

# Effects of low zinc status and arsenic exposure in mice

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## BACKGROUND

### Role of zinc

- Zinc is an essential micronutrient which is involved in numerous cellular processes including its role as an antioxidant, and maintaining DNA integrity
- Approximately 12% of Americans do not consume the estimated average requirement for zinc

### Arsenic exposure

- Arsenic is a naturally occurring element found within the earth's crust
- Humans typically come into contact with arsenic through contaminated food and water sources
- Arsenic exposure is associated with an increase in reactive oxygen species (ROS) which have many negative health effects
- It is estimated that 34 million Americans are drinking water containing arsenic above tolerable levels

### Low zinc status and arsenic exposure are associated similar health concerns

- Zinc deficiency and arsenic exposure are associated with the onset and progression of diabetes, cancer, and liver disease
- Both have been shown to elicit oxidative stress which is a contributing factor to the development of these diseases
- Irregular levels of zinc or arsenic may affect overall mineral balance leading to secondary deficiency

## HYPOTHESIS

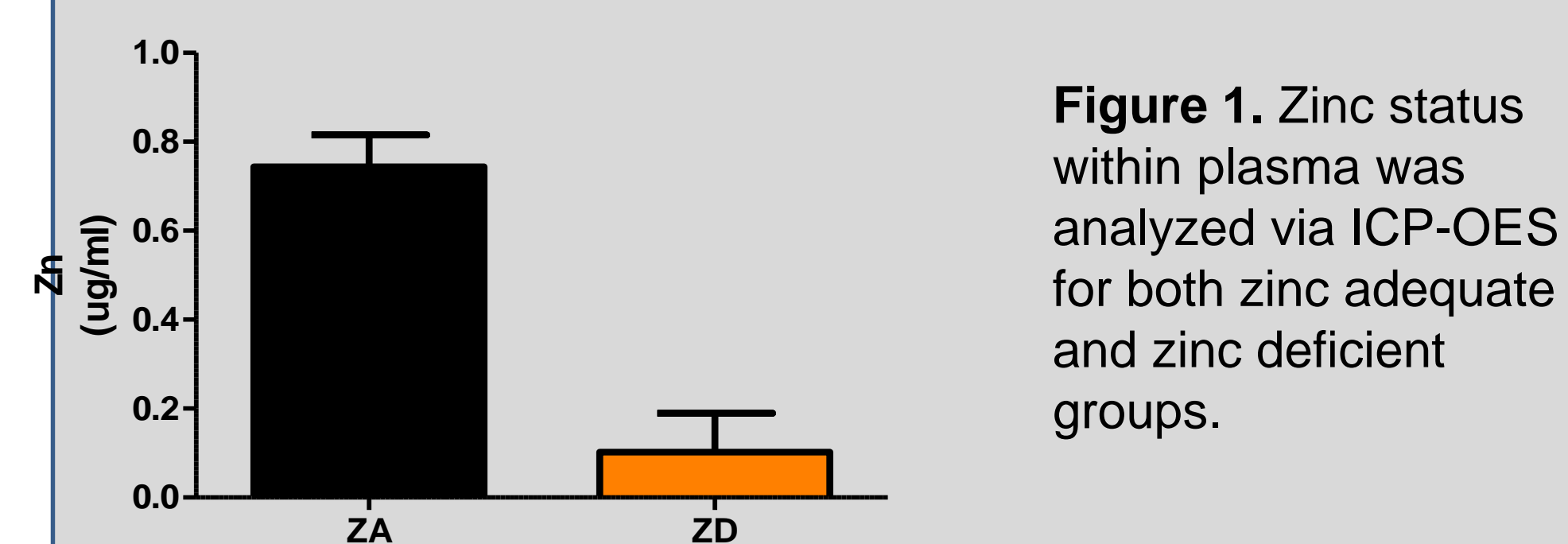
### Overall Goal:

The goal of this study was to determine if zinc deficiency or arsenic exposure caused an increase in oxidative damage and affected overall mineral content

### Hypothesis:

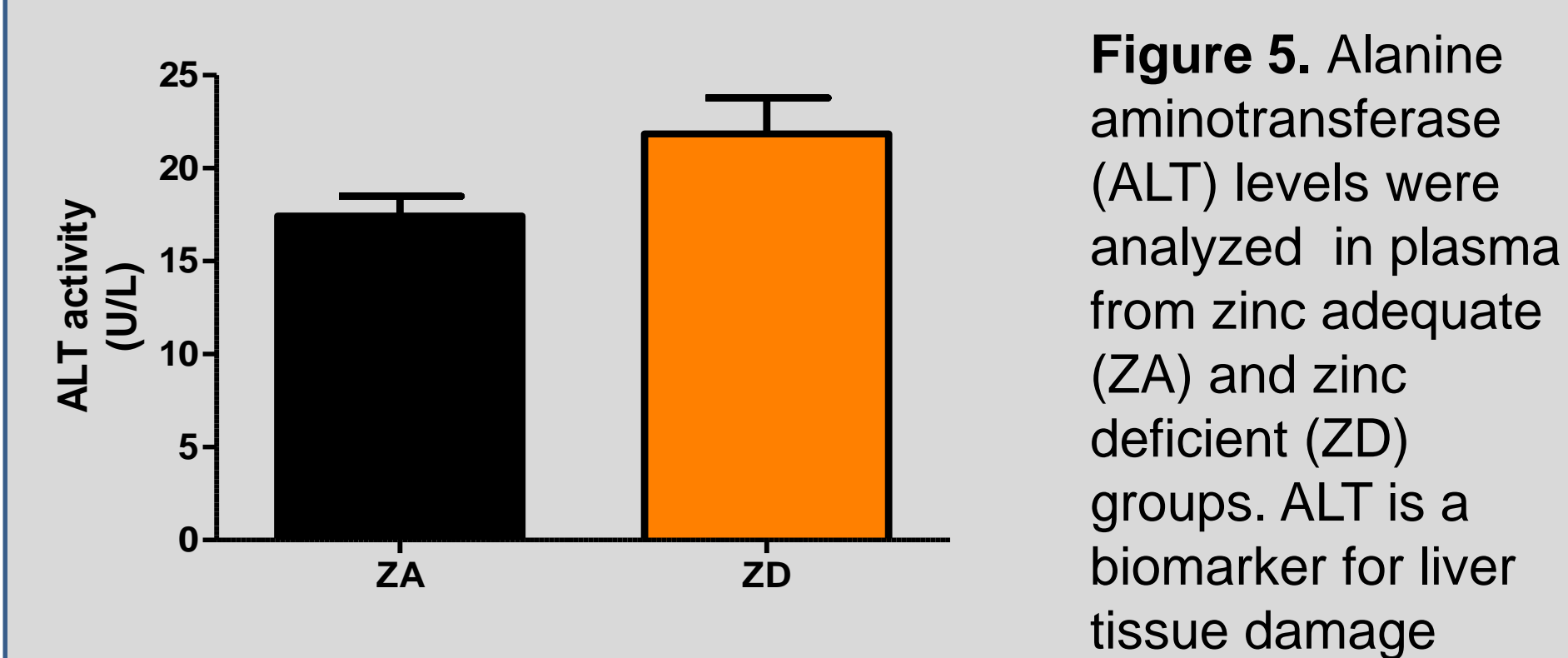
Our hypothesis is that arsenic exposure will cause mineral imbalance and that both arsenic and zinc deficiency will enhance oxidative damage

## ZINC DEFICIENT DIET RESULTED IN LOW ZINC STATUS



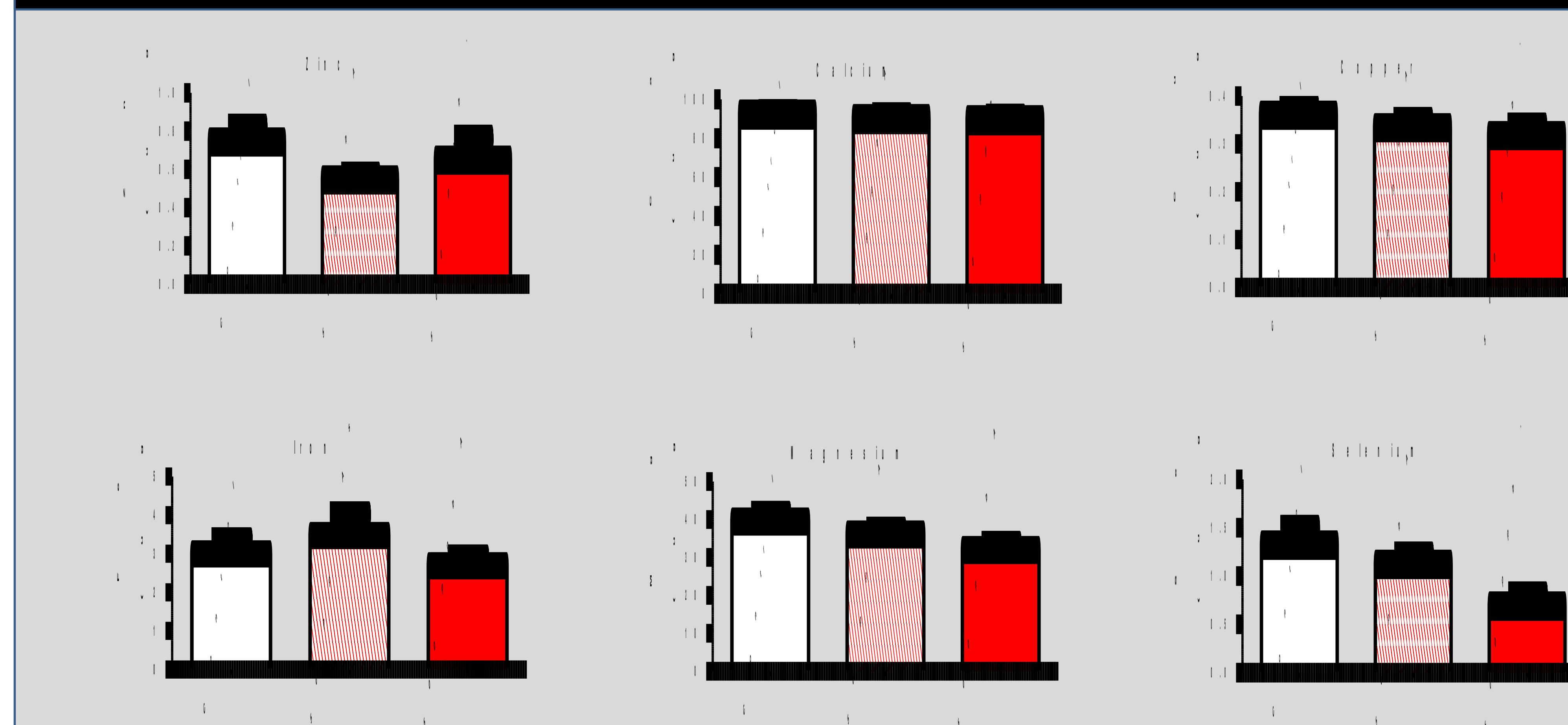
**Figure 1.** Zinc status within plasma was analyzed via ICP-OES for both zinc adequate and zinc deficient groups.

## ZINC DEFICIENCY INCREASED LIVER TISSUE DAMAGE



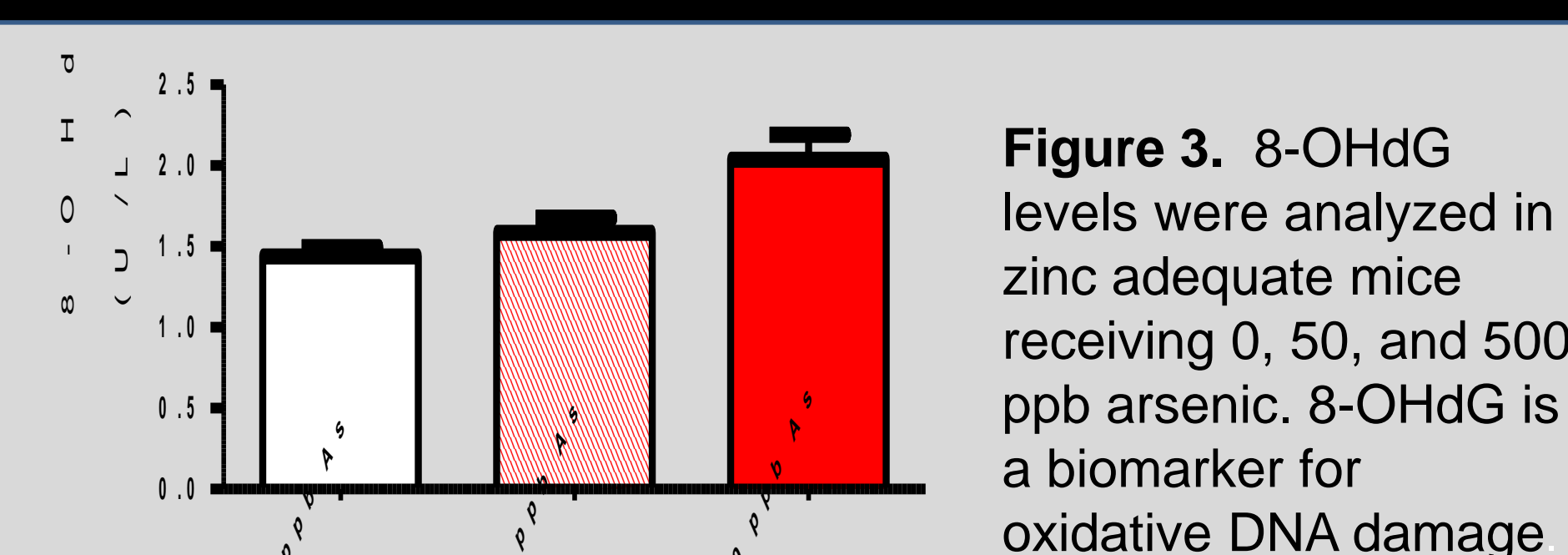
**Figure 5.** Alanine aminotransferase (ALT) levels were analyzed in plasma from zinc adequate (ZA) and zinc deficient (ZD) groups. ALT is a biomarker for liver tissue damage

## ARSENIC EXPOSURE REDUCED MAGNESIUM AND SELENIUM CONTENT IN PLASMA



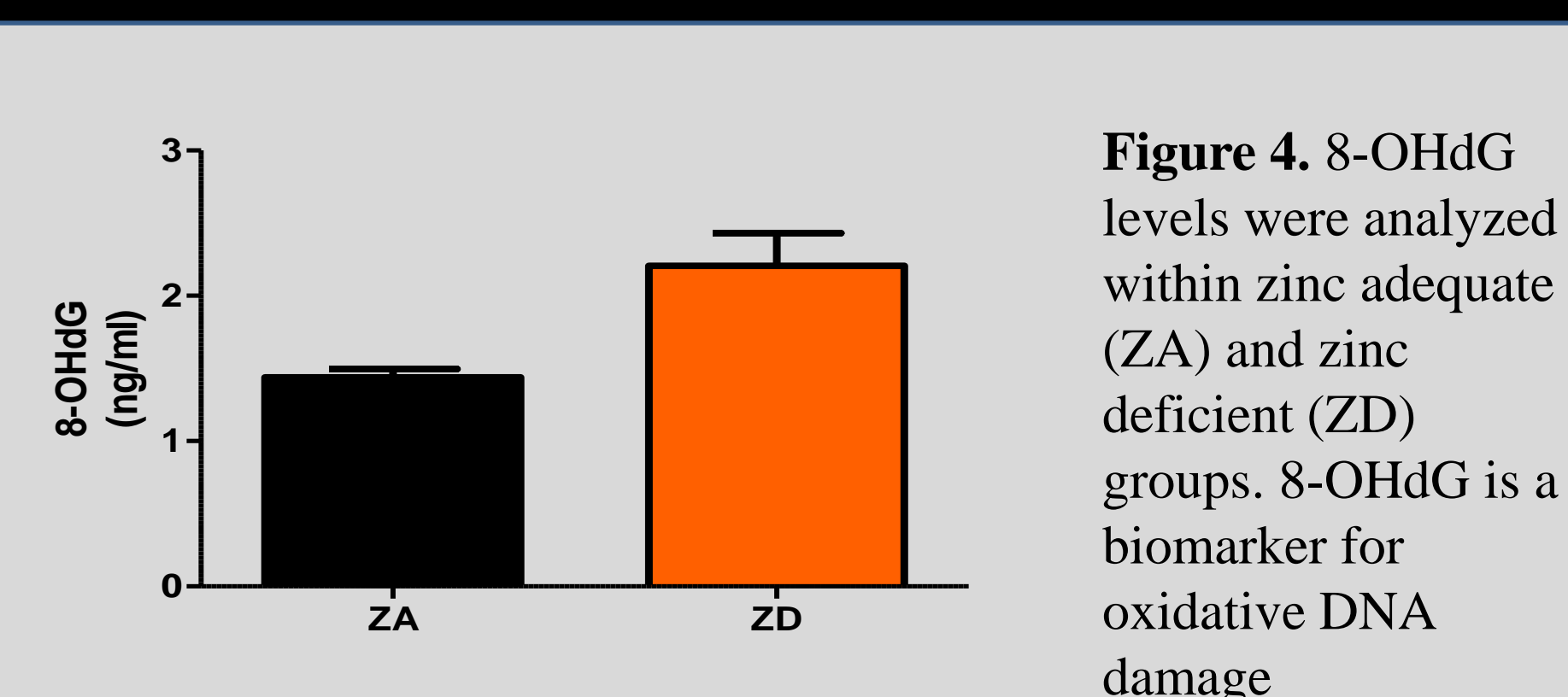
**Figure 2.** Mineral status within plasma was analyzed via ICP-OES to determine mineral content for calcium, copper, iron magnesium, selenium, and zinc. Although arsenic exposure effected magnesium, and selenium content, it did not have an impact on the other listed minerals

## ARSENIC EXPOSURE INCREASED OXIDATIVE DNA DAMAGE



**Figure 3.** 8-OHdG levels were analyzed in zinc adequate mice receiving 0, 50, and 500 ppb arsenic. 8-OHdG is a biomarker for oxidative DNA damage

## ZINC DEFICIENCY INCREASED OXIDATIVE DNA DAMAGE



**Figure 4.** 8-OHdG levels were analyzed within zinc adequate (ZA) and zinc deficient (ZD) groups. 8-OHdG is a biomarker for oxidative DNA damage

## STUDY DESIGN

| Zinc deficiency     | N |
|---------------------|---|
| Zinc adequate (ZA)  | 8 |
| Zinc deficient (ZD) | 8 |
| Arsenic exposure    | N |
| Control (0 ppb As)  | 8 |
| 50 ppb As           | 8 |
| 500 ppb As          | 8 |

- 3 wk old C57Bl/6 females were randomly assigned to dietary or arsenic treatment for 4 wk in single housed wire suspension cages.

## MATERIALS AND METHODS

- Diet: Purified egg white based AIN-93G Diets were made by Research Diets Inc. Zinc adequate diet contains 30ppm zinc, and zinc deficient diet contains 0ppm zinc.
- Arsenic was added in the drinking water at 0, 50, and 500 ppb and were fed the 30ppm zinc adequate diet.
- Mineral analyses: Mineral analyses were done using ICP-OES (inductively coupled plasma optical emission spectrometry) at W. M. Keck Collaboratory for Plasma Spectrometry
- Liver damage: Plasma ALT (alanine aminotransferase) levels were determined as a biomarker for liver damage (Thermo Scientific).
- Oxidative DNA damage: Oxidative DNA damage was determined in liver genomic DNA using 8-OHdG DNA Damage ELISA (Cell Biolabs, Inc.)

## SUMMARY

- Arsenic exposure reduced magnesium and selenium content within plasma, but did not appear to effect the status of zinc, calcium, copper or iron
- Both zinc deficiency and arsenic exposure increased levels of 8-OHdG, which is a marker for oxidative DNA damage
- Zinc deficiency increased levels of ALT, which is an indicator of tissue damage in the liver

- Future studies are needed to determine if the effects of zinc deficiency enhance the damaging effects of arsenic exposure. Future studies will also utilize a more relevant "moderate" zinc deficient diet