

The Effect of Acetylsalicylic Acid on the Odontogenesis of Human Dental Pulp Cells

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Acetylsalicylic Acid (ASA, Aspirin)



Pharmacological Category

- Analgesic, Non-opioid
- Anti-platelet Agent
- Non-steroidal Anti-inflammatory Drug (NSAID), Oral
- Salicylate

“Epidemiologic studies revealed that **current aspirin users had significantly higher bone mineral density** compared with non-users according to quantitative computed tomography data”

(Carbone et al., 2003)

“A study has highlighted the **positive effect of aspirin in the treatment of ovariectomy-induced osteoporosis** through activating osteoblasts by increasing telomerase activity and inhibiting osteoclasts”

(Yamaza et al., 2008)

Cells that have been studied with Aspirin

- Stem cells from exfoliated deciduous teeth (SHEDs)
- Bone marrow stem cells (BMSCs)
- Periodontal ligament stem cells (PDLSCs)
- **Human dental pulp stem cells (hDPSCs)**



Osteogenesis

- Stem cells from apical papilla (SCAPs)



Odontogenesis

Acetylsalicylic Acid Treatment and Suppressive Regulation of AKT Accelerate Odontogenic Differentiation of Stem Cells from the Apical Papilla

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Aspirin Accelerates in Odontogenic Differentiation of SCAPs

- ASA accelerates **in vitro and in vivo odontogenic differentiation** of SCAPs
- Functional suppression of the PI3K-AKT signaling pathway was associated with **RUNX2 down-regulation and DSPP up-regulation** in odontogenic differentiation of SCAPs under ASA stimulation.

(Tanaka et al., 2019)

Aspirin promotes osteogenic differentiation of human dental pulp stem cells

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- Aspirin was **non-toxic** to hDPSCs at a concentration of $\leq 100 \mu\text{g/ml}$ and **enhanced the osteogenesis** of hDPSCs *in vitro*.
- Aspirin significantly **increased hDPSC-based bone formation in vivo** in the rat cranial defect model at 8 or 12 weeks post-implantation

(Yuan et al., 2018)

Research Questions

- Does the ASA have an inductive effect on **the proliferation, odontogenic differentiation and mineralization** of dental pulp cells in vitro?
- If yes, what is the optimal concentration of ASA that can mostly enhance the inductive effect on **the proliferation, odontogenic differentiation and mineralization** of dental pulp cells in vitro?

Hypothesis

The acetylsalicylic acid (ASA) at an optimal concentration has an **inductive effect** on dental pulp cell proliferation, differentiation and mineralization *in vitro*

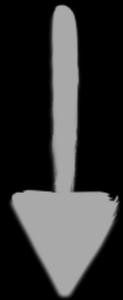
Expected Outcome

The ASA would be beneficial for future development of **new composition of the pulp capping materials** leading to clinical success of dental tissue reparation and regeneration

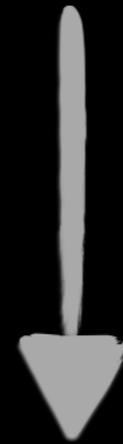
Materials and Metho

Concentration in This Study

0, 25, 50, 75, 100, 200 $\mu\text{g/ml}$



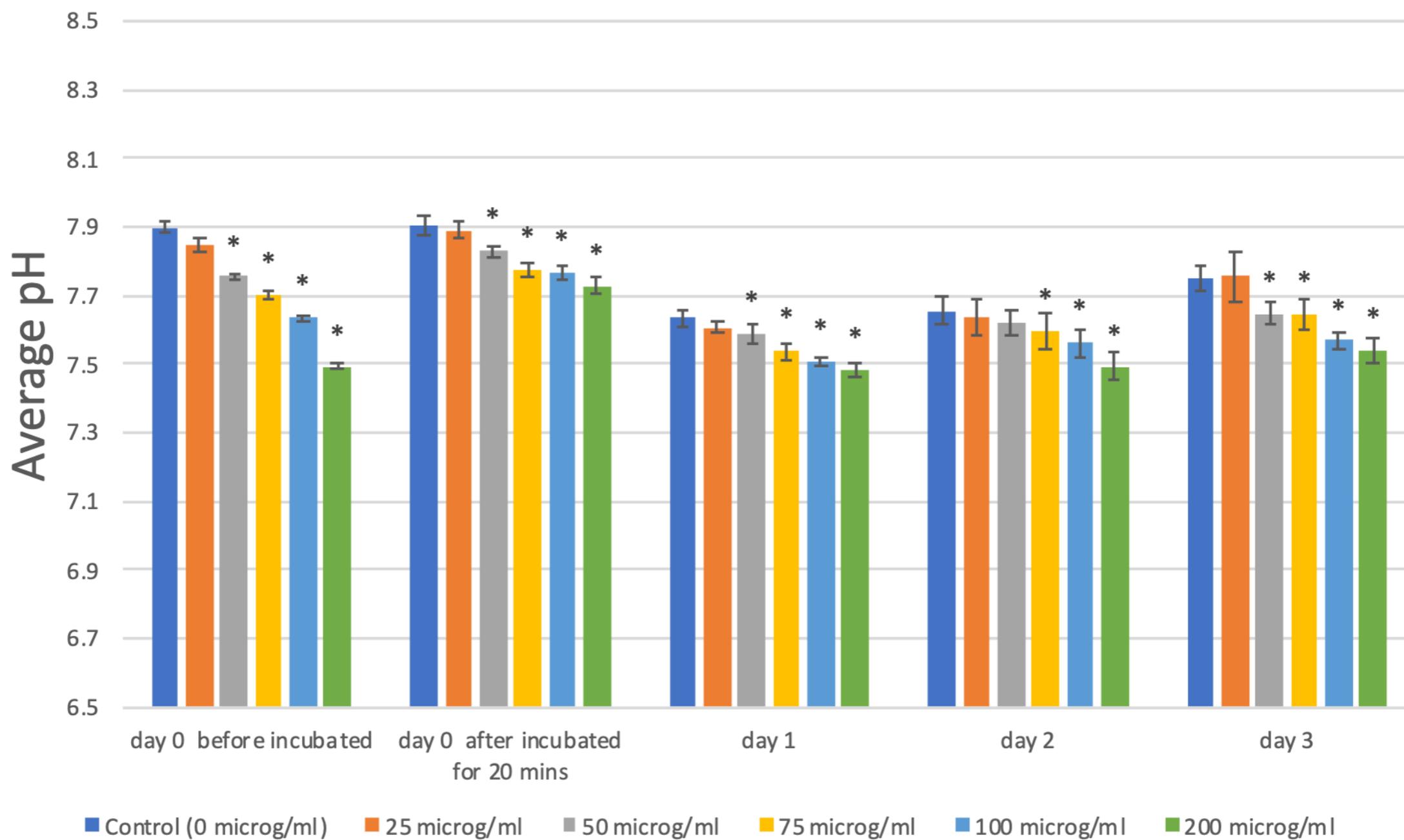
Control



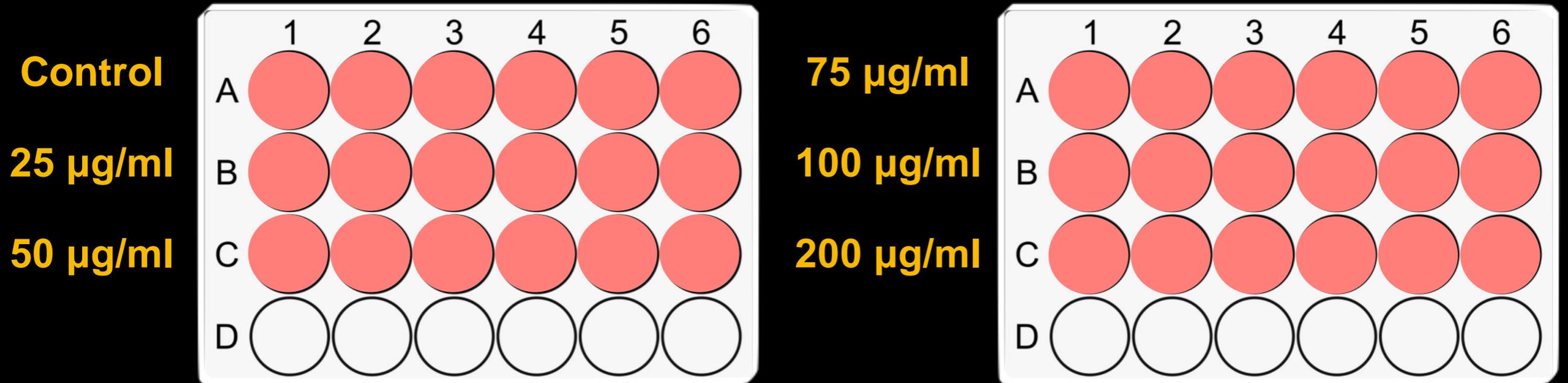
**To see
the negative effect**

ASA pH

ASA pH Monitoring Graph
(3 day-incubation)



Experimental Design



6 Groups
for 4 time points

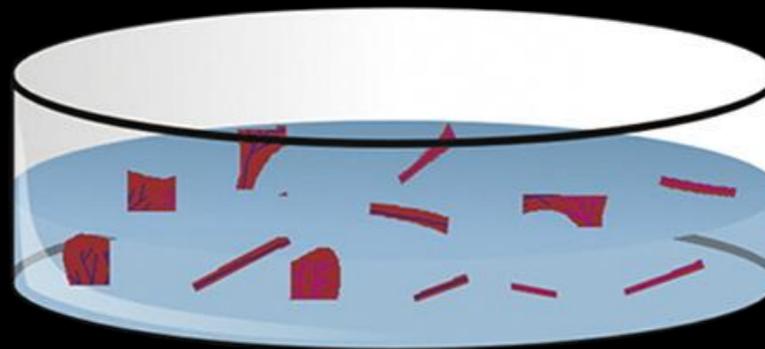
16h

7d

14d

21d

Isolation and Culture of Human Dental Pulp Cells



Laboratory culture

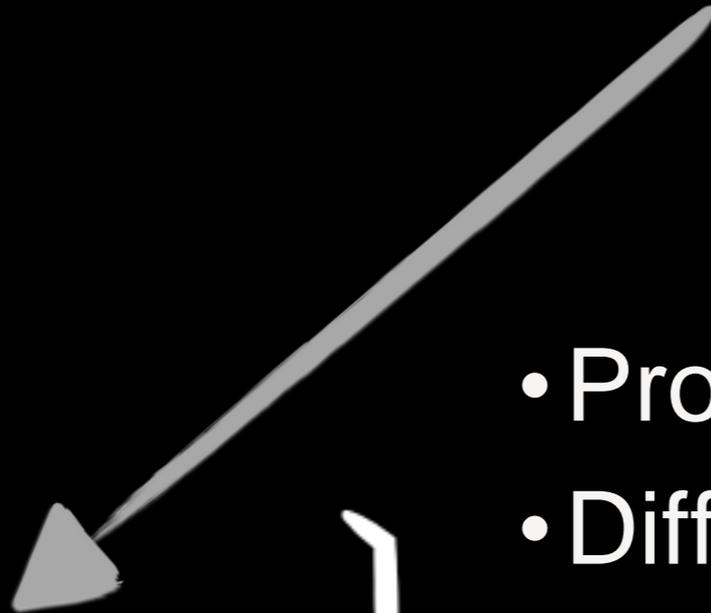


1st passage



80-90% cell
confluence

2nd passage

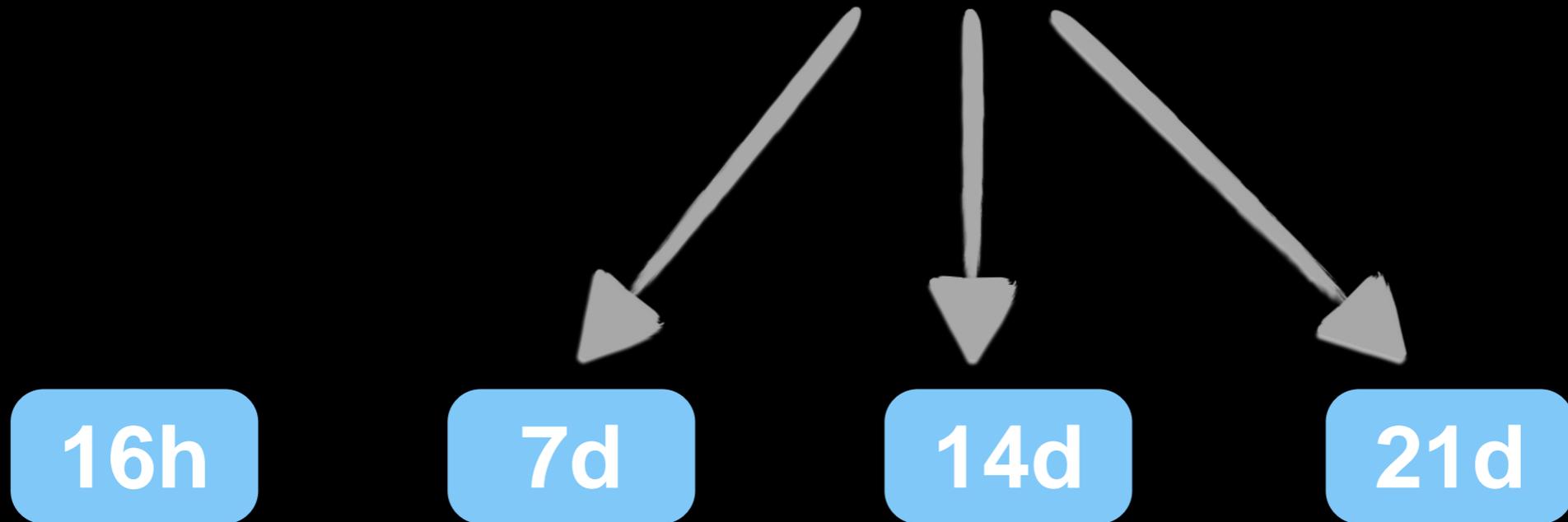


- Proliferation
- Differentiation
- Mineralization

Experiments

**ANOVA
&
T-test**

Add differentiation media

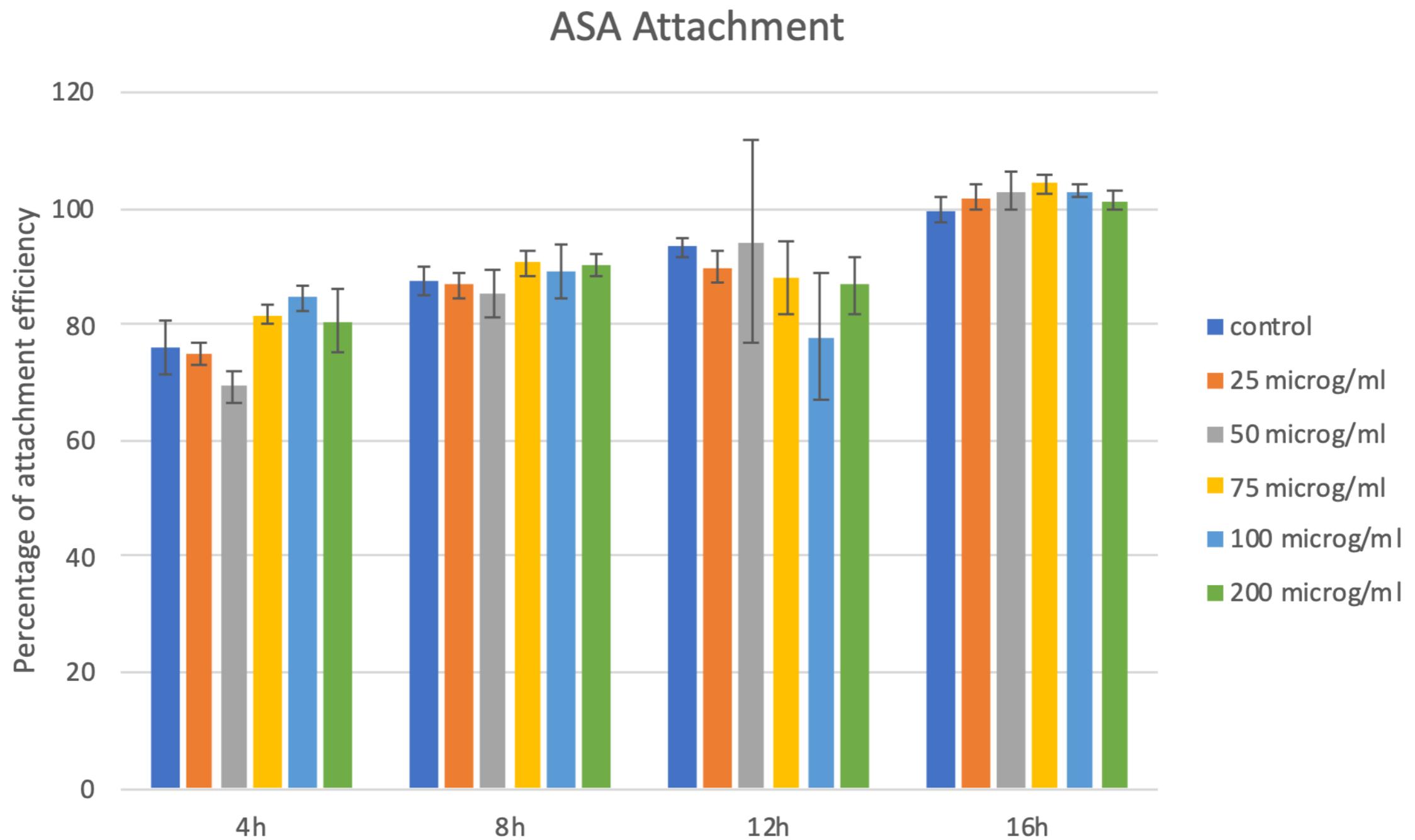


Collect supernatant > ALP assay

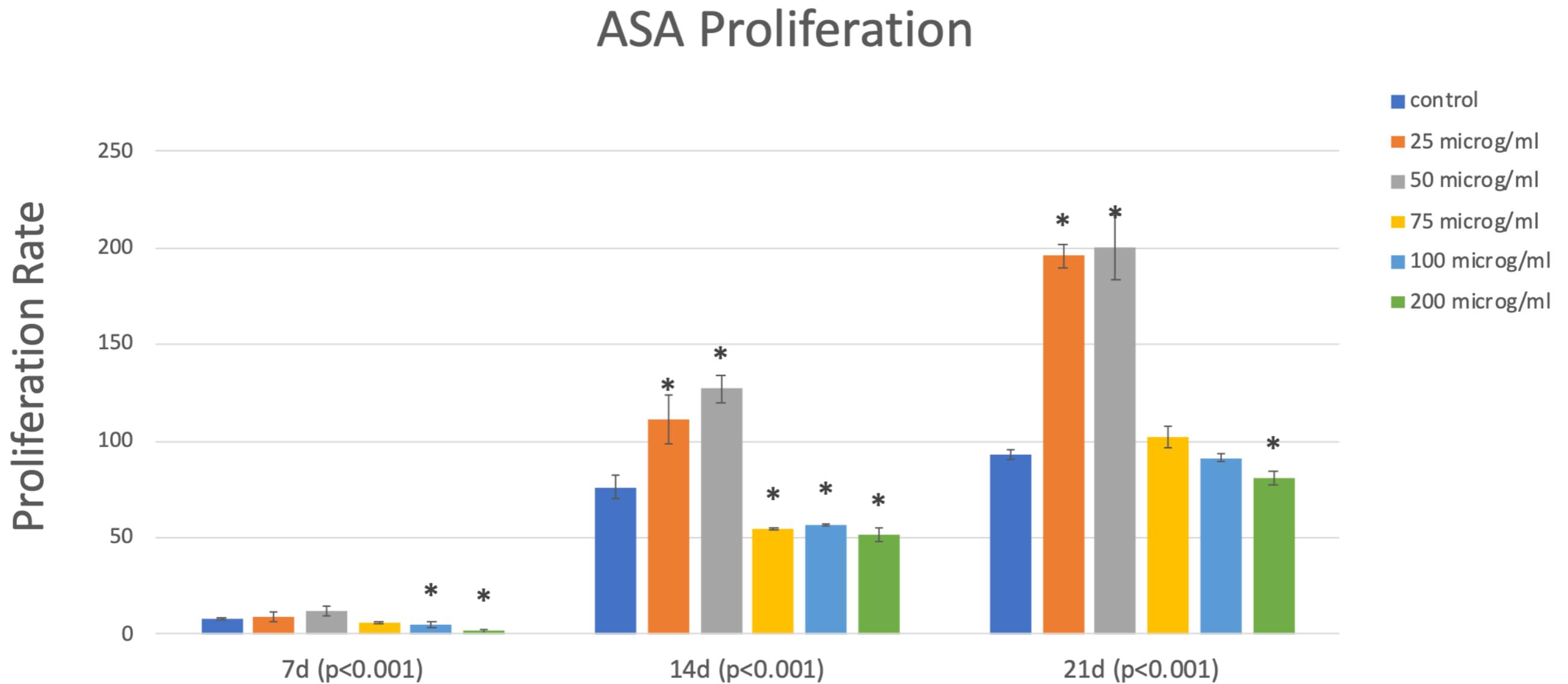
Fixation & Staining > Proliferation and Mineralization

Results

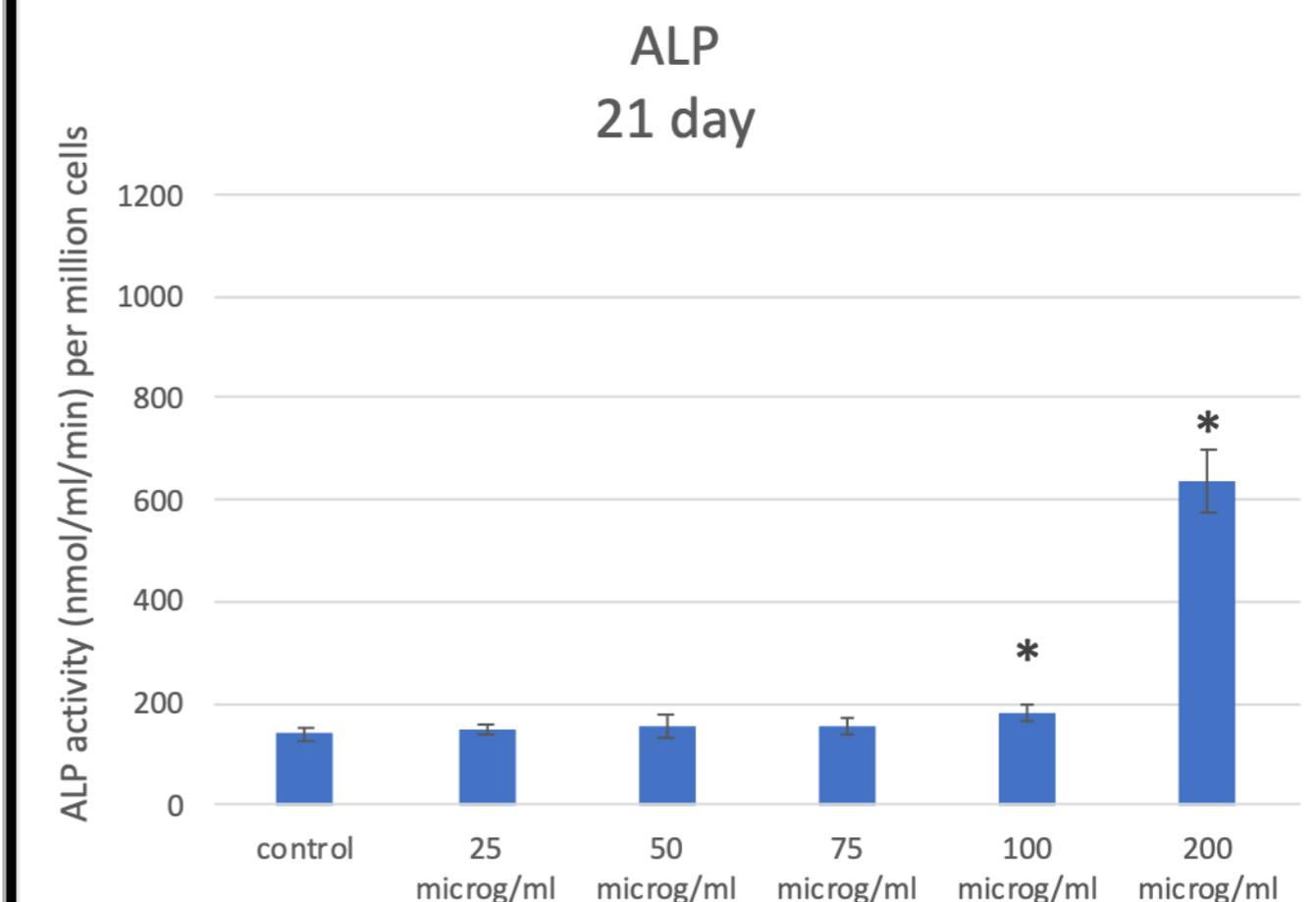
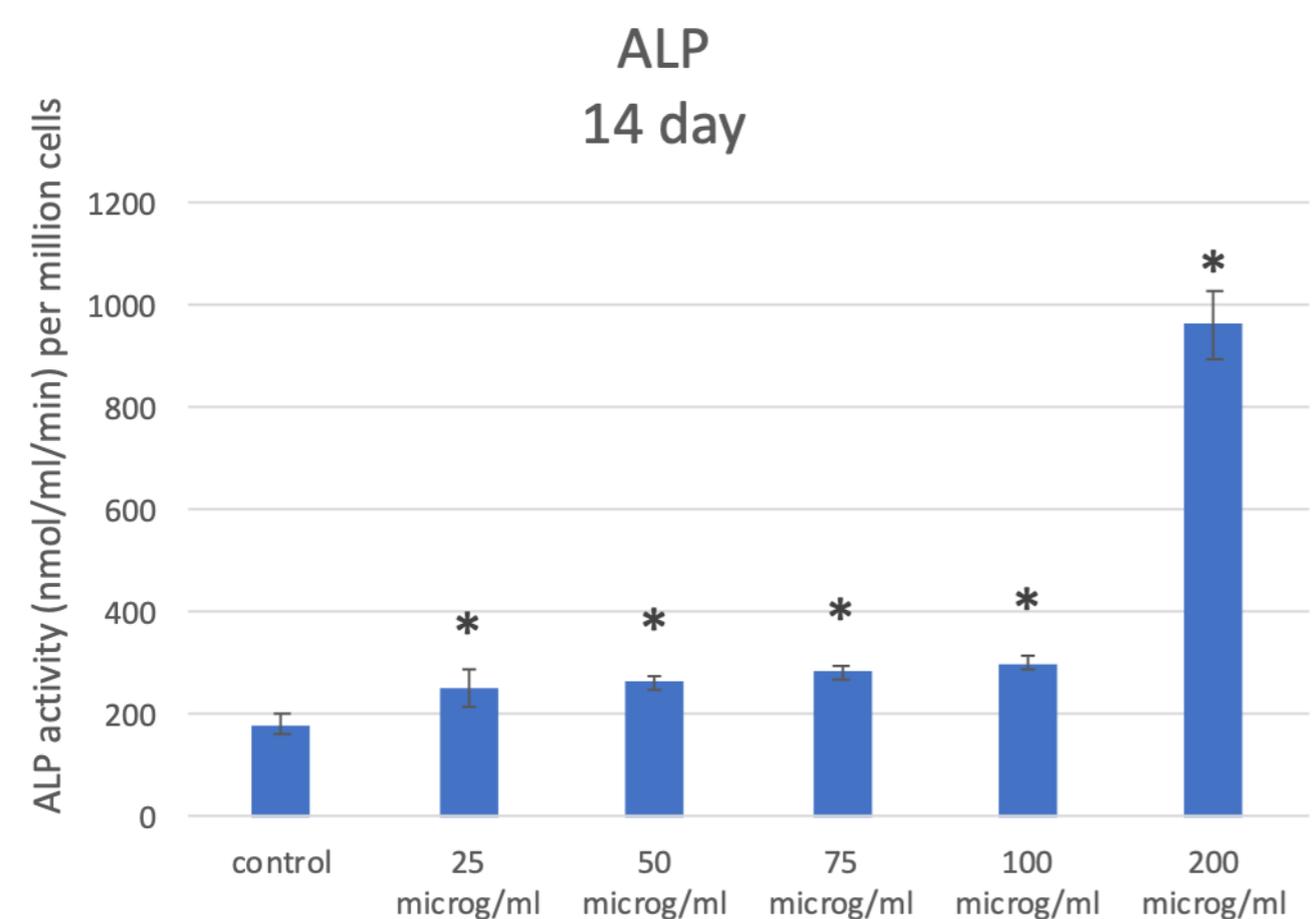
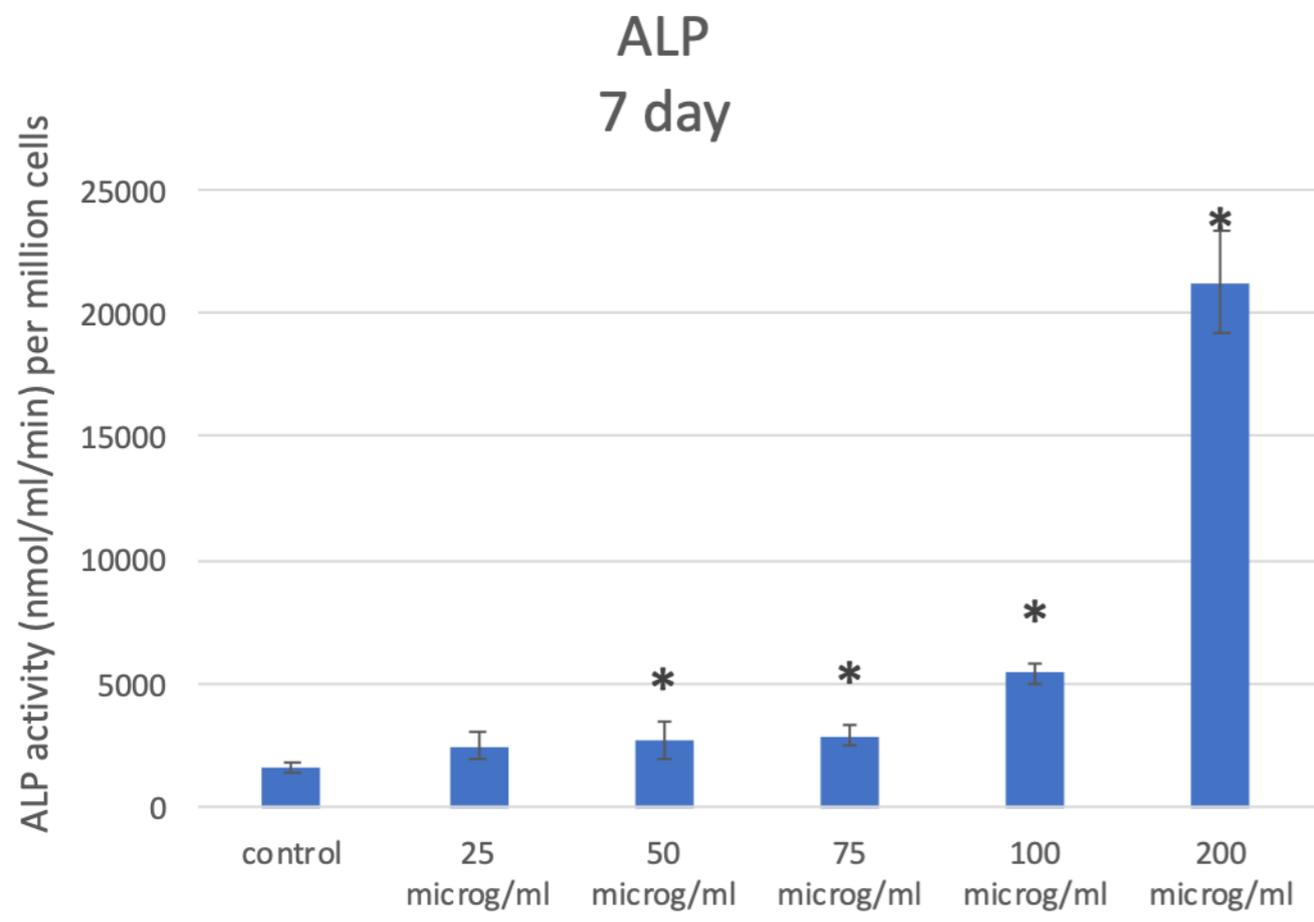
Attachment



Proliferation

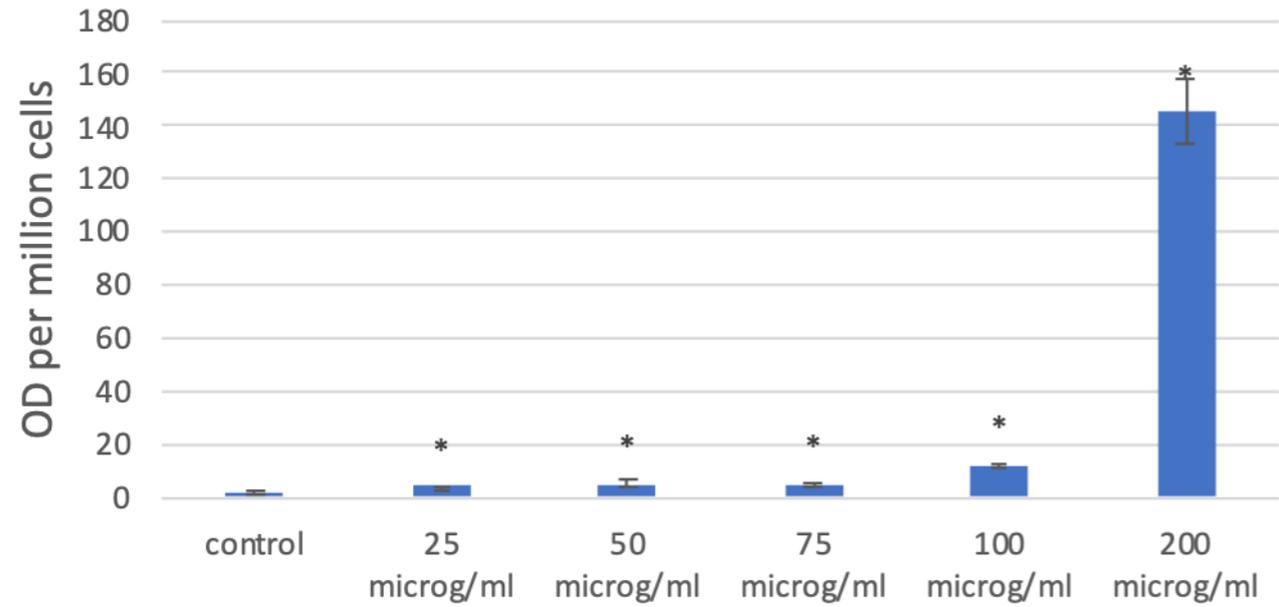


ALP

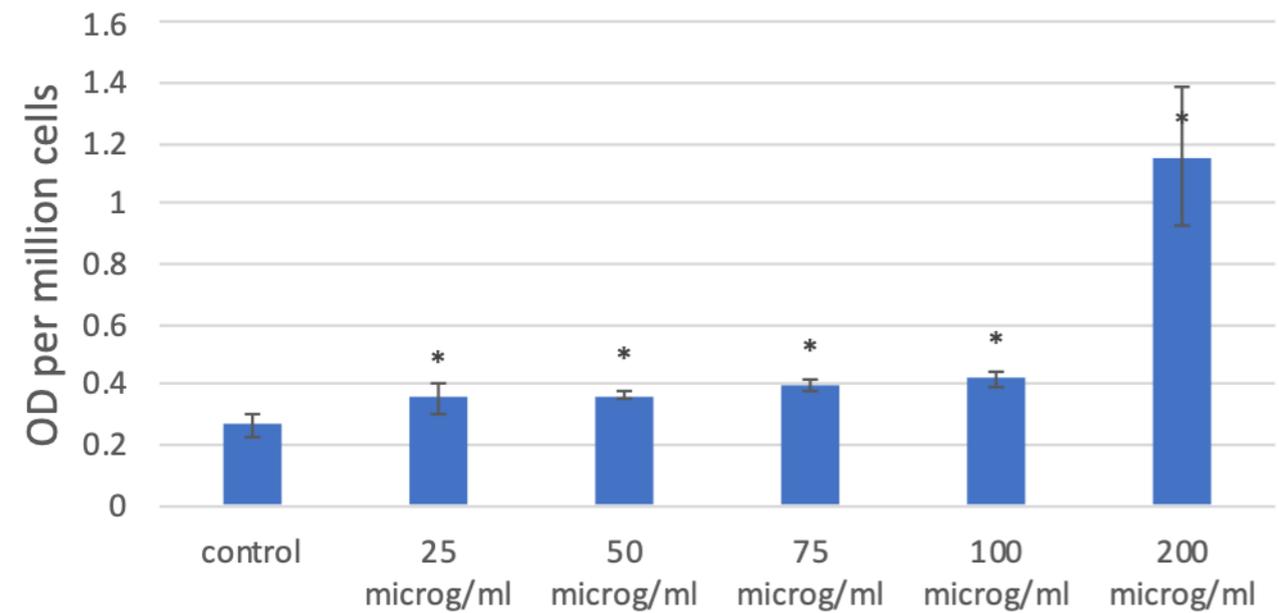


Mineralization

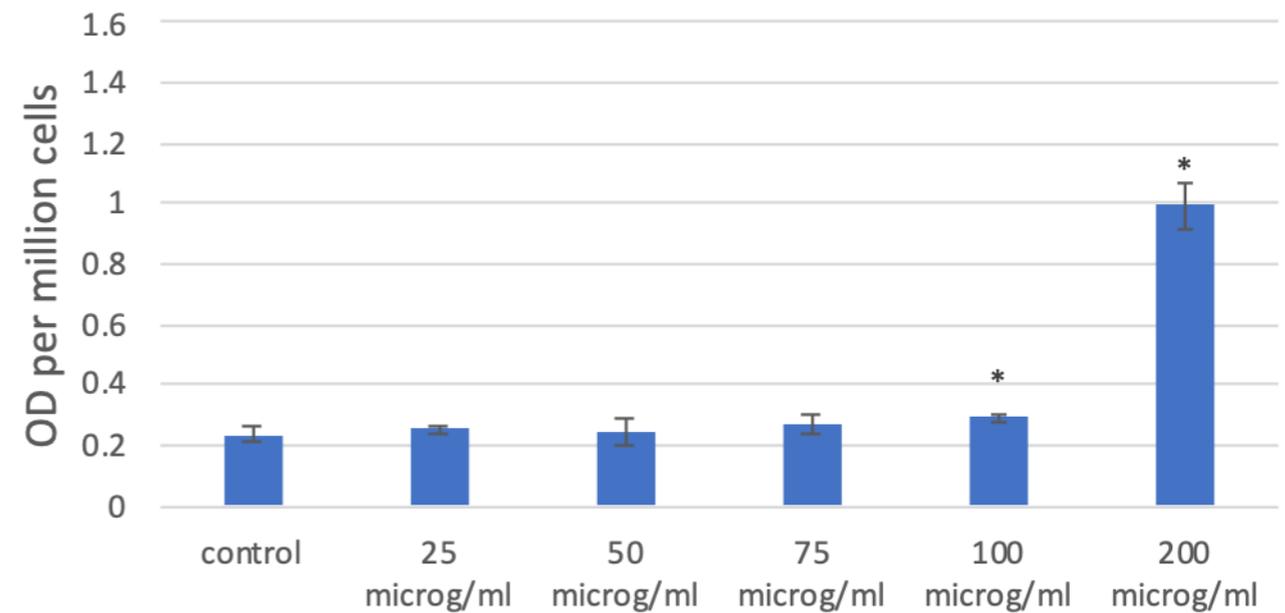
Mineralization 7d



Mineralization 14d



Mineralization 21d



Conclusions

- Low concentrations of aspirin (25-50 $\mu\text{g}/\text{mL}$) yielded significantly higher proliferation levels of HDPCs than the control at 14 and 21 days ($P < 0.05$)
- All concentrations of aspirin yielded significantly higher levels of mineralization and ALP activity in a dose-dependent manner ($P < 0.05$).

Further Study

The effect of acetylsalicylic acid (ASA) at an optimal concentration on dental pulp cell differentiation *at transcriptional and post-transcriptional levels*

Thank you :)