

co-ordinated with the Director of the Institute / Research Unit

**Research Unit of Radiation Cytogenetics**

**PSP-Element:**

G-501000-001

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**Title of the highlight:**

Dose-dependent expression of CLIP2 in post-Chernobyl papillary thyroid carcinoma

**Keywords:**

Thyroid carcinoma, Chernobyl, logistic Regression, Biomarker, dose-dependency

**Central statement of the highlight in one sentence:**

The expression of the CLIP2 protein shows a dose-dependent expression in tumors from young thyroid carcinoma patients who were operated before the age of 20 years.

**Text of the highlight:**

Previous studies conducted by the Research Unit of Radiation Cytogenetic revealed a radiation specific genomic copy number gain and an overexpression at the mRNA and the protein level of the CLIP2 gene. Further, it was shown, that the CLIP2 expression has the potential to serve as biomarker for radiation induced papillary thyroid carcinoma (PTC).

In this study we could confirm the hypothesis of a dose-dependent expression of the CLIP2 radiation marker in PTC by logistic regression. However, of note the dose-dependency is only present for patients who were operated before the age of 20 years or have been exposed to ionising radiation before the age of 5 years, respectively. Interestingly, the dose-dependent probability for a CLIP2 overexpression obtained from the logistic regression analysis are in good accordance with the probabilities derived from a mechanistic two path model for the carcinogenesis of PTC, which was developed by the Institute of Radiation Protection (manuscript in preparation).

**Publication:**

**Selmansberger M**, Kaiser JC, Hess J, Guethlin D, Likhtarov I, Shpak V, Tronko M, Brenner A, Abend M, Blettner M et al: **Dose-dependent expression of CLIP2 in post-Chernobyl papillary thyroid carcinomas**. Carcinogenesis 2015.

**Taking account of the HMGU mission:**

The impact of ionising radiation from environmental, medical, and technical sources on human health is of great importance for a large group of the population. The understanding of radiation-associated effects on human health has the potential to improve radiation protection as well as radiotherapy of a multitude of cancers.

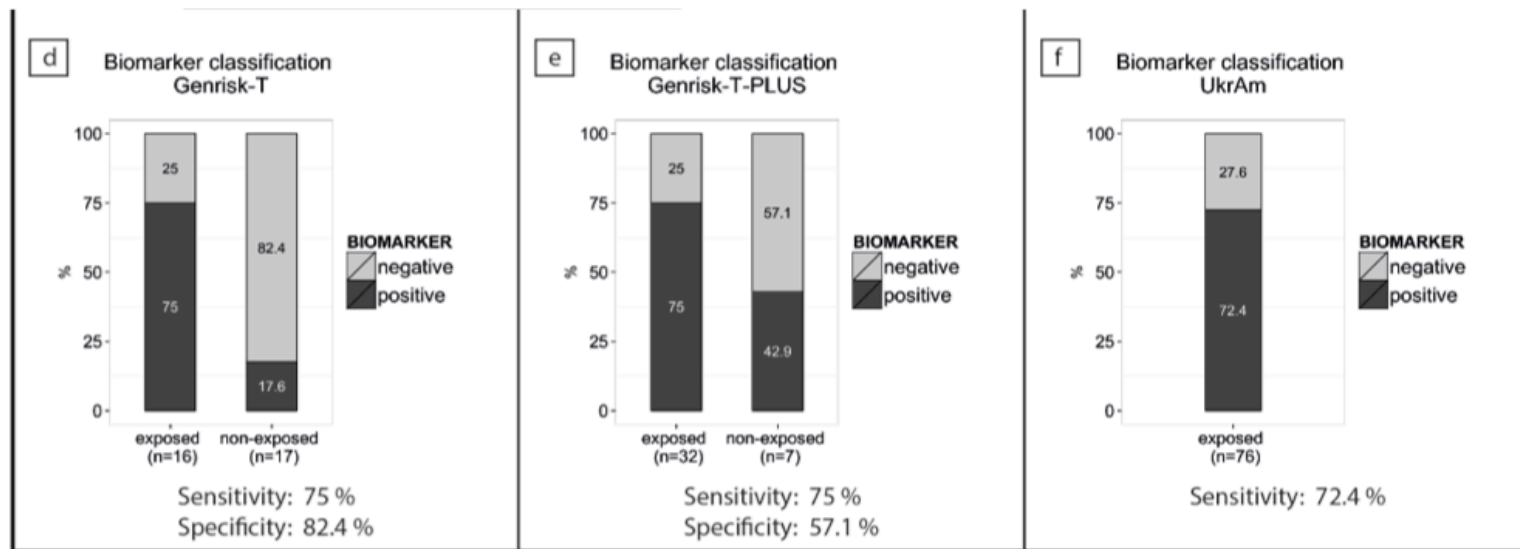
**The internal HMGU co-operation partners with whom the highlight was compiled, if appropriate:**

Institute of Radiation Protection (ISS)

Hypothesis: probability to observe a positive CLIP2 marker is dose-dependent (stochastic effect)

Method: logistic regression    dependent variable -> binary (CLIP2 marker status)  
independent variables -> continuous / binary

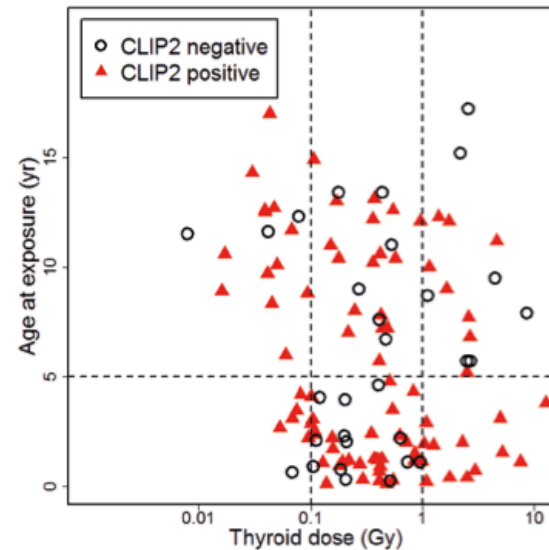
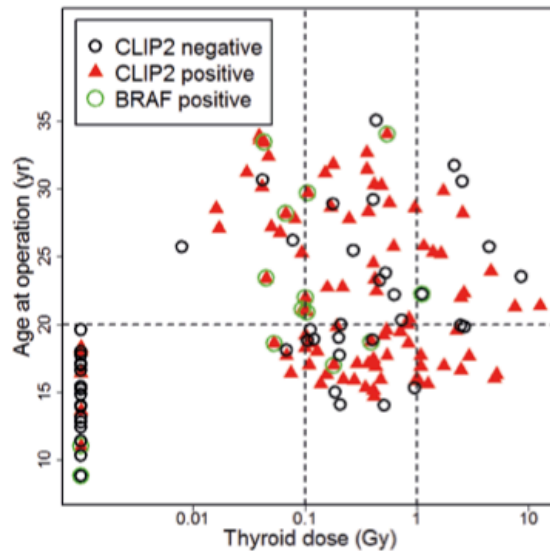
Data set: CLIP2 typing data Selmansberger et al. with assigned thyroid doses



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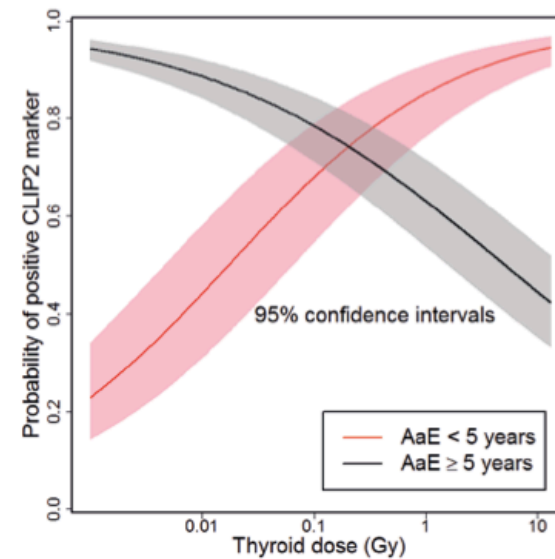
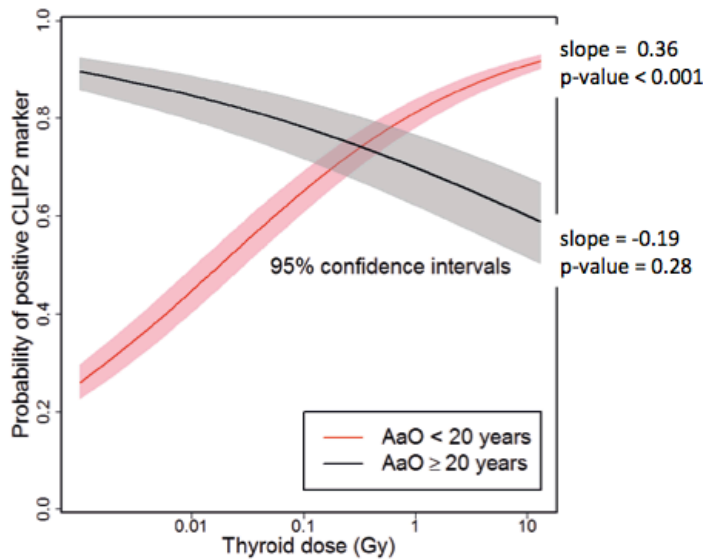


**Model 1:** 141 exposed and non-exposed cases  
(117 exposed, 24 non-exposed)

**Model 2:** 117 exposed cases

Intercept + log(Dose) + AaO.cat + log(Dose) \* AaO.cat

Intercept + log(Dose) + AaE.cat + log(Dose) \* AaE.cat



Positive dose-response of CLIP2 marker for young patients (AaO < 20, AaE < 5)

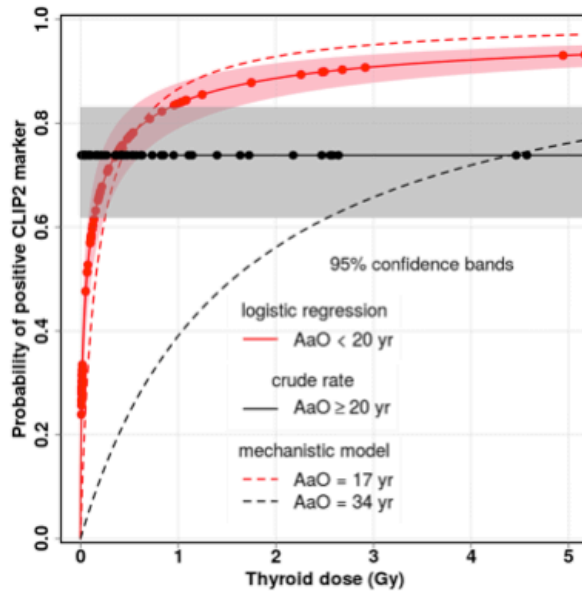
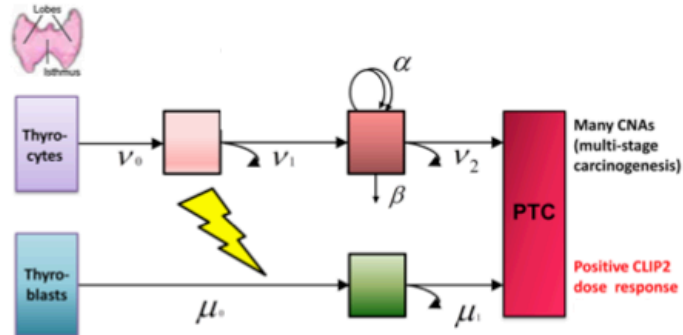
Different molecular mechanisms in CLIP2 positive (radiation induced) PTC and “other”/sporadic PTC (dose dependent probability of radiation-induced PTC for young patients)

Selmansberger et al., 2015, Carcinogenesis

## Two path mechanistic model:

Upper path: sporadic PTCs

Lower path: radiation induced PTCs



Remarkable **agreement** of probability estimates from **logistic regression and the two path mechanistic model** for patients operated at young ages (< 20 years)

Manuscript in preparation by ISS