

Long-term radiobiological effects of ^{131}I exposure -dose, age and time related transcriptomic and proteo- mic response in rats

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, onsdag den 14 april 2021, klockan 9.00

av Malin Larsson

Fakultetsopponent:

Bo Baldetorp, Professor

Lunds Universitet, Sverige

Avhandlingen baseras på följande delarbeten

- I. **Larsson, M.**, Rudqvist, N., Spetz, J., Shubbar, E., Parris, TZ., Langen, B., Helou, K., Forssell-Aronsson, E. *Long-term transcriptomic and proteomic effects in Sprague Dawley rat thyroid and plasma after internal low dose ^{131}I exposure.* PloS One 2020;15(12):e0244098
- II. **Larsson, M.**, Rudqvist, N., Spetz, J., Parris, TZ., Langen, B. Helou, K., Forssell-Aronsson, E. *Age related long-term response in rat thyroid tissue and plasma after internal low dose exposure to ^{131}I .*
- III. **Larsson, M.**, Shubbar, E., Spetz, J., Parris, TZ., Langen, B., Berger, E., Helou, K., Forssell-Aronsson, E. *Late age-related effects on the proteome of thyroid tissue in rats after ^{131}I exposure.*

**SAHLGRENKA AKADEMIN
INSTITUTIONEN FÖR KLINISKA VETENSKAPER**



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Abstract

^{131}I is commonly used in the clinic for treating thyroid diseases, using the physiological uptake of iodine in thyroid, but also for other target tissues. ^{131}I is also commonly released during nuclear accidents. Children are in general more radiation sensitive, and an increased number of thyroid cancers was seen in children but not in adults after the Chernobyl accident. There is a lack of knowledge about long-term radiobiological mechanisms and response in vivo.

The aim of this thesis was to study the ^{131}I induced long-term effects in rat thyroid tissue and plasma by investigating the transcriptional and translational expression, and to propose potential biomarkers related to age at exposure, time after exposure, and dose.

The radiation induced transcriptomic and proteomic response was studied in thyroid tissue and plasma from young and adult rats, 3-12 months after ^{131}I injection, using mRNA microarray technique and mass spectrometry. The number of significant transcripts and proteins was in general highest for low doses (5-50 kBq) and for young rats, but showed no general time-related trend. From these transcripts and proteins, biomarker candidates were identified. Biological functions associated to the significant transcripts and proteins were identified, and metabolic and hormonal effects were in common in most studies. Young rats demonstrated more affected canonical signaling pathways than adults one year after exposure.

In conclusion, radiobiological effects were detected late after exposure (3-12 months), and biomarker candidates (single markers and panels) were proposed for ^{131}I exposure, dose, age, and time after exposure, some connected to thyroid function and cancer. The results increase the knowledge in radiobiology, and may be valuable for improvement of radiation therapy and radiation protection.

Keywords: radiation, thyroid, plasma late effects, biomarkers, transcript, protein