigenetic/genetic profiles) in conjunction with epidemiologic data
- Prevalence of pre-leukaemic clone (e.g., ETV6-RUNX1) has to be determined; this is crucial for understanding intrinsic vs. external RF
- Develop deep sequencing of leukaemia cases/subtypes
- Re-evaluation of existing material (e.g., from GWAS studies) in view of new hypotheses (e.g. comparing rural versus urban area) is promising
- It is time for networking and combining disciplines