

The impact of Zinc Status and bioavailability on enterocytes as model for the gastrointestinal tract to understand gut-brain signalling in health and disease

Clara Emilia Vitense

Introduction

- In the past decades, the prevalence of autism spectrum disorders (ASD) especially in children has increased significantly. Comparing periods from 1994-1999 and 2015-2019 the global prevalence for ASD increased by nearly 400% [1]. ASD are not only a challenge to families but also socio-economically.
- Interestingly, apart from their core behavioural symptoms, many individuals with ASD show symptoms associated with abnormalities in the gastrointestinal (GI) tract, such as leaky gut syndrome, inflammatory bowel diseases, and constipation/diarrhoea.
- Recently, the maternal zinc status has been proposed as ASD risk factor, contributing disruptions in central nervous system but also the GI system, including compromised gut lining integrity.
- This phenomenon has the potential of contributing to the understanding of how GI comorbidities and ASD are linked and thus give more information about the gut-brain axis.

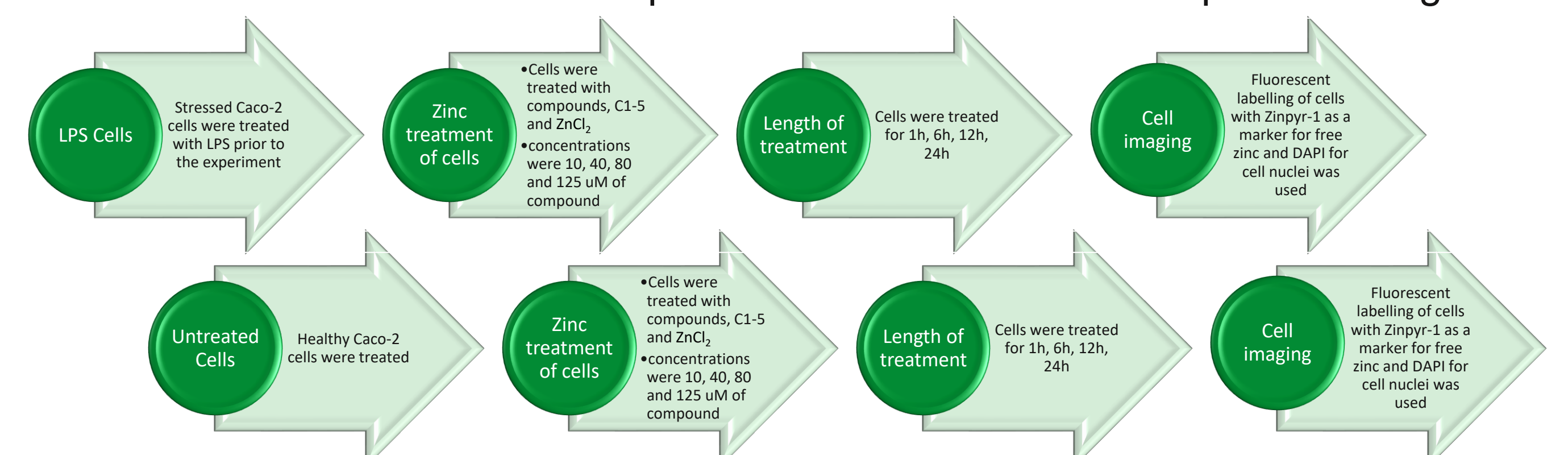
Here, the effect of different zinc supplements, concentrations and lengths of treatment on the growth of immortalized Colorectal Adenocarcinoma cells (Caco-2) as model for the GI system and the impact of zinc status is investigated

Objectives

1. Investigate the effect of different zinc supplements on zinc status in the gut using Caco-2 cells as a 2D model, while exposing the cells to different zinc concentrations and treatment durations.
2. Understand the effect inflammation (modelled by pre-treatment with LPS for 24h) has on zinc status of enterocytes modelled by Caco-2 cells

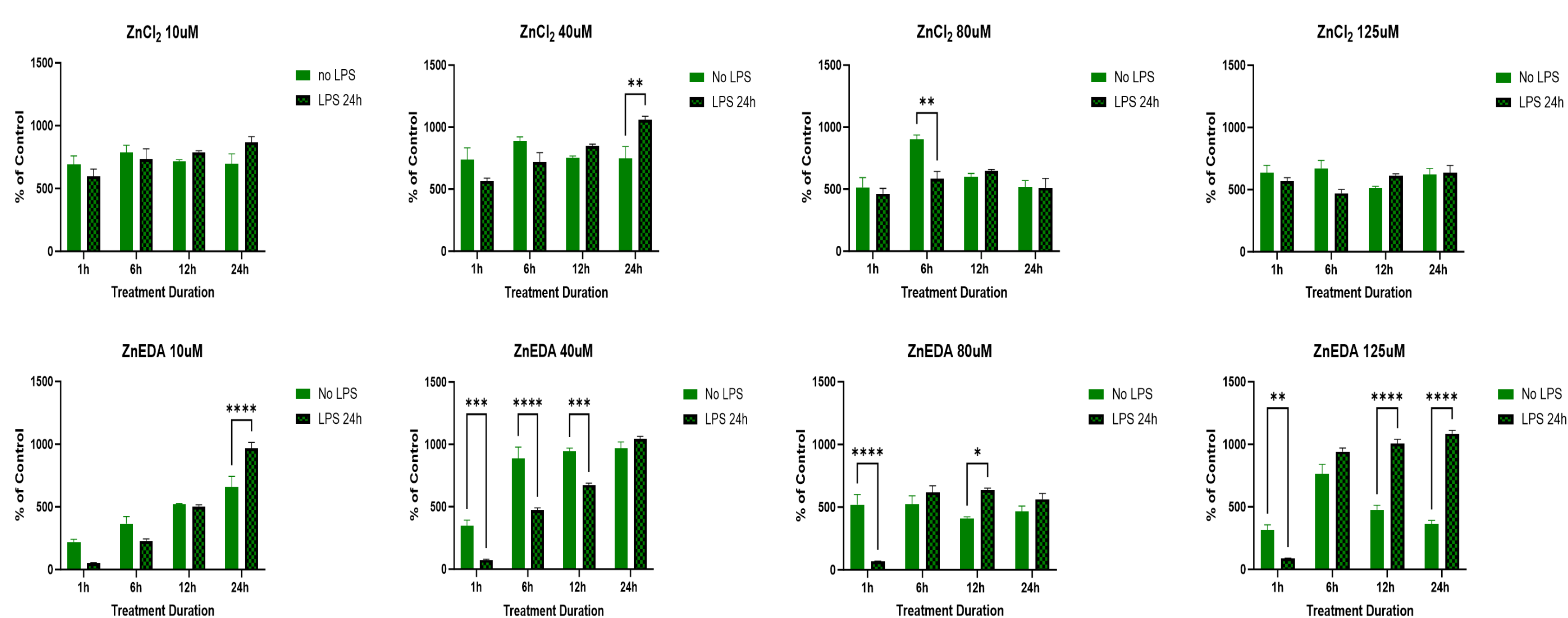
Methodology

Caco-2 cells were seeded in 24- well plates on PLL coated coverslips according to:



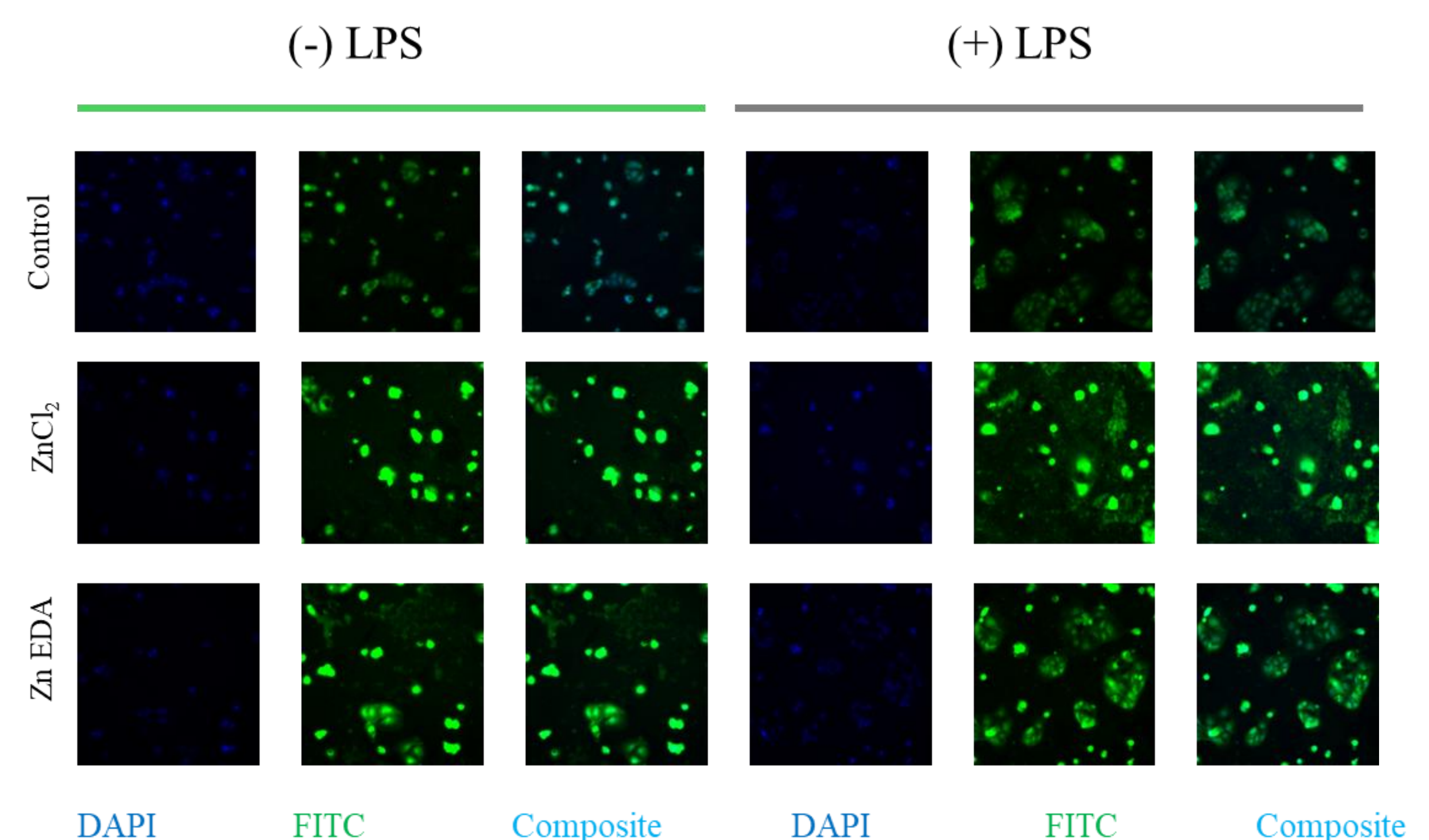
- High-resolution imaging using ImageXpress Confocal microscope was performed to evaluate the final zinc uptake by the cells.
- Using the mean grey value the amount of zinc taken up was determined.

Results



The diagrams represent different lengths of ZnEDA and ZnCl₂ at inclining concentrations with respect to the percentage control of untreated cells

Exemplary Images



Exemplary images taken of caco-2 cells pre-treated with LPS and not pre-treated with LPS for 24h and subsequently treated with ZnCl₂, ZnEDA and Availa Zn for 12h. Cells were stained with DAPI and Zinpyr-1 and imaged using fluorescent microscopy

Discussion

Cells treated with LPS were observed to have a lowered zinc uptake rate when the bioavailability of zinc was low at various treatment lengths compared to the healthy cells. In contrast, the zinc uptake rate of cells treated with LPS at higher concentrations of zinc compounds and lengths of treatment was higher than in the cells without prior treatment. The results showed that zinc supplementation is feasible using a broad range of concentrations and treatment durations

Conclusion

This research provided better understanding of zinc uptake and its link to cell health. The results will feed into further research to determine potentially beneficial effects using the optimal concentrations for zinc supplementation and using more complex cell systems such as intestinal organoids. Furthermore, there is the prospect of developing nutritional supplements to support maternal zinc adequacy during pregnancy.

Acknowledgments

I would like to thank the University of Limerick that enabled me to do this research. Special thanks to Dr. Andreas Grabrucker for his guidance, and to Katelyn O'Grady for her invaluable assistance.

References

- [1] Talantseva OI et al. The global prevalence of autism spectrum disorder: A three-level meta-analysis. Front Psychiatry. 2023 Feb 9;14:1071181. doi: 10.3389/fpsy.2023.1071181. PMID: 36846240; PMCID: PMC9947250.