The Mellanby Centre
for bone research

The University Of Sheffield.

HANNAH'S WILLBERRY WONDER PONY
#KICKINGCANCERSBUTT

Preclinical Bone Cancer Research

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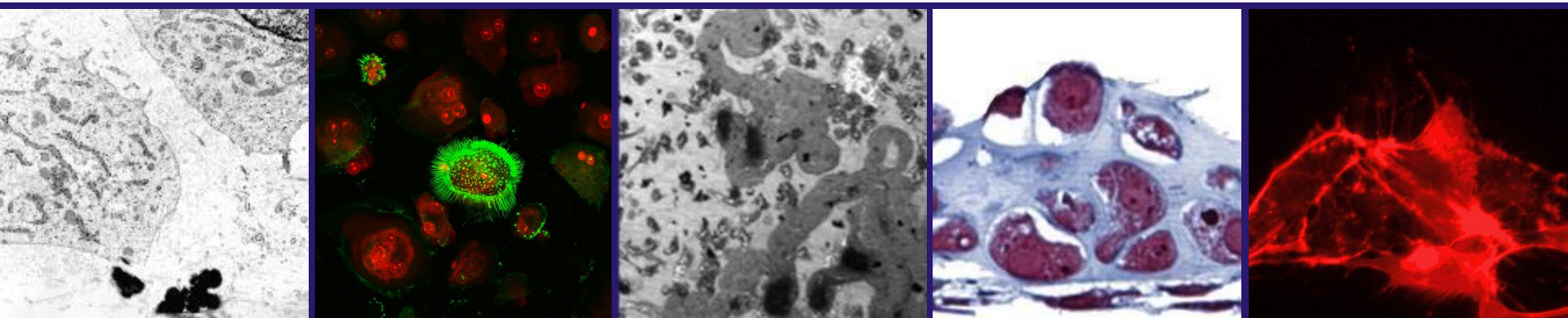
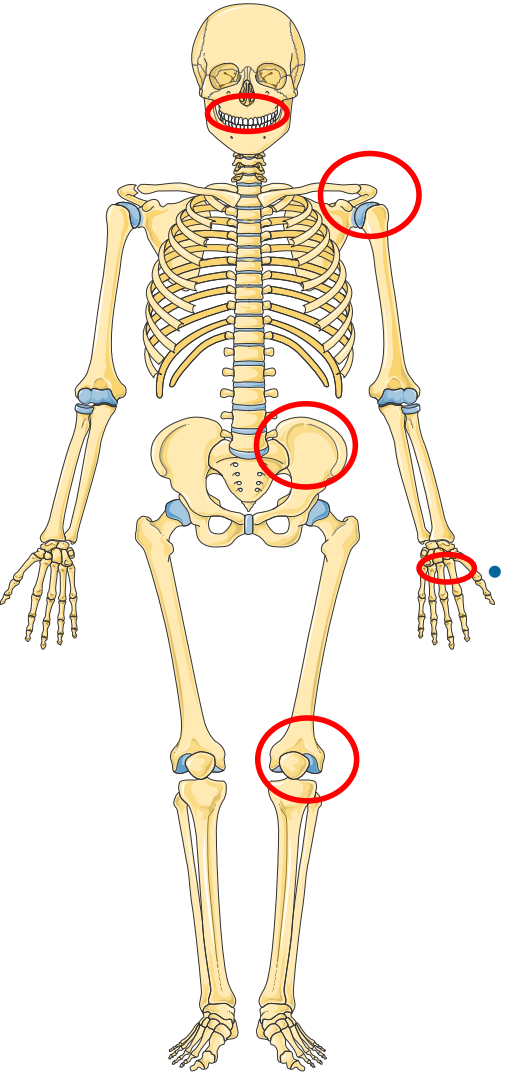


Overview

- Osteosarcoma background
- High throughput drug screening
- *In vitro* validation of hits
- *In vivo* models used in our lab group

Osteosarcoma- Background



- Osteosarcoma is the most common type of primary bone cancer
- Originates from osteoblasts
- Osteosarcoma affects young people with a peak age of incidence at 18
- Most commonly occurs in the limbs (90%) but can affect any bone in the body
- Males are affected more than females
- It occurs at a rate of 1-5 cases per million people per year

Osteosarcoma- Background

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Standard treatments for osteosarcoma haven't changed for around 40 years

Survival statistics remain the same

Lack of new effective drugs

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High throughput screening

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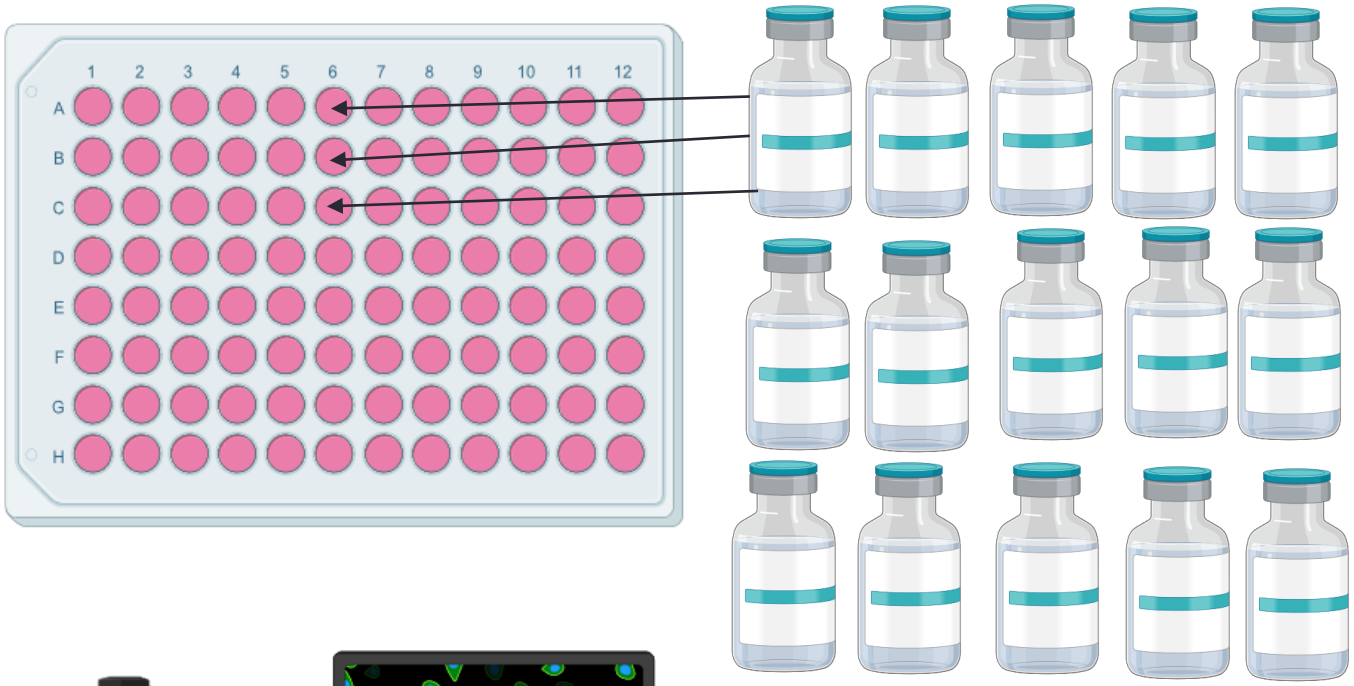
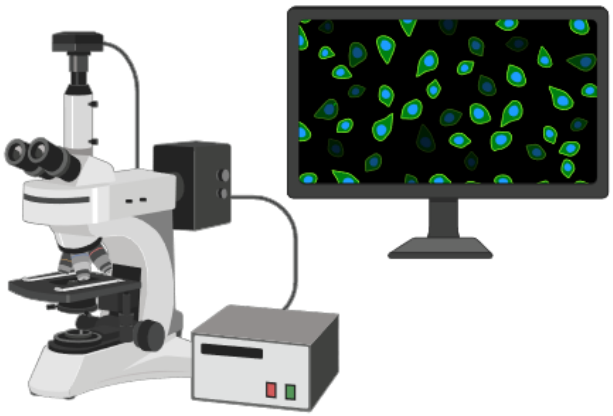


Compound libraries



High throughput screening

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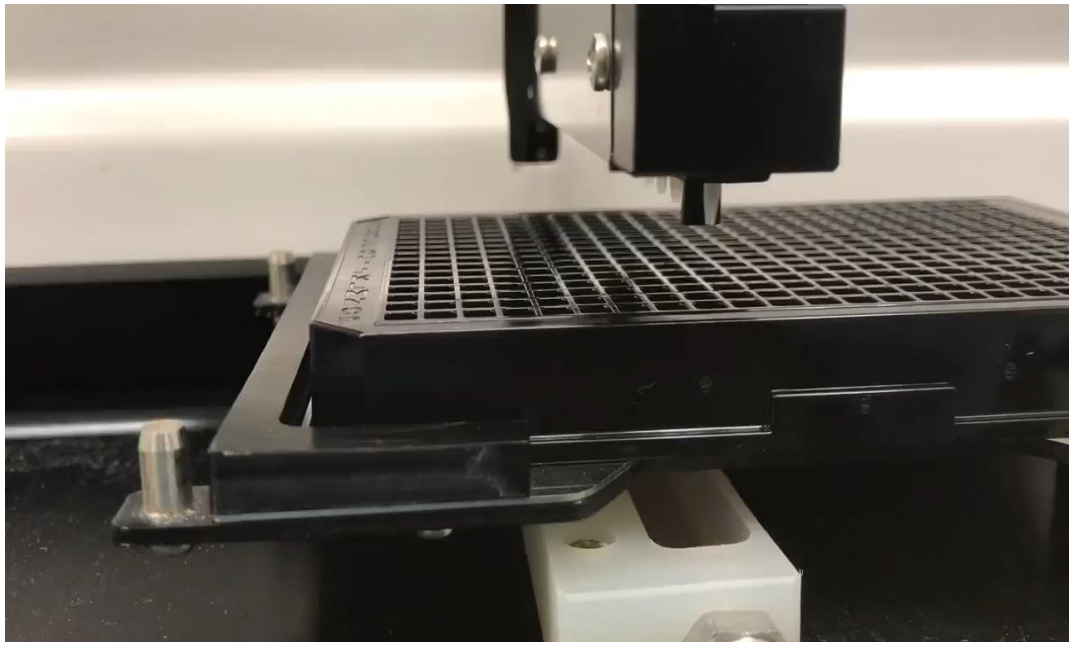
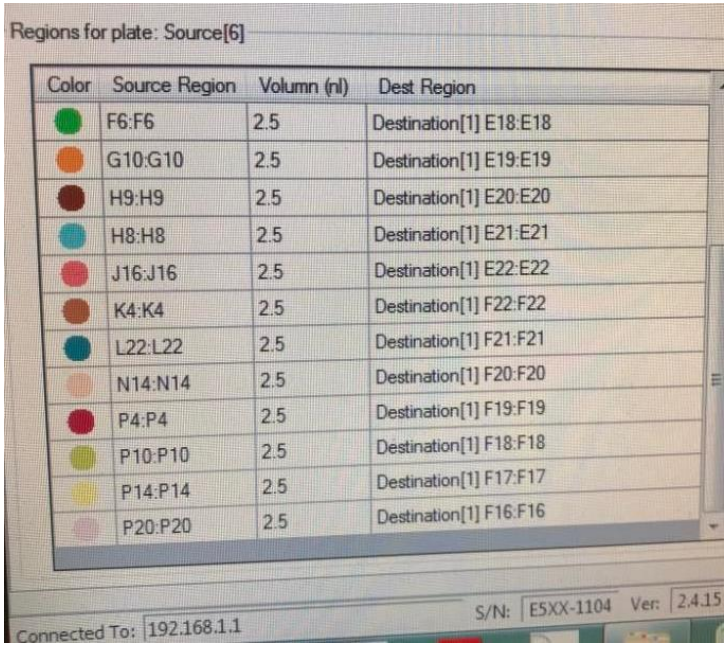
Automated cell plating



Automated drug treatments



Individual compounds

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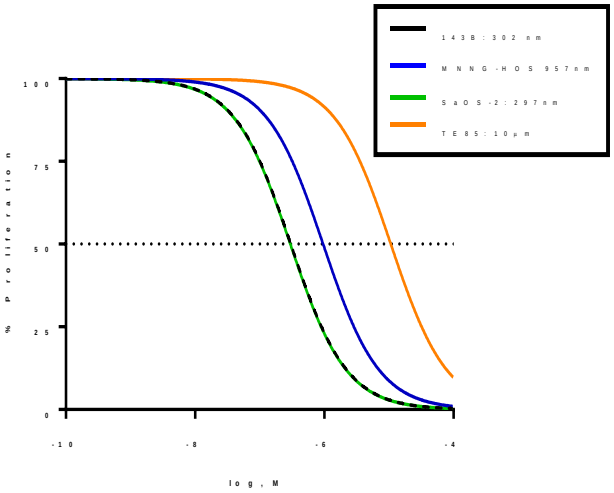
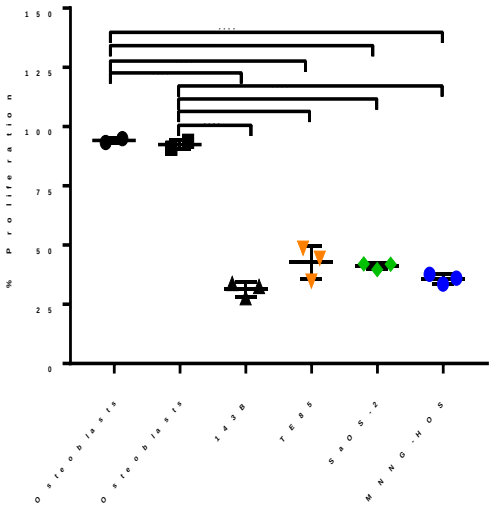
In vitro validation

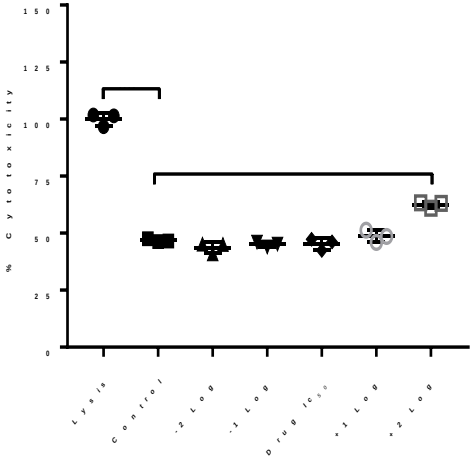
IC50 across cell lines



Effect on osteoblasts



LDH release



Growth rates

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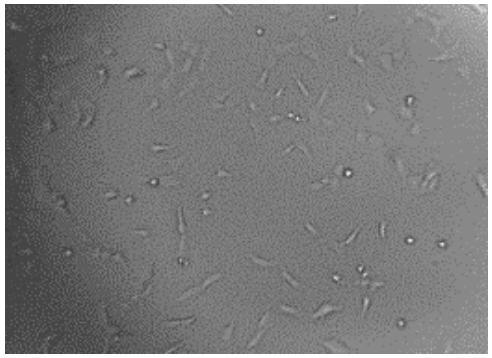
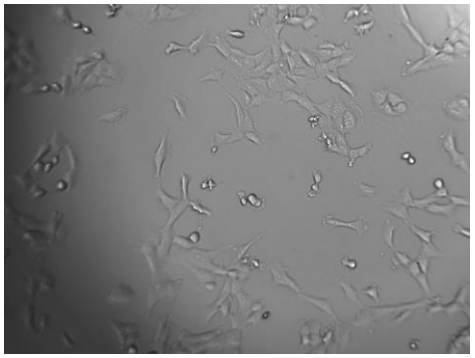
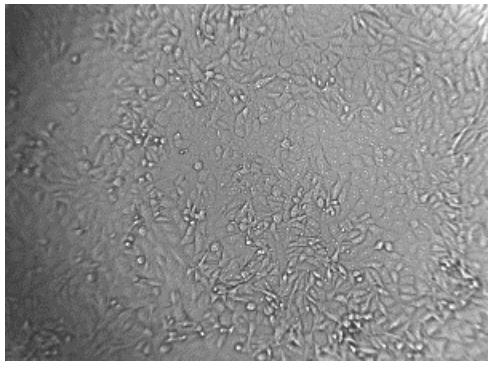
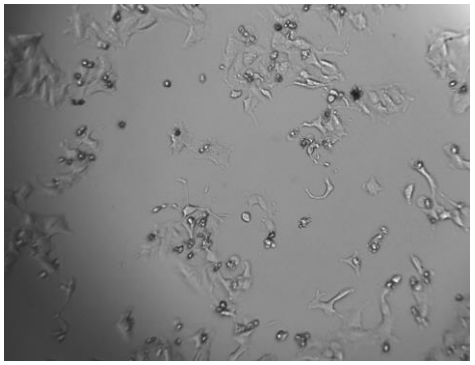
0 hours

48 hours







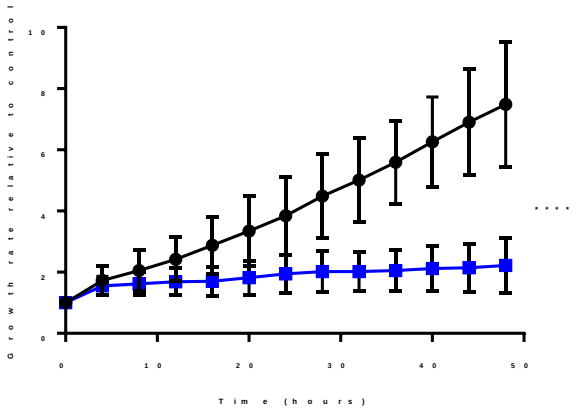


Control

Drug

Control

Compound



Migration

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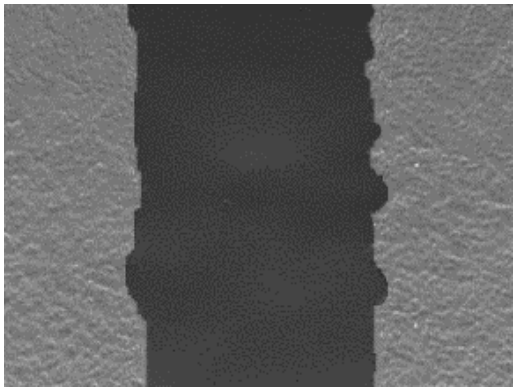
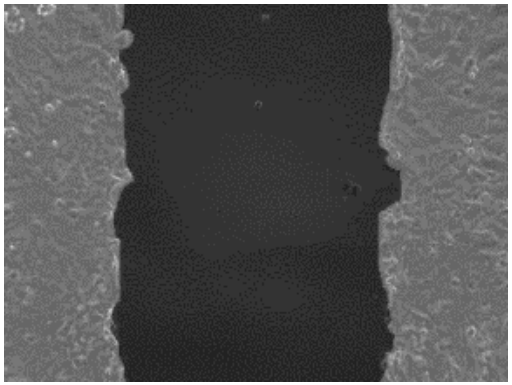
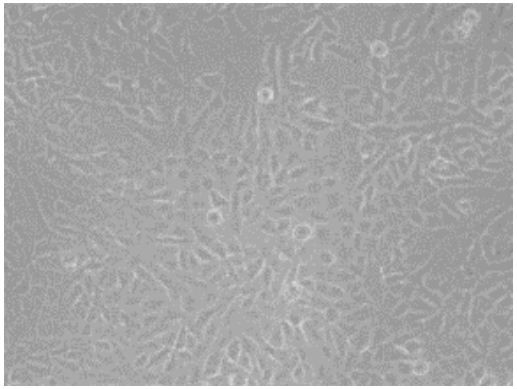
0 hours

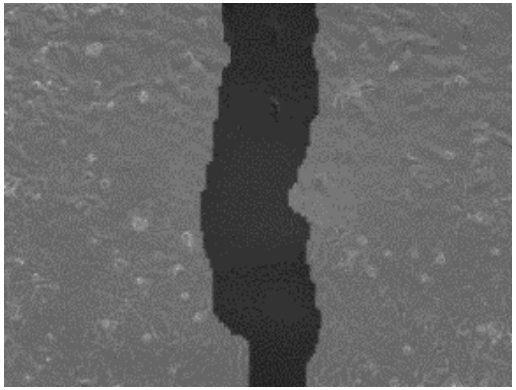


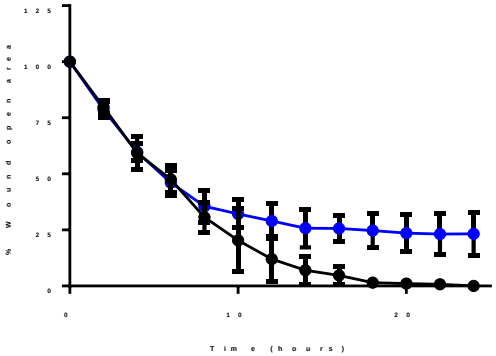


Control
Compound

24 hours



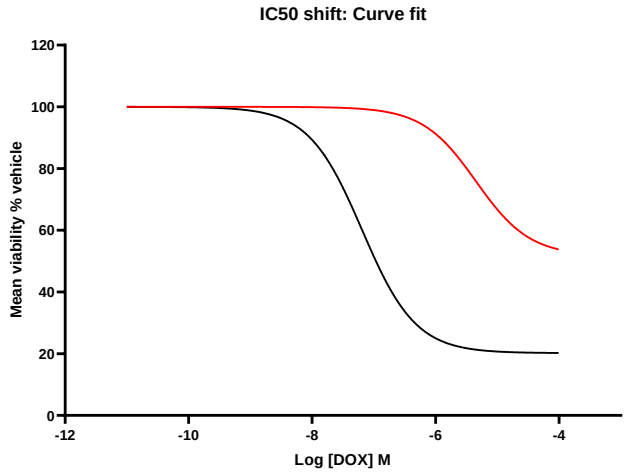




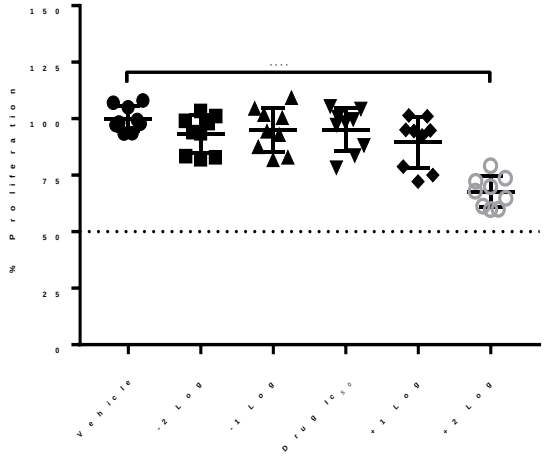
Control

Drug

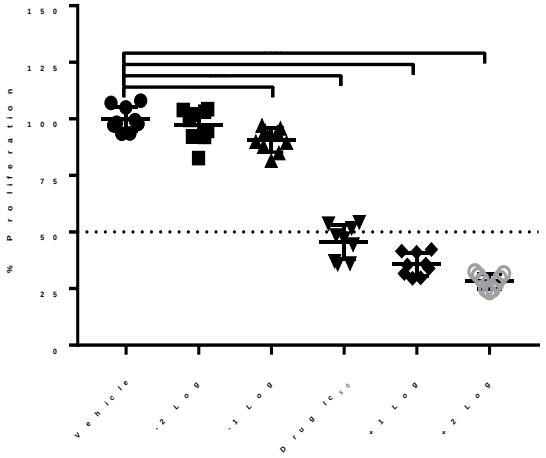
Effect on doxorubicin resistant cells



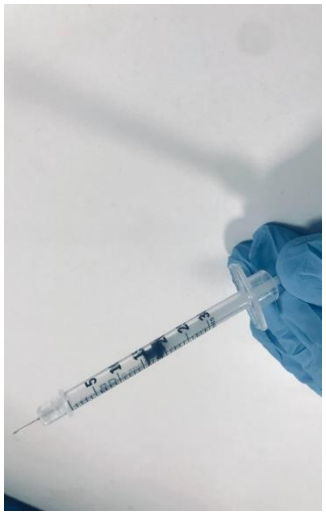
Doxorubicin



Drug



In vivo studies



250,000 MNNG-HOS /143B+GFP-LUC

Tumour formation

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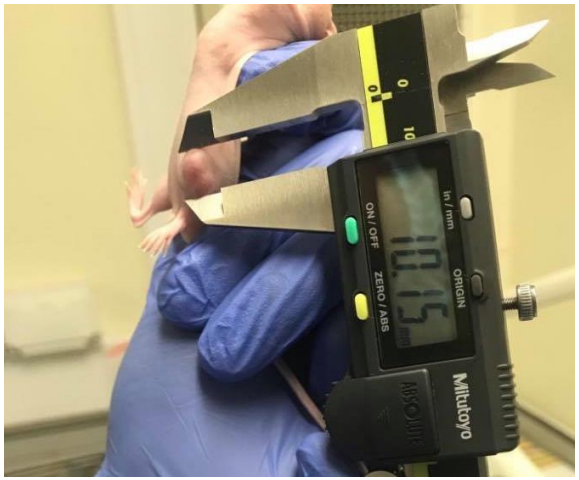

Non-tumour bearing

Tumour bearing

Calliper measurements twice a week

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IVIS imaging – 143B

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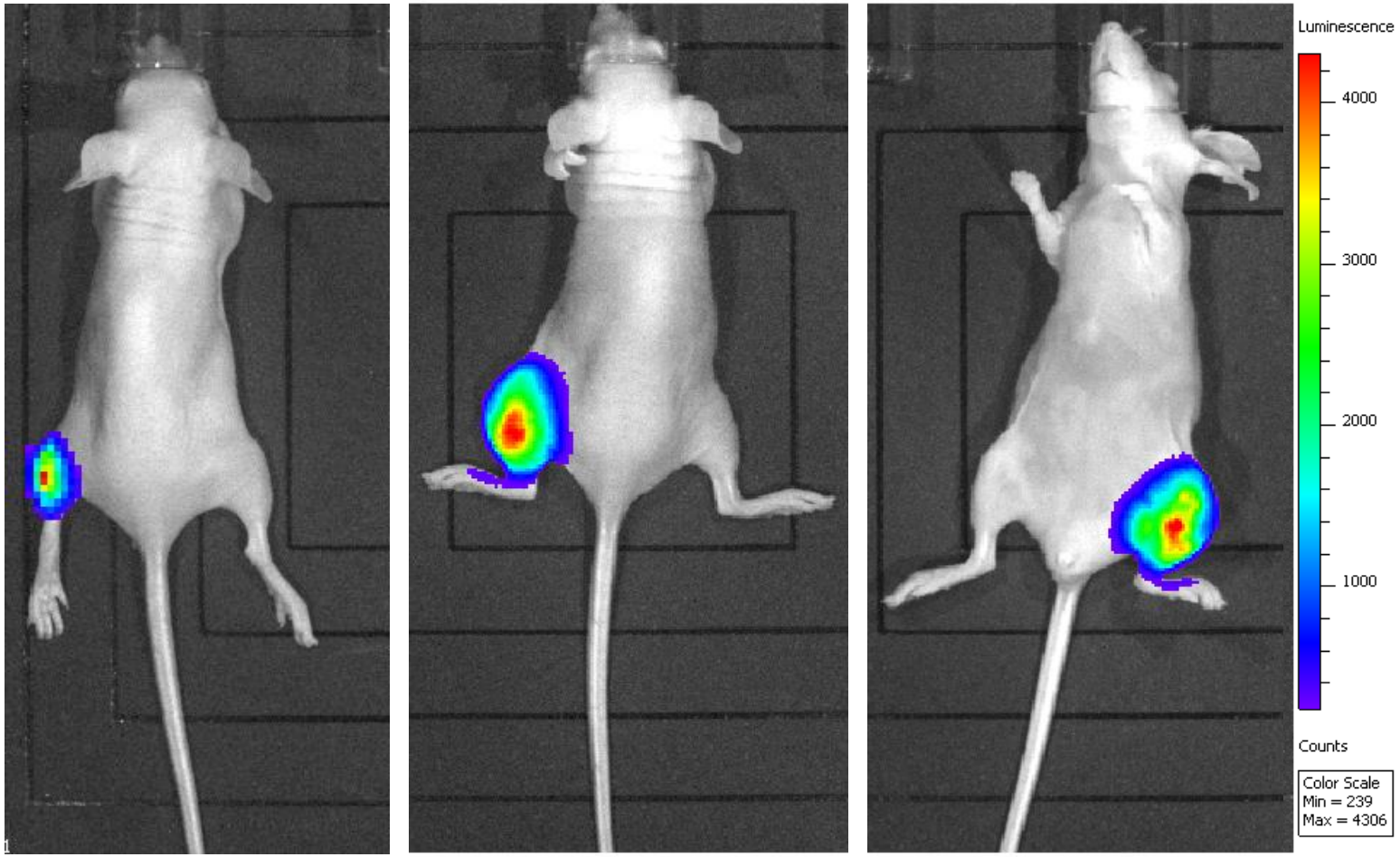

First IVIS day (Day 4)

Cull day (Day 31)

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EX Vivo

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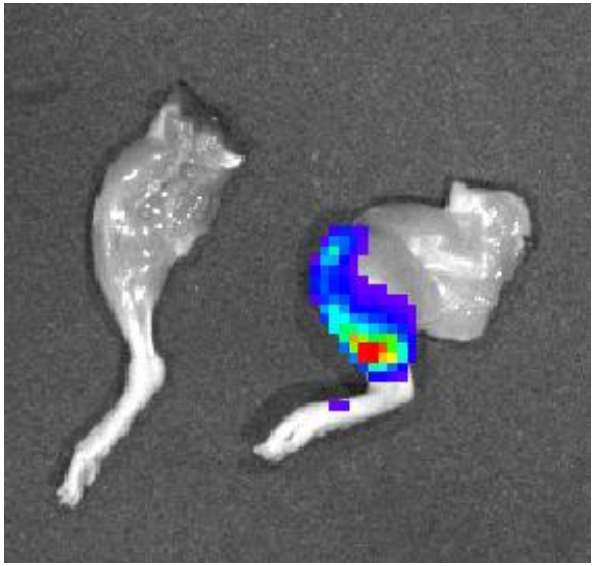
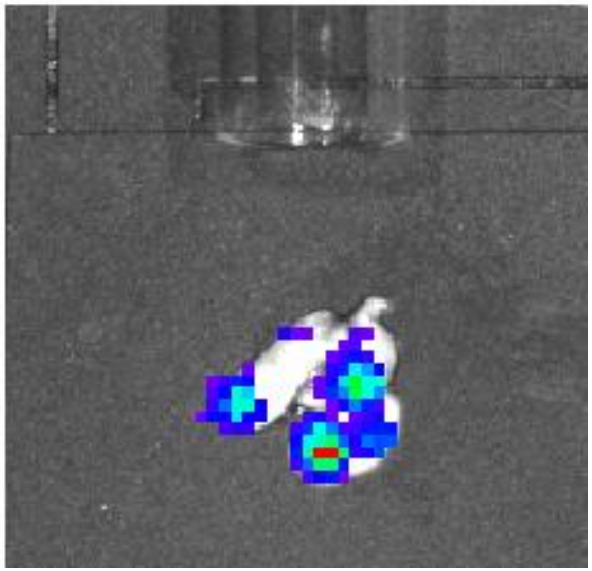
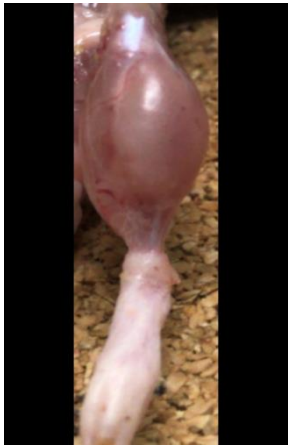
Limbs





Lungs



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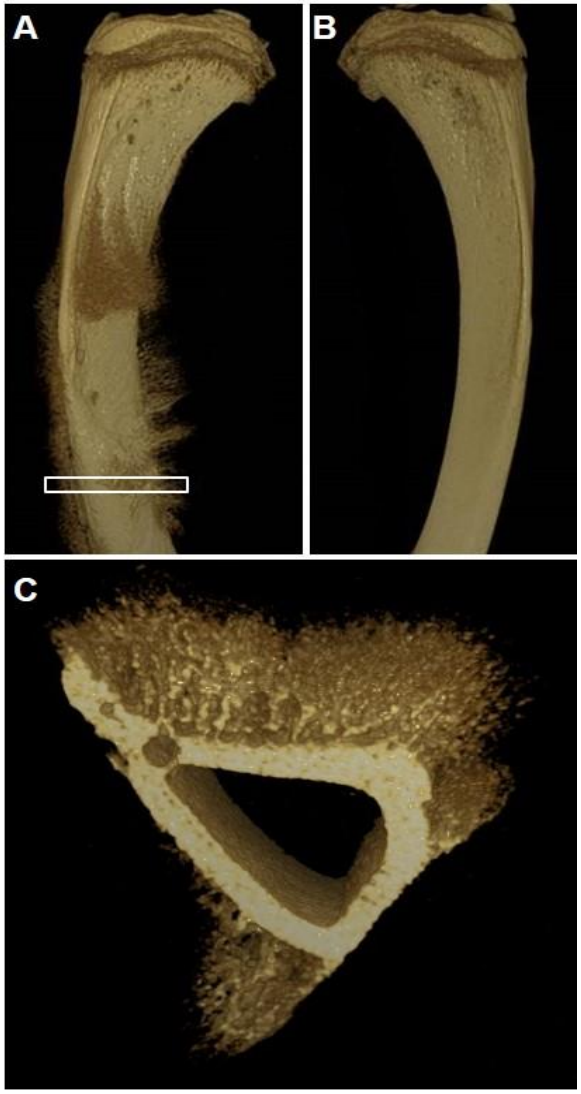
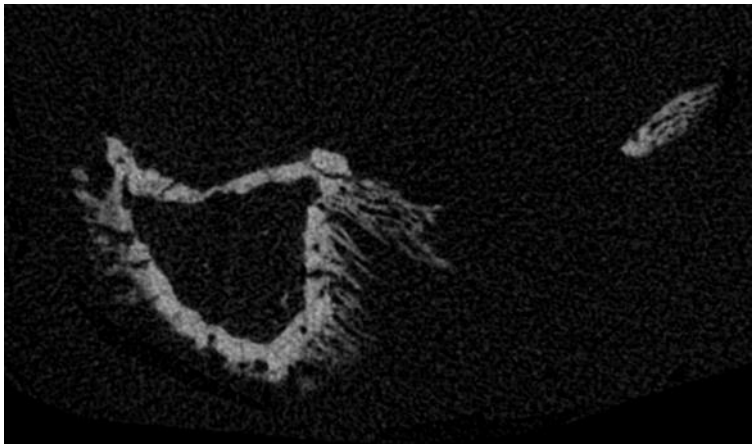
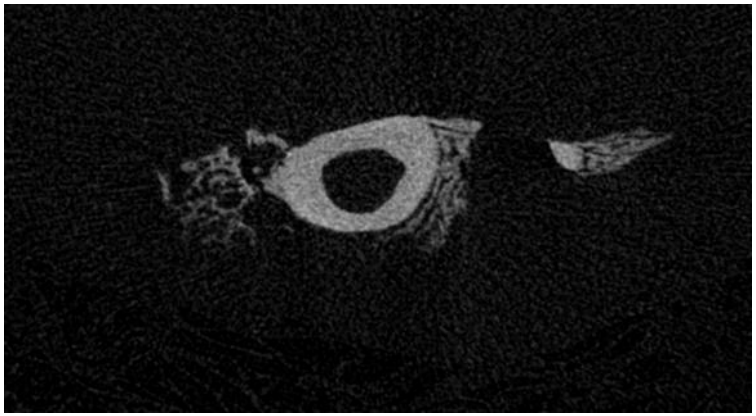
MNNG-HOS model - bone







Ectopic bone builds up around the bone

Displaying the typical ‘sunburst’ pattern seen in patients

143B model - bone

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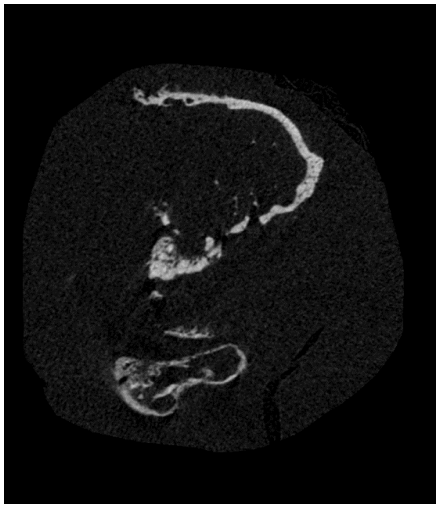
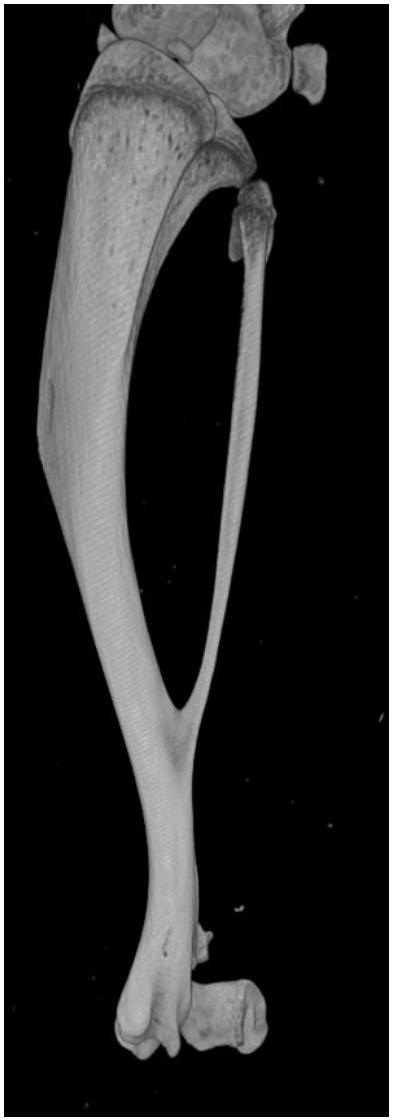
Lesions





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Comparison of models

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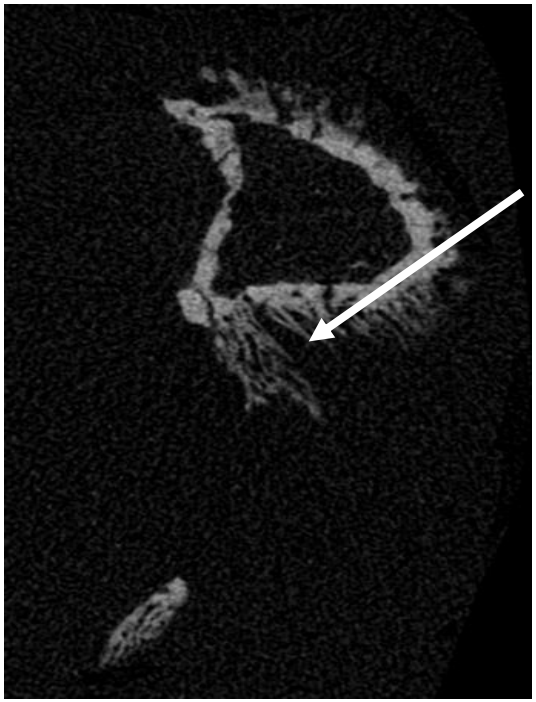
143B

MNNG-HOS

Lesions



Ectopic bone

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OS lung metastasis

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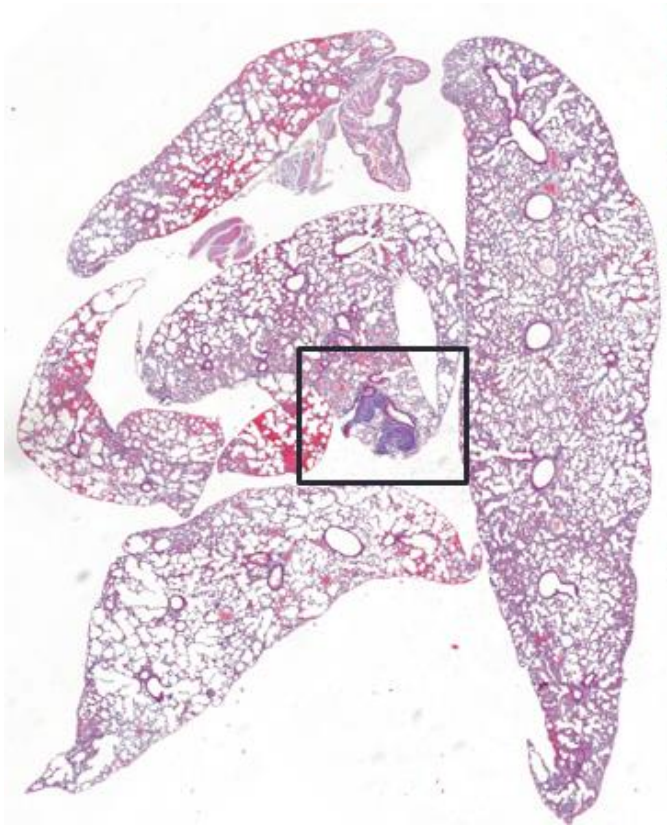
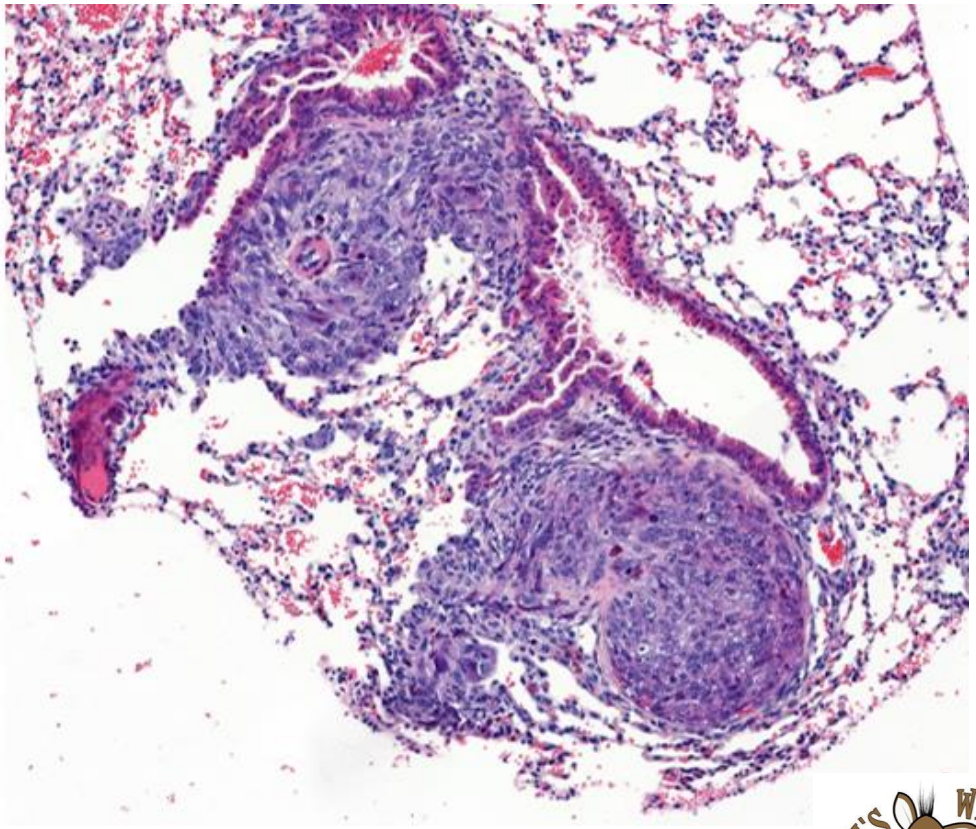
Lung section



Metastasis



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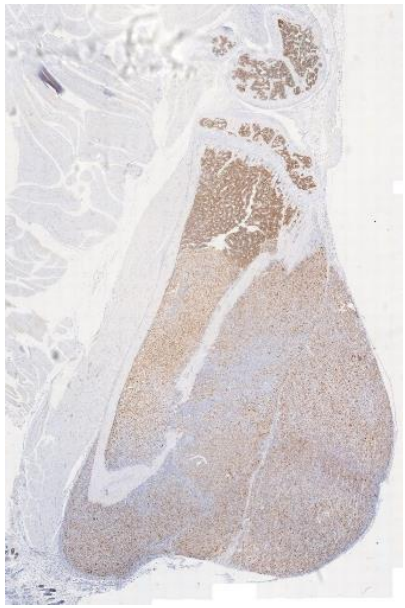
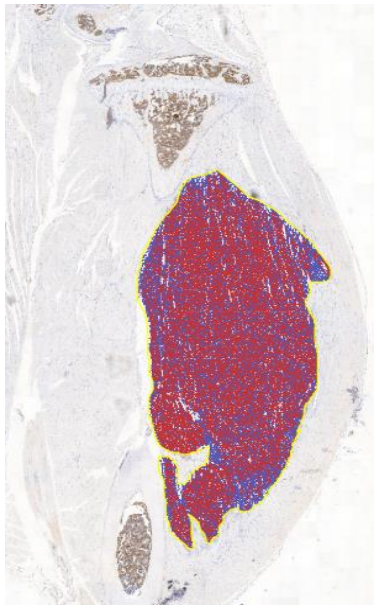
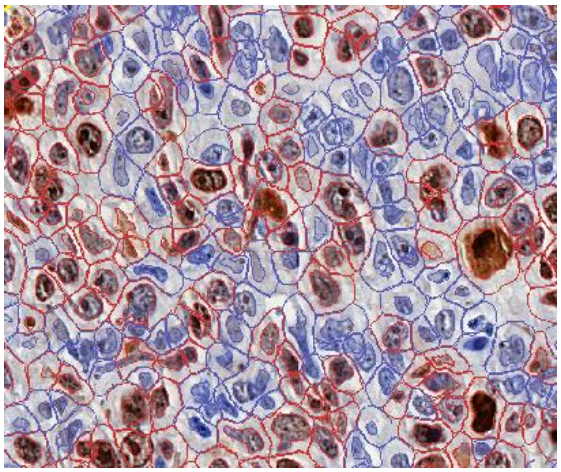
OS Histology







H&E staining

IHC- Ki-67 for proliferation

Acknowledgements

Prof Allie Gartland

Dr Adrian Higginbottom

Miss Victoria Tippett