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Exploring Selenium-Mercury Interactions in Human Systems: Insights from Controlled Fish Consumption and Biomarker Analysis

Adna Alilović[1], Polona Klemenčič[2], Marta Jagodic Hudobivnik[2], Igor Živković[1,2], Janja Snoj Tratnik[1,2], Ingrid Falnoga[2], Neža Palir[1,2], Darja Mazej[2], Milena Horvat[1,2]

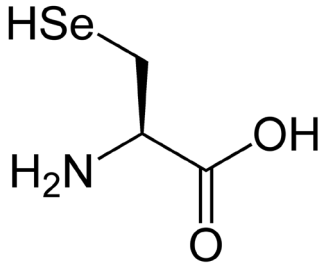
[1]International Postgraduate School Jožef Stefan, Ljubljana, Slovenia
[2]Institute Jožef Stefan, Ljubljana, Slovenia

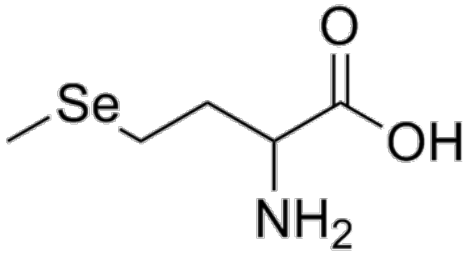
Introduction

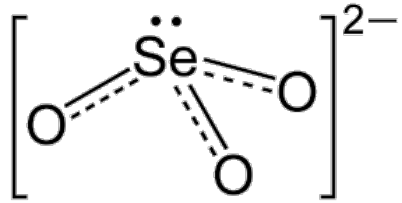
- **Mercury** – non-essential and toxic

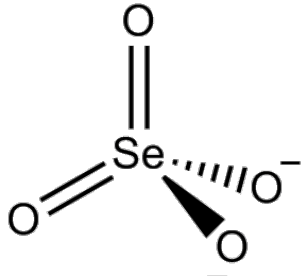
- **Selenium** – essential, incorporated as **SeCys** residue in various antioxidant enzymes (glutathione peroxidase, thioredoxin reductase, iodothyronine deiodinase, selenoprotein P…)

selenocysteine (SeCys), **selenomethionine** (SeMet), **selenite** (SeO_3^{2-}), **selenate** (SeO_4^{2-})

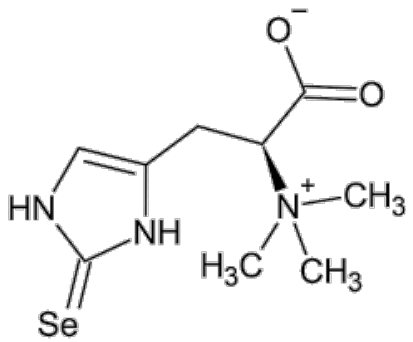






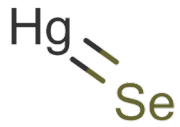


selenoneine was discovered as the main organic Se in the blood and tissues of bluefin tuna



- all Se forms except selenoneine – utilized for selenoprotein synthesis
- selenoneine - unique metabolic pathway, unrelated to the central metabolic pathway; dominant species in the RBC of fish-eating populations

- many *in vitro* and *in vivo* studies show protective effects of Se against (Me)Hg toxicity in birds, mammals, fish, but the exact mechanism still unclear
  - by increasing the organism's antioxidant ability
  - by binding Hg into poorly soluble, inert complexes, with drastically reduced bioavailability and toxicity
  - by increasing demethylation of MeHg



To what extent can laboratory results be extrapolated to real-life situations?

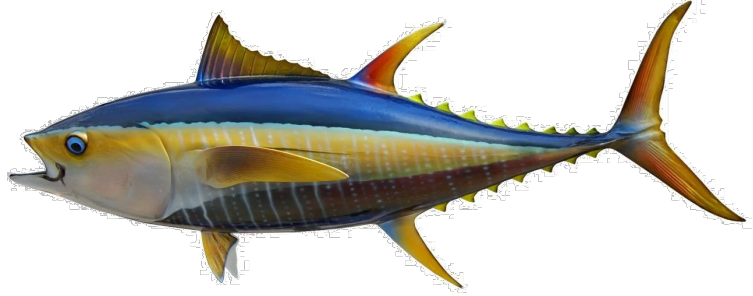
MeHgCl, $HgCl_2$…selenite

MeHgCys, SeMet, SeCys, SeN

- **the absence of neurological symptoms in studies of highly MeHg-exposed populations suggests existence of certain protective factors against MeHg toxicity**
- several studies on human populations have reported a **positive correlation between Hg and Se levels in plasma and/or blood**
  - consequence of **co-exposure** to both elements through a common dietary source (correlations found in fish-eating populations) **?**
  - existing bodily Se depots **dynamically respond** to increased Hg exposure (studies in Hg miners) **?**

Fish is a rich source of Se, which could potentially provide **natural protection against Hg toxicity.**

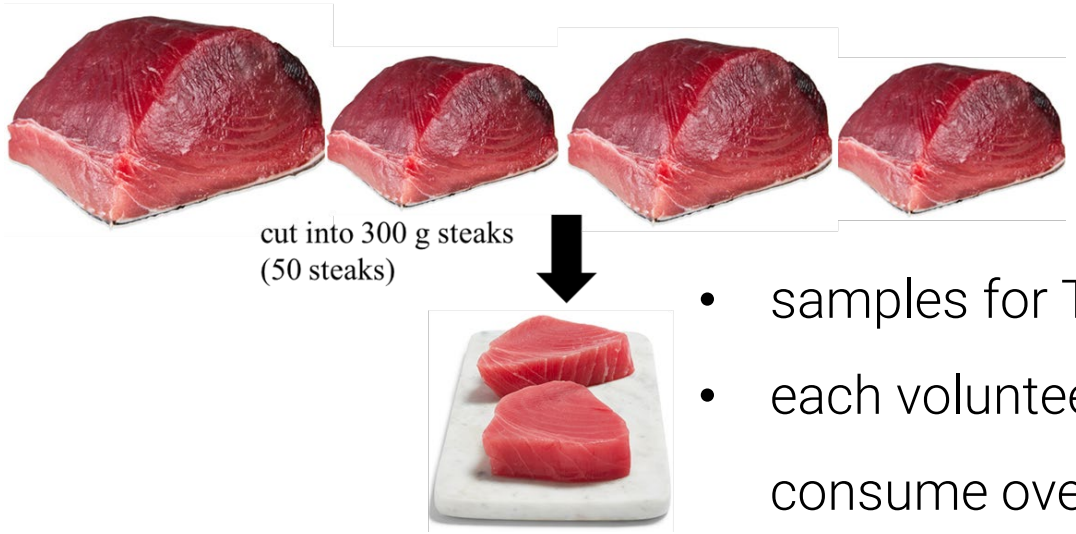
The tuna experiment



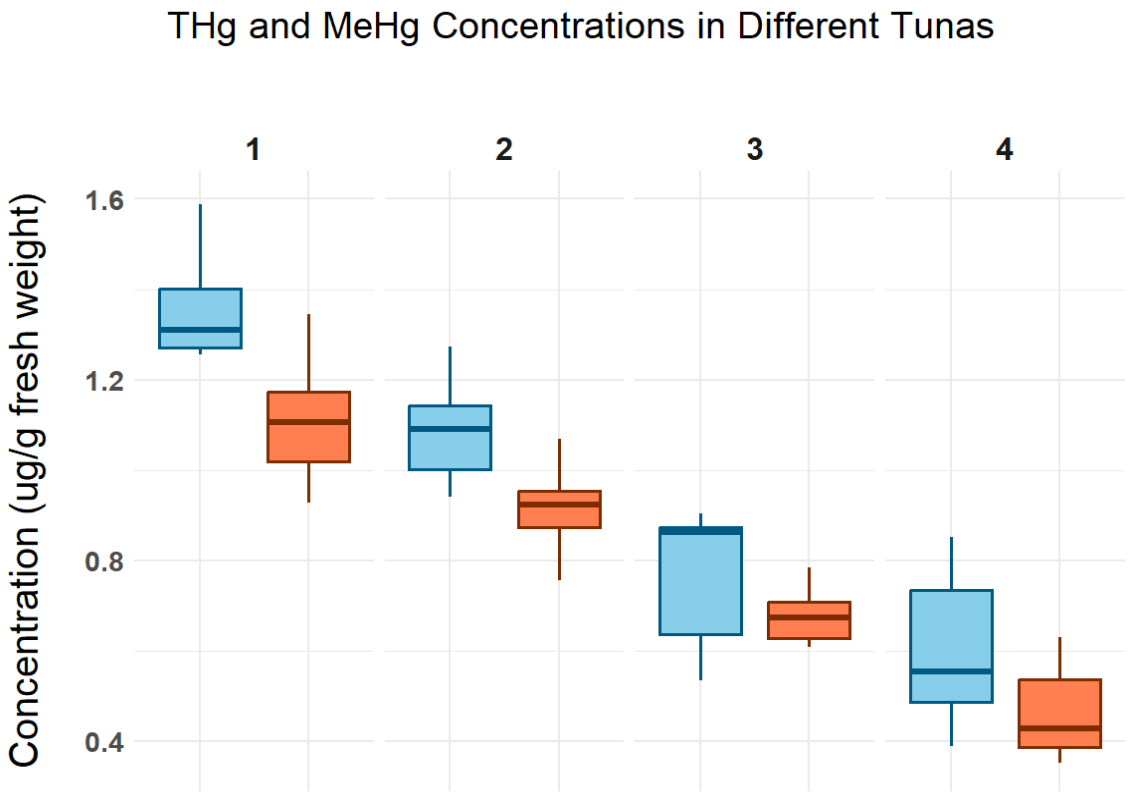
- creation of a **controlled** and realistic exposure scenario and subsequent measurements of **THg, MeHg, Se** in **multiple** biological samples

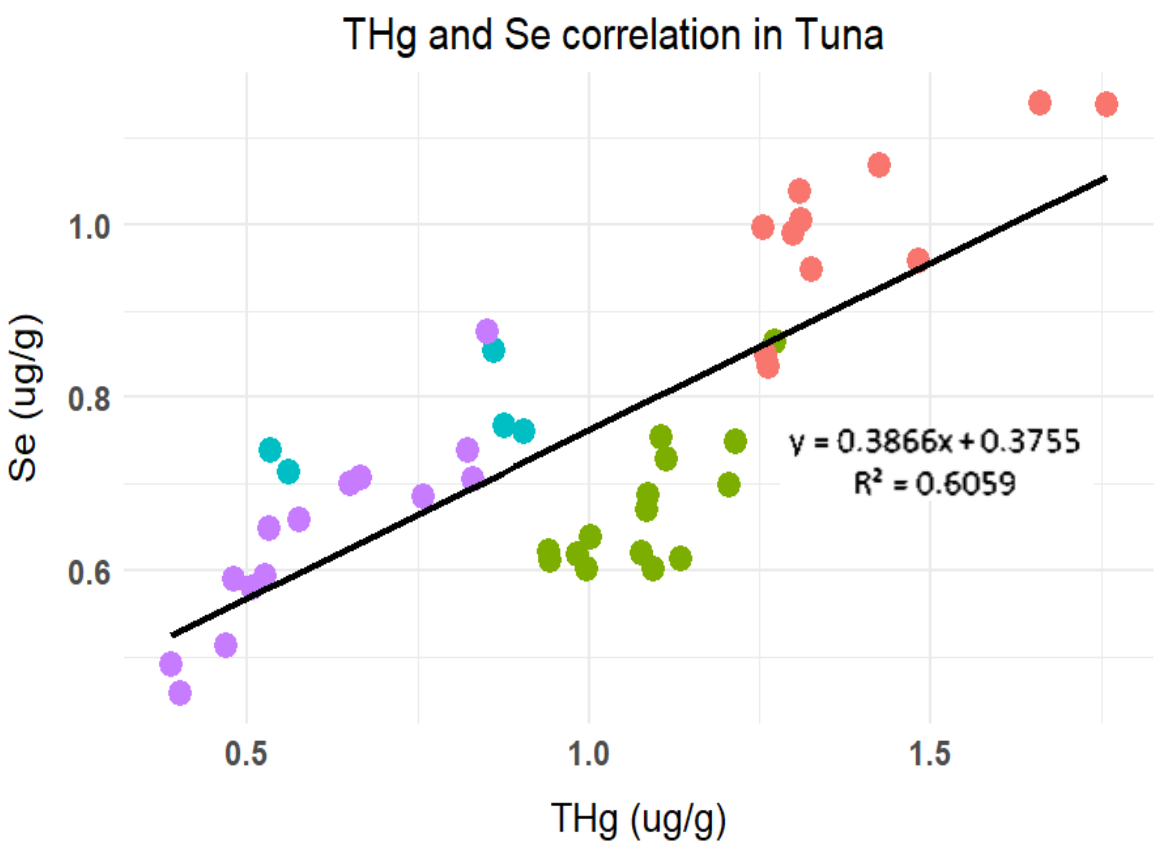
  16 volunteers (10 experimental + 6 controls)

  Yellowfin tuna (Thunnus albacares)



- samples for THg and MeHg measurements taken from each steak
- each volunteer in the experimental group was given 5 steaks to consume over 5 consecutive days



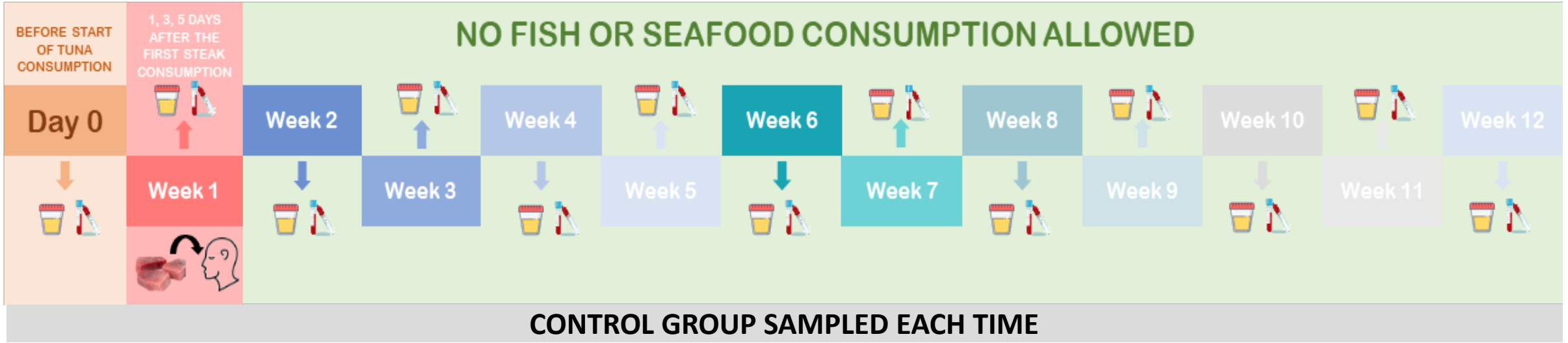


THg: 0.4 – 1.6 µg g^{-1} fresh weight

Se: 0.5 – 1.2 µg g^{-1} fresh weight

~ 80% MeHg

The sampling regimen



Day 0 – sampling to establish initial state of exposure

5 days of fish consumption (experimental group), 3 samplings (also control group)

No fish consumption, continuous periodical sampling until 89 days post-exposure

The initial state

Significant positive correlations between:

- **whole blood THg and whole blood Se**

  stronger when THg > median of 0.97 ng/g (**r=0.893**)

- **erythrocyte THg (MeHg) and erythrocyte Se**

  stronger when THg > median of 1.95 ng/g (**r=0.801**)

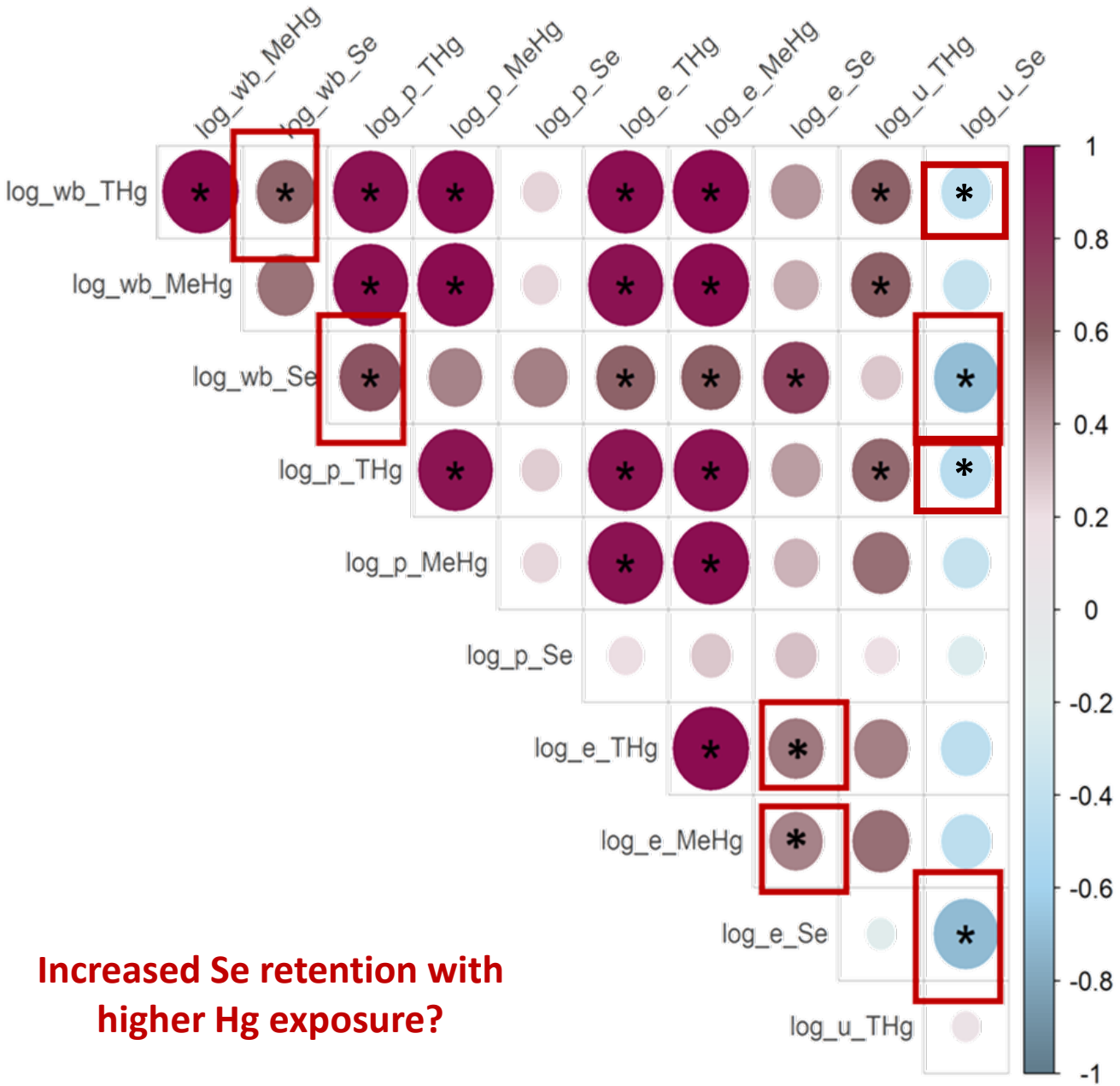
No significant correlations were found between:

- **plasma Se and plasma THg or MeHg**
- **urinary Se and Hg**

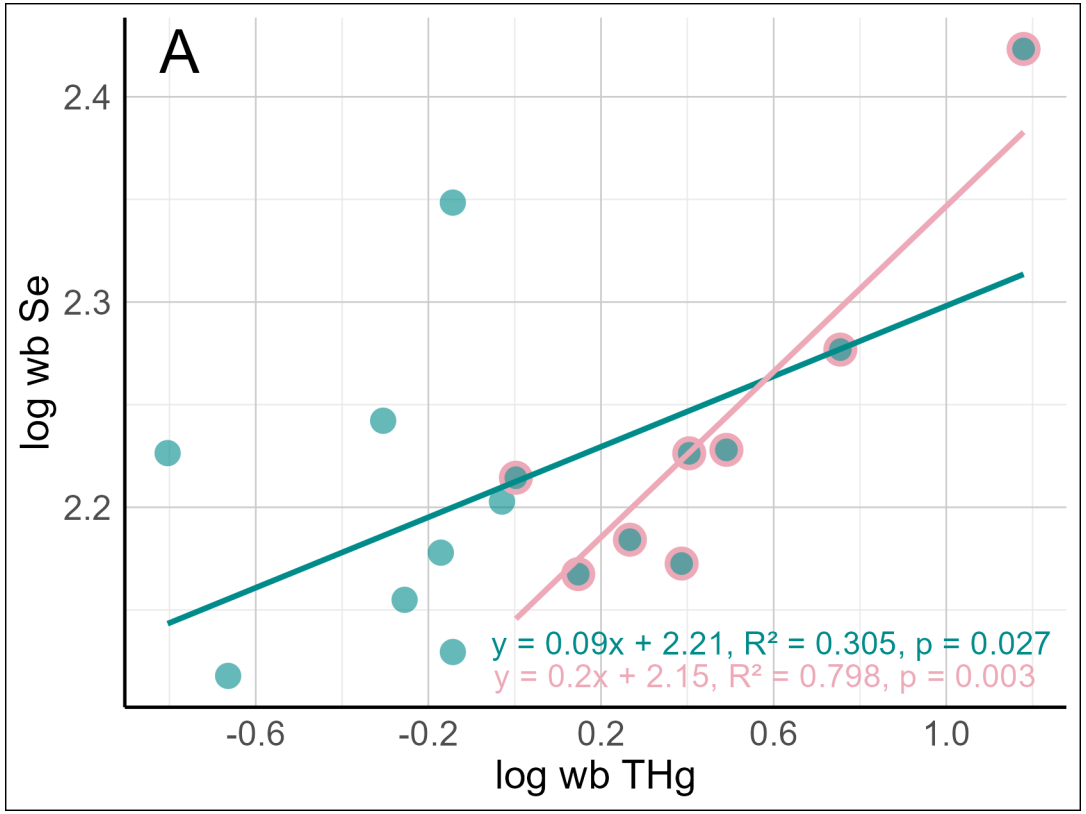
Significant negative correlations between:

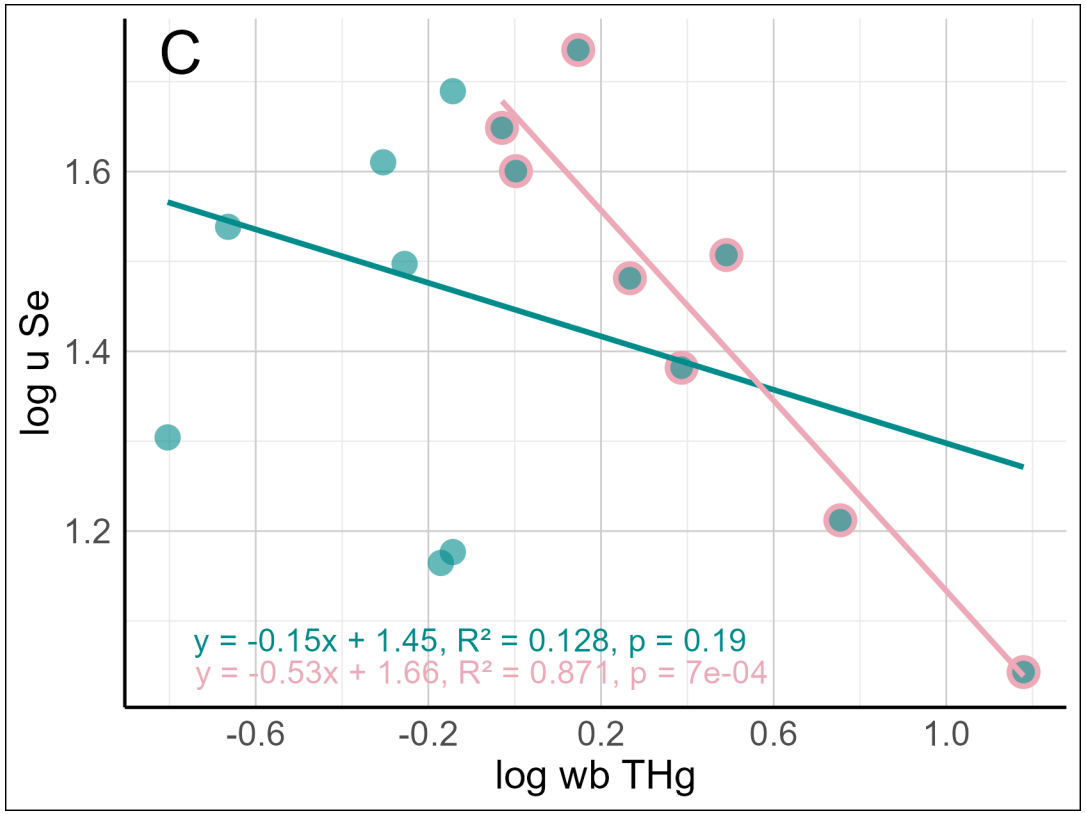
- **whole blood Se and urinary Se**
- **whole blood and plasma THg and urinary Se**

  stronger when wb THg > median (**r=-0.950**)



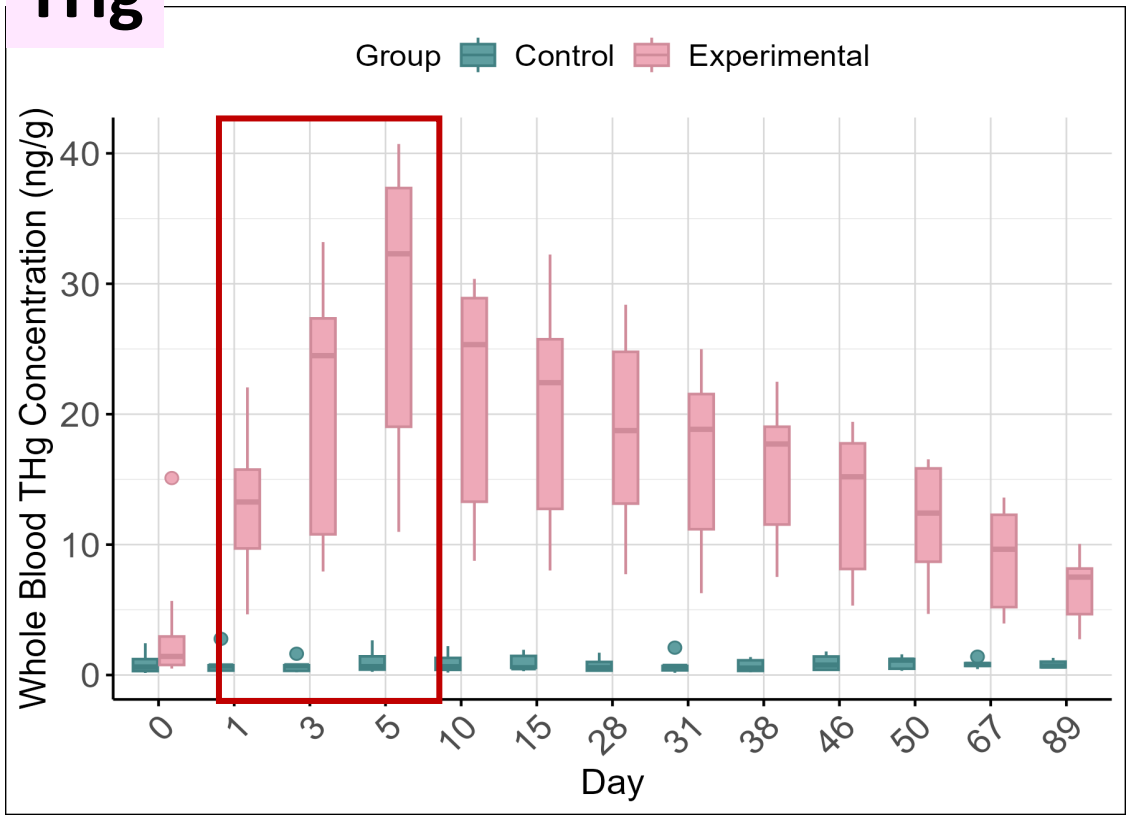
Increased Se retention with higher Hg exposure?


A
2.4
2.3
2.2
log wb Se
-0.6
-0.2
0.2
0.6
1.0
log wb THg
y = 0.09x + 2.21, R² = 0.305, p = 0.027
y = 0.2x + 2.15, R² = 0.798, p = 0.003

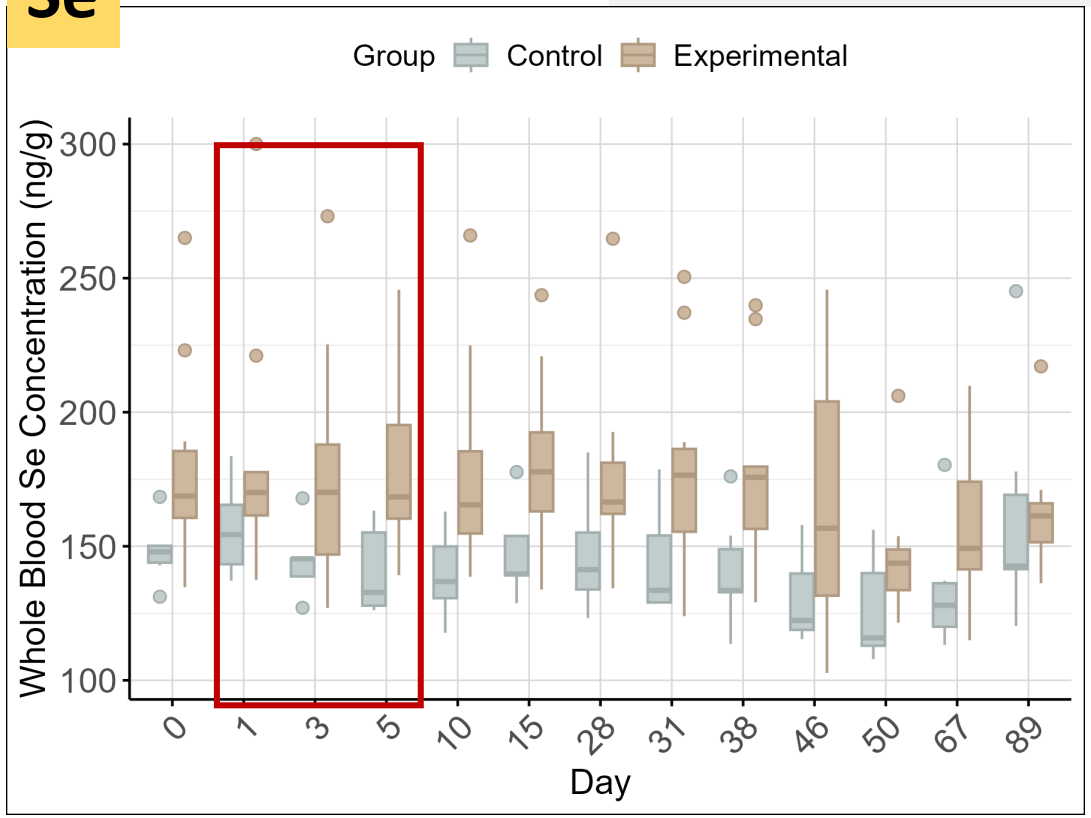

C
1.6
1.4
1.2
log u Se
-0.6
-0.2
0.2
0.6
1.0
log wb THg
y = -0.15x + 1.45, R² = 0.128, p = 0.19
y = -0.53x + 1.66, R² = 0.871, p = 7e-04

WHOLE BLOOD

THg



Se



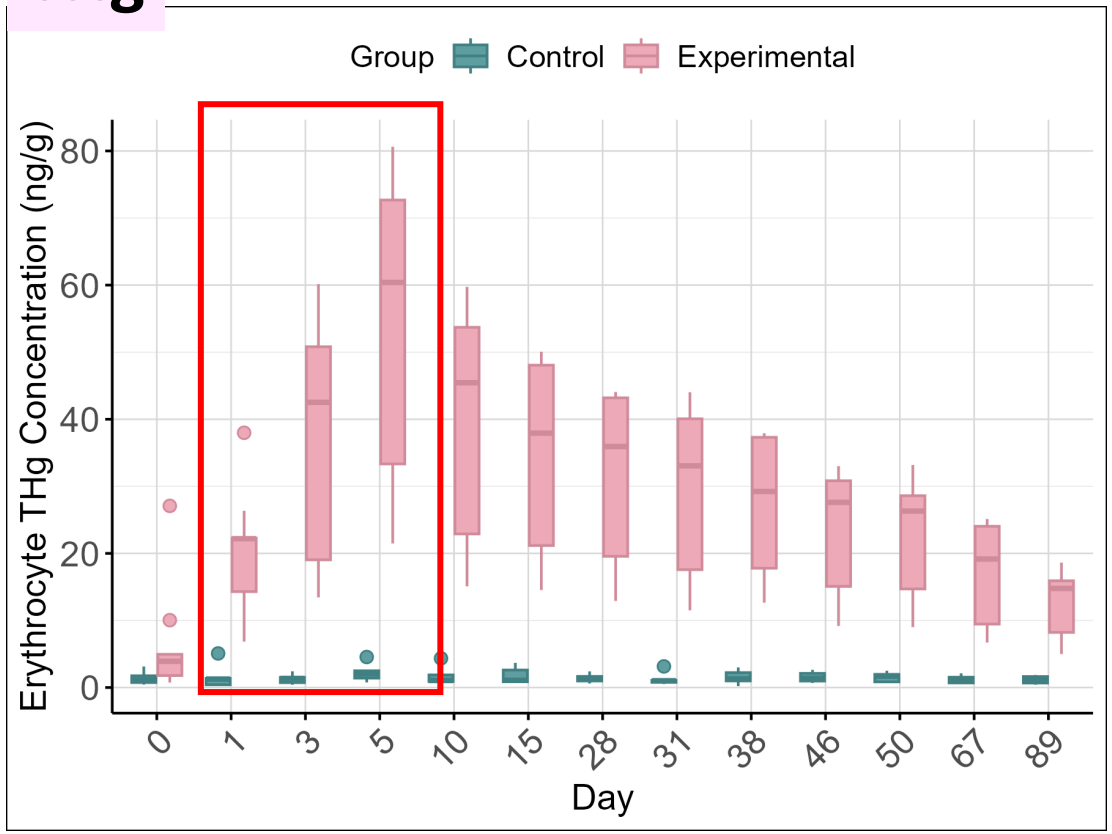
During the exposure:

- the increase in wb THg and wb MeHg proportional to dose per kg body weight
- the increase in whole blood Se was within a few percent of their initial values

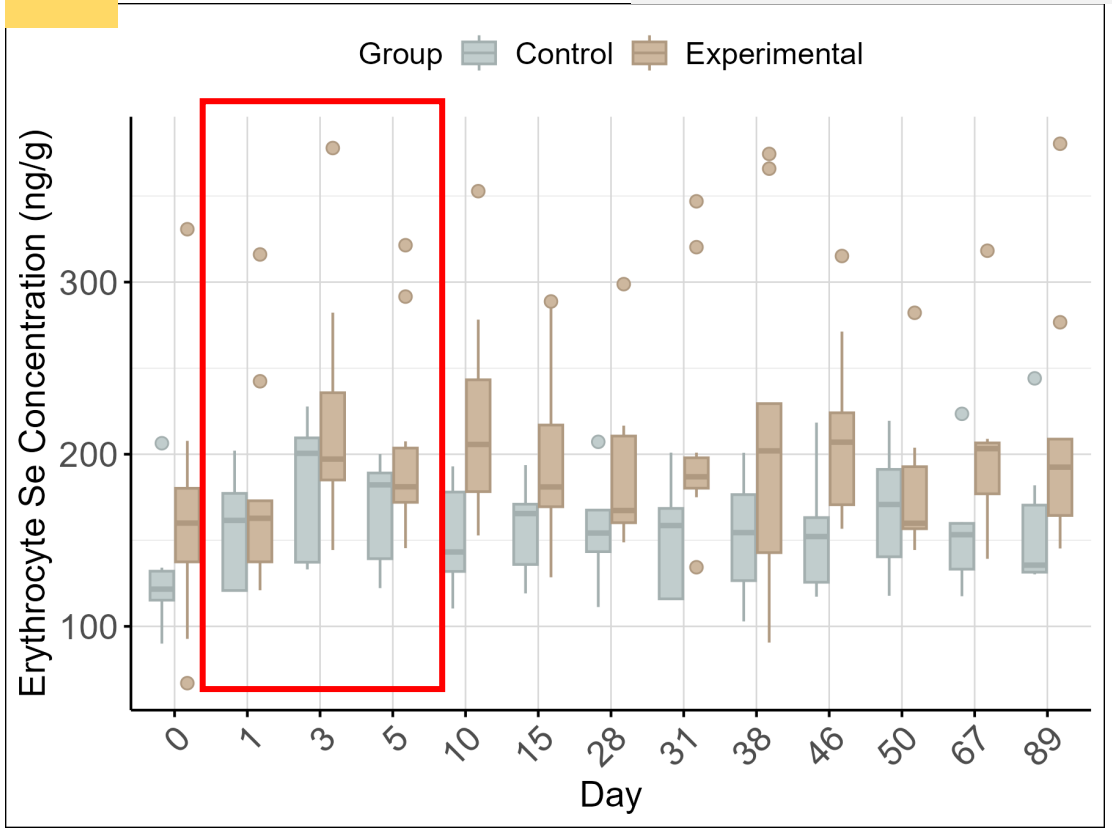
Increase in whole blood Se was not dependent on the Se dose ingested, nor did it follow the THg (MeHg) trend in the whole blood.

ERYTHROCYTES

THg



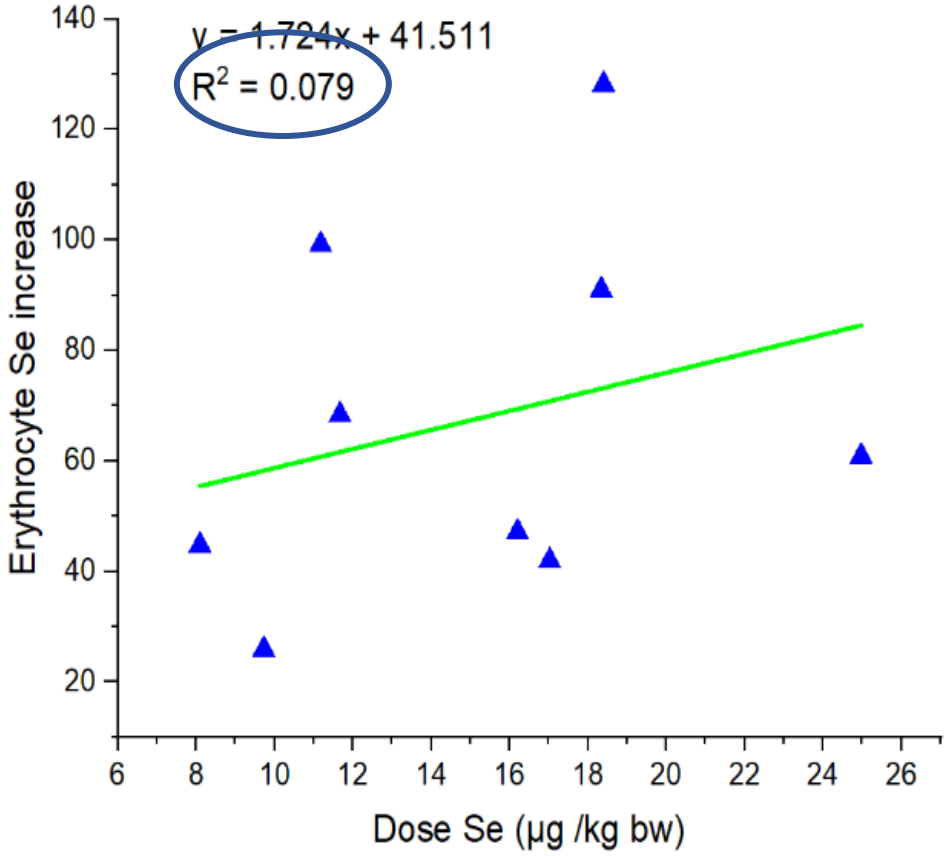
Se

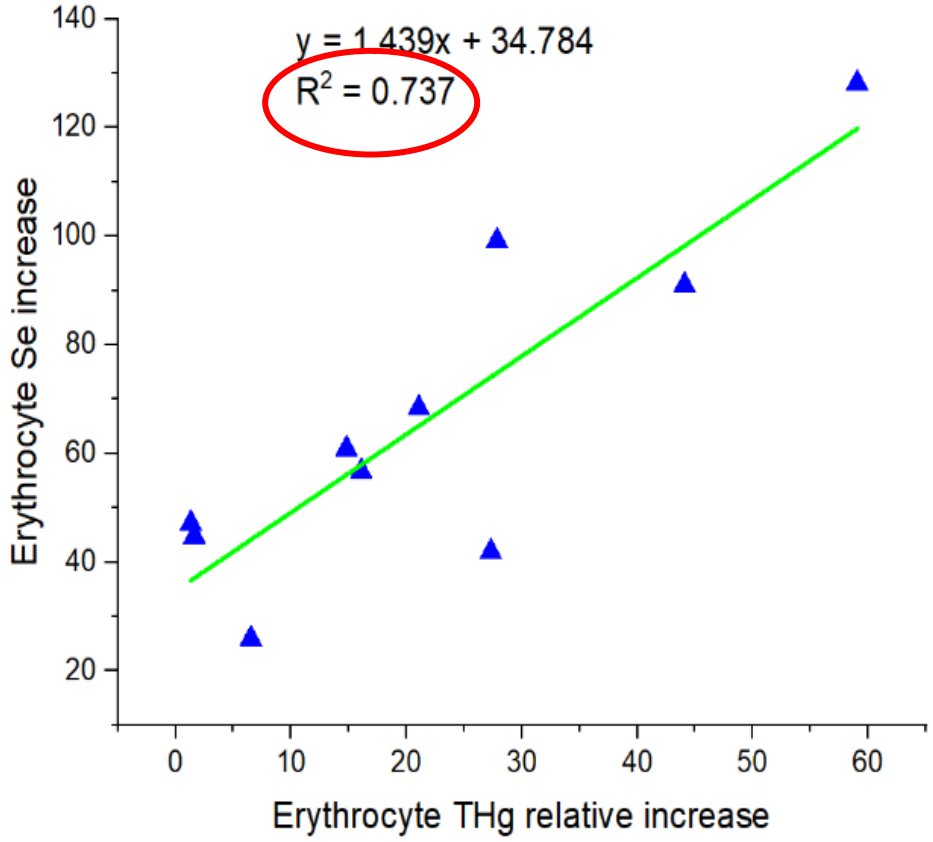


Se levels in the erythrocytes **rose significantly** following tuna consumption, and also **remained elevated** significantly above their initial values for the whole duration of the experiment.

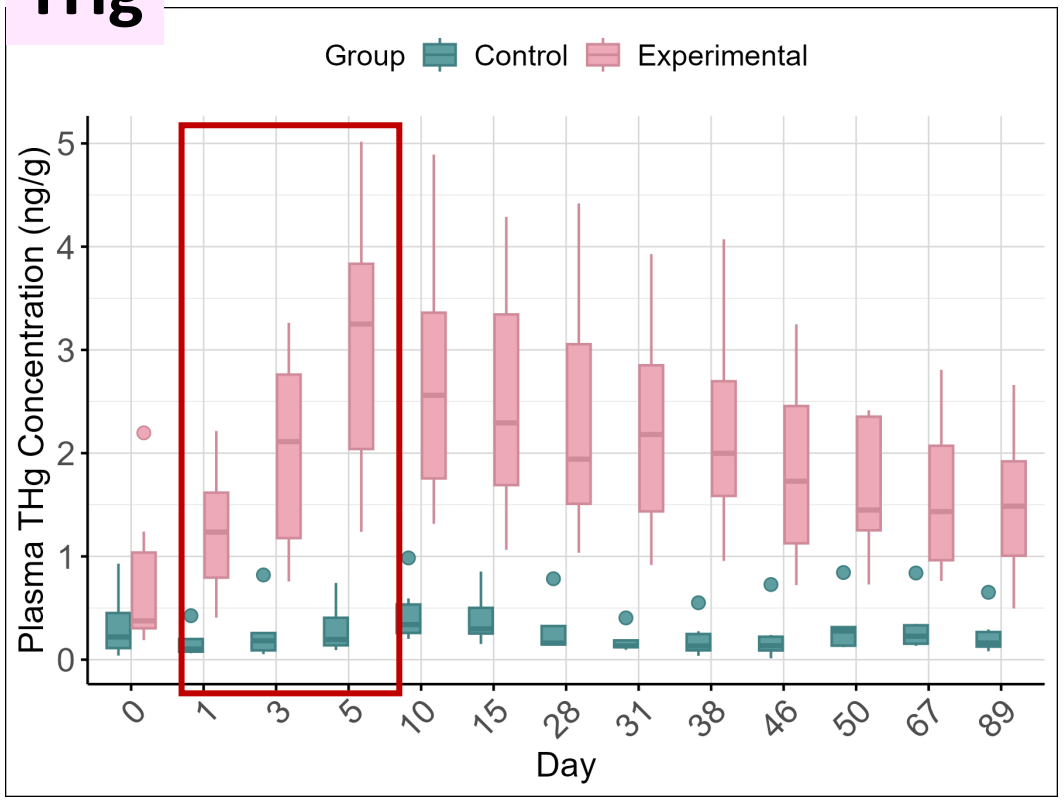
On the group level, **the maximum increases in erythrocyte Se were very weakly correlated with the dose Se ingested**.

The **maximum increases of erythrocyte Se were strongly correlated with the relative increase of erythrocyte THg.**

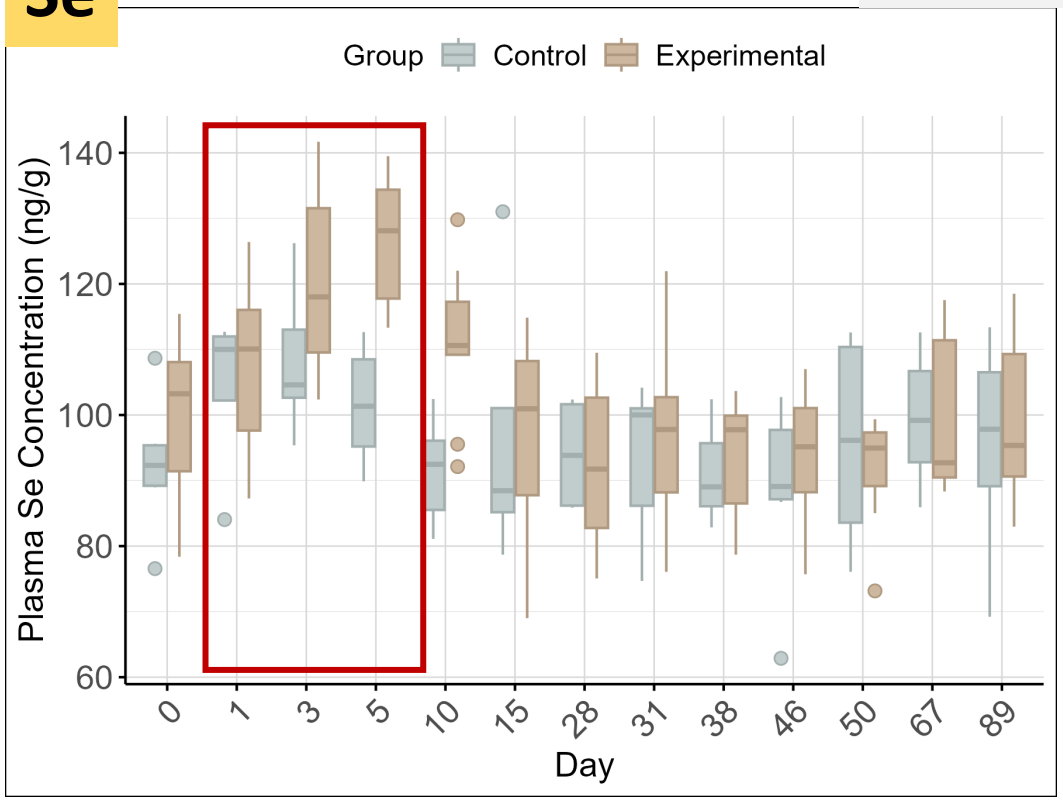




THg



Se

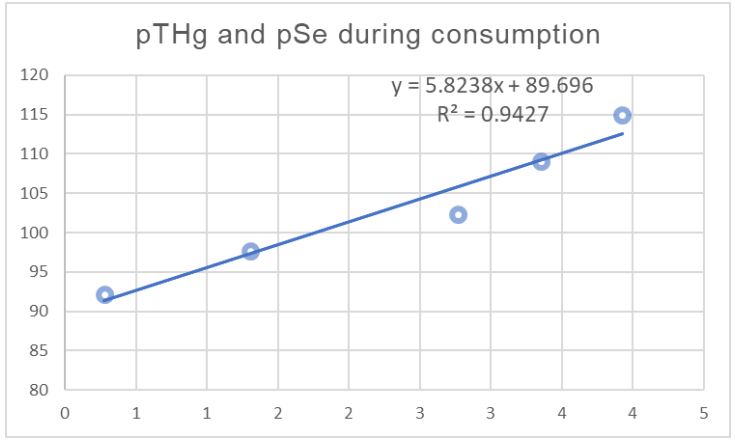


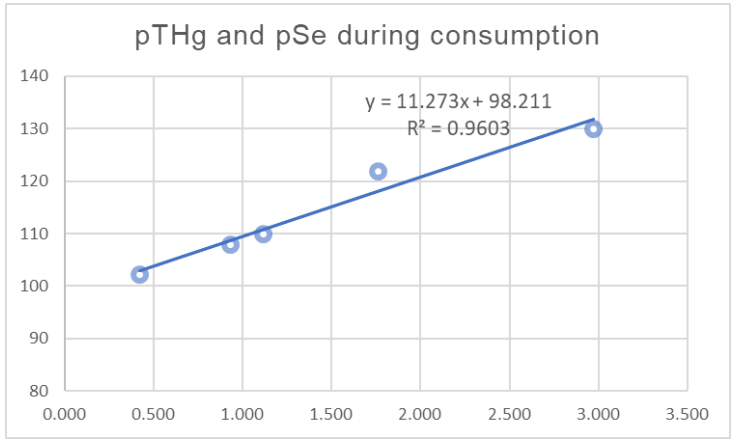
Plasma Se **rises throughout the exposure week**, reaching the maximum at the same time as THg (MeHg).

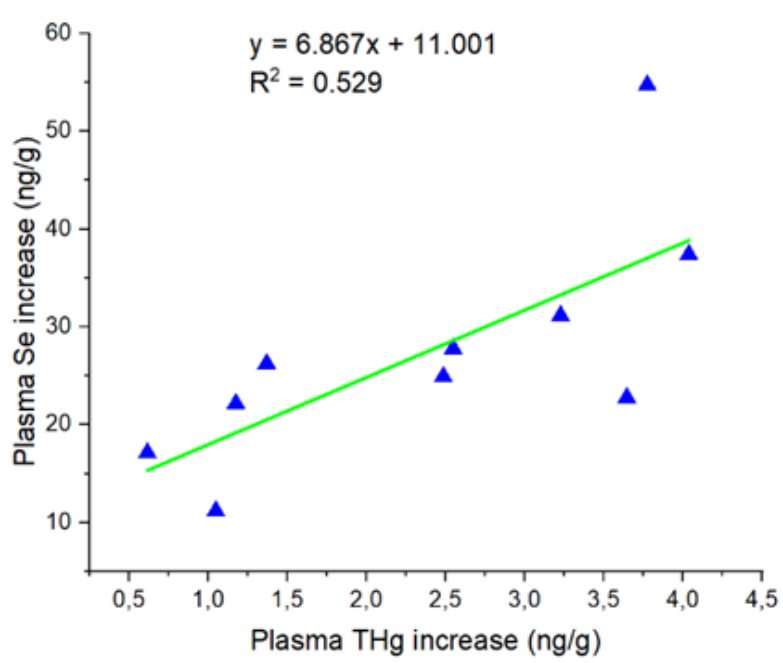
Plasma Se **did not remain elevated** for the rest of the experiment.

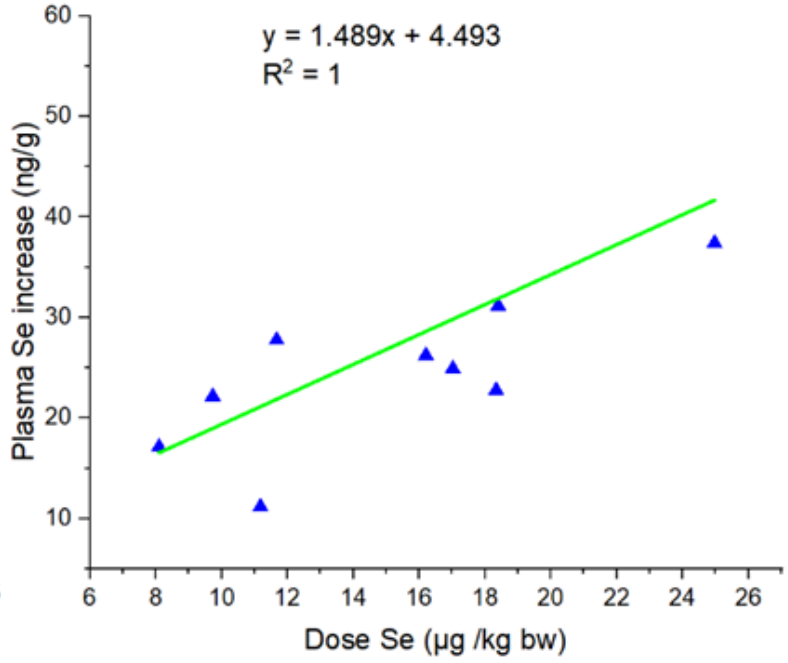
On individual level, plasma Se and plasma THg (MeHg) were positively correlated during the tuna consumption week.

On the group level, the maximum increases in plasma Se were strongly positively correlated with the maximum increases in plasma THg and plasma MeHg **but also** with the dose Se per kg bw.



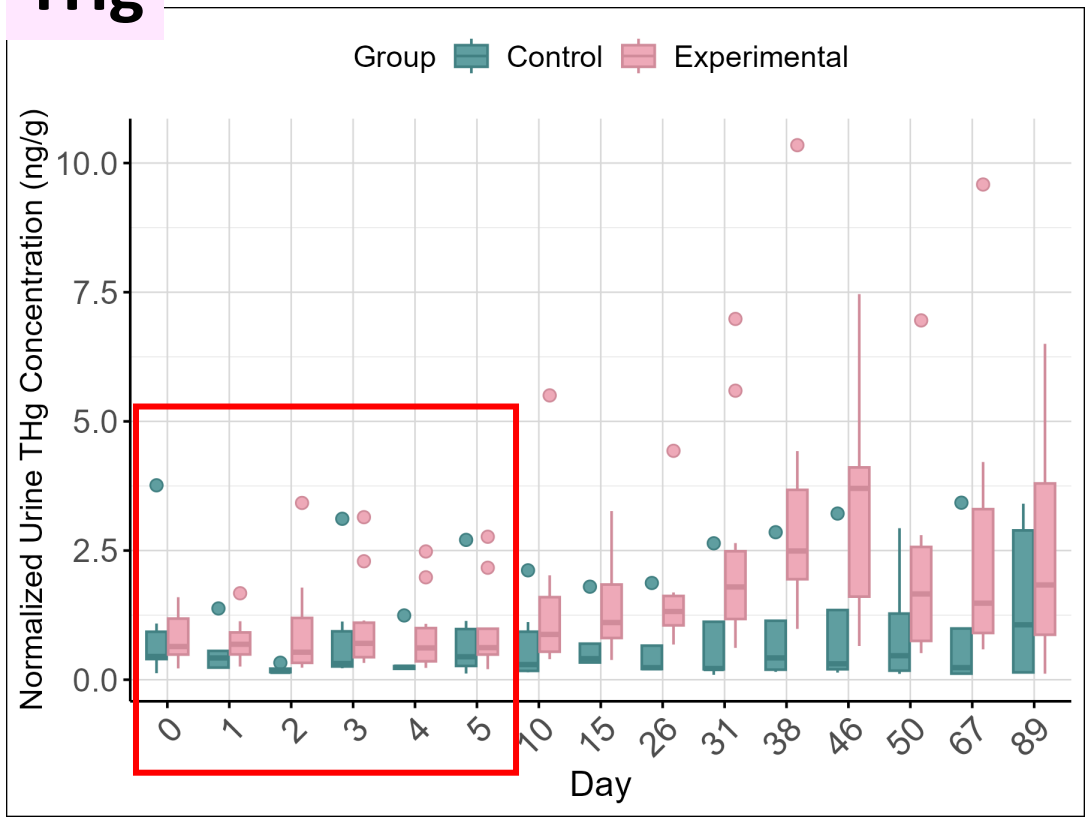




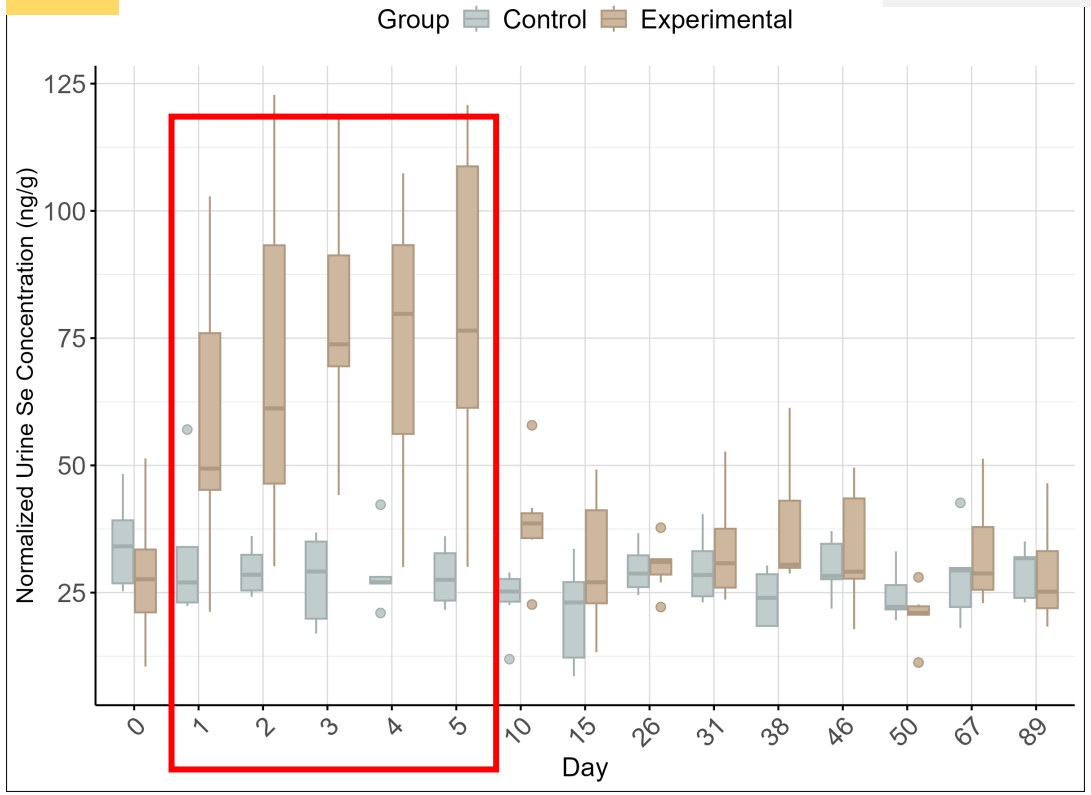


URINE

THg

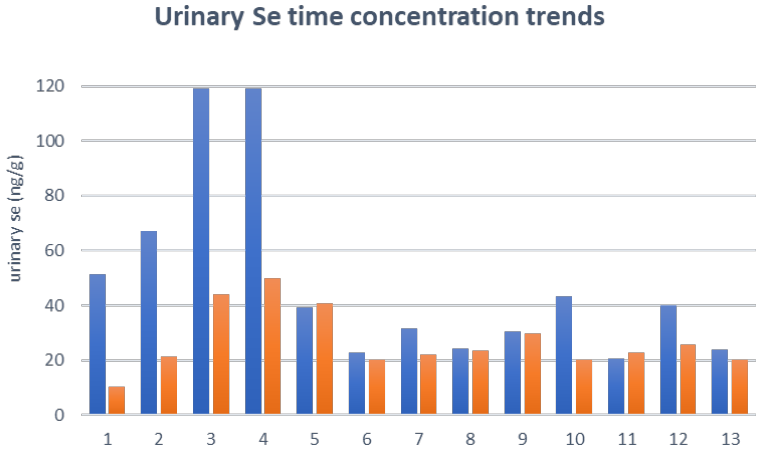


Se



THg and Se in urine did not follow the same trend. During the exposure week, urinary **THg did not change significantly**, while there was an **immediate increased excretion of Se**.

Large individual differences of time-concentration profiles of Se in urine!



Discussion and conclusions

Without the speciation, it is very difficult to draw conclusions!

- **Whole blood Se almost unchanged throughout - did not show any conclusive trends.**
- **In the plasma, Se concentrations increased over the tuna consumption period:**
  - could be a consequence of ingested Se from fish **OR**
  - a dynamic response to increasing Hg concentrations

Plasma response to dietary Se is **dependent on the Se species** (according to the literature, SeN will not lead to an increase in plasma selenoproteins)

- **In the erythrocytes**, Se increase was very weakly dependent on the Se dose, but was strongly positively correlated with the relative increase in erythrocyte (Me)Hg **AND** remained elevated for the rest of experiment – **indicative of a dynamic response**?

Thank You for Your attention!

adna.alilovic@ijs.si
milena.horvat@ijs.si

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