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Abstract

The lens of the eye is known to be more radiosensitive than previously thought but, despite a substantial reduction in occupational dose limits based on recent epidemiological information and reanalyses, the mechanisms of low dose radiation cataract induction are still unclear. This is an important current public health issue, for instance for medical radiation workers, many of whom will need to amend their working practices despite a clear understanding of the effects of chronic, low dose, ionising radiation exposure.

The LDLensRad project aims to bring together experts from across Europe to answer a number of key research questions on this topic, including: how does low dose radiation cause cataracts; is there a dose rate effect, and how does genetic background influence cataract development after radiation exposure. CONCERT Deliverable 9.58 describes progress in preparation of a special issue of Radiation Research, a peer reviewed journal, devoted to the main research outputs of the LDLensRad project.

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Special issue of Radiation Research

The LD LensRad Management Board (MB) met to discuss how best to achieve scientific dissemination in Autumn 2019. It was agreed to approach the chief editor of Radiation Research to ask whether the journal would consider a special issue focused on the combined outputs of the project. This was done and the editor has agreed that they will be happy to host the special issue.

At the final project meeting in Rome in December 2019, it was agreed that each task leader will collate data into a rough draft paper to be ready for circulation amongst the partners by July 2020. Further discussion will take place regarding how to best organise the data for publication, with manuscripts to be ready for submission by end November 2020. Publication of the special issue should then take place ~ March 2021.

It was also agreed that the project PhD students and others who have a more pressing need to publish as soon as possible are welcome to submit to the special issue as soon as the papers are ready as online publication will, as usual, occur as soon as manuscripts are accepted.

Finally, it was agreed to approach a separate journal, likely Mutation Research Reviews, with a list of related reviews, including:

Review: What is a cataract? Evidence has accumulated for radiation cataracts, but definition of lens opacities and cataracts, suitability of cataract surgery as a surrogate for vision impairing cataracts remain obscure, the lens opacification classification system suitable for radiation cataracts, which will be discussed in this review article (Nobby Hamada + Roy Quinlan, Jochen Graw + ophthalmological expert colleagues external to the project and others)

Timeline

Publication by Spring 2021 means hard submission deadline latest end November 2020; circulation of first draft papers/ideas amongst the partners end July 2020.

Proposed list of papers (corresponding author(s))

- 1) Commentary on the LD LensRad project as a whole: Overview of the project aims and how the project has advanced knowledge on how ionising radiation contributes to cataract (Liz Ainsbury, All LD LensRad partners + EAB)
 - a. Discussion of inconsistencies between data that haven't been explained – new research questions!
- 2) Factors affecting cataract formation in mouse models at 10 weeks of age: PHE, HMGU and ENEA data 18 months post IR – dose, dose rate, strain, age and sex effects on lens opacification quantified by Scheimpflug (Claudia Dalke)
- 3) Cataract formation in Ptch mice exposed at P2, including comparison with 10 wk data, mechanistic indications based on Ptch response + medulloblastoma + cancer risk + neurogenesis (Mariateresa Mancuso)
- 4) Long-term observations of adult B6C3F1 with OCT, Histology (lens+retina+cornea), IHC (lens+retina+cornea) and visual acuity (Daniel Pawliczek)
- 5) Survival analysis and wider pathology in B6C3F1 mice (dose rate effects in comparison to INSTRA) (HMGU TBC)

- 6) Short-term effects in adult B6C3F1 mice including IHC of lens epithelium repair sites and kinetics (HMGU TBC)
- 7) DNA damage, proliferation and cellular morphology in mouse models (Steve Barnard and Alice Uwineza)
- 8) NGS and pathway analyses for mechanistic hypothesis generation, linking to data in a above papers (Barbara Tanno)
- 9) Long-term effects of radiation on behaviour: Effects of a single radiation event (0, 0.5, 1, 2 Gy, 0.3 Gy/min) at age 10 weeks on spontaneous behaviour and cognition 4, 12 and 18 months p.i. in male and female B6C3F1 and heterozygous *Ercc2*^{S737P} mice on the same genetic background (Sabine Hoelter-Koch)
- 10) In vitro investigations in support of mechanisms of radiation cataractogenesis (Maryam Ahmadi)
- 11) Statistical modelling revealing adverse outcome pathways for radiation induced cataracts (Liz Ainsbury)
- 12) Short summary paper – implications of the results for RP and future research directions discussed in full (Liz Ainsbury, Nobby Hamada, All LDLenRad partners + EAB)