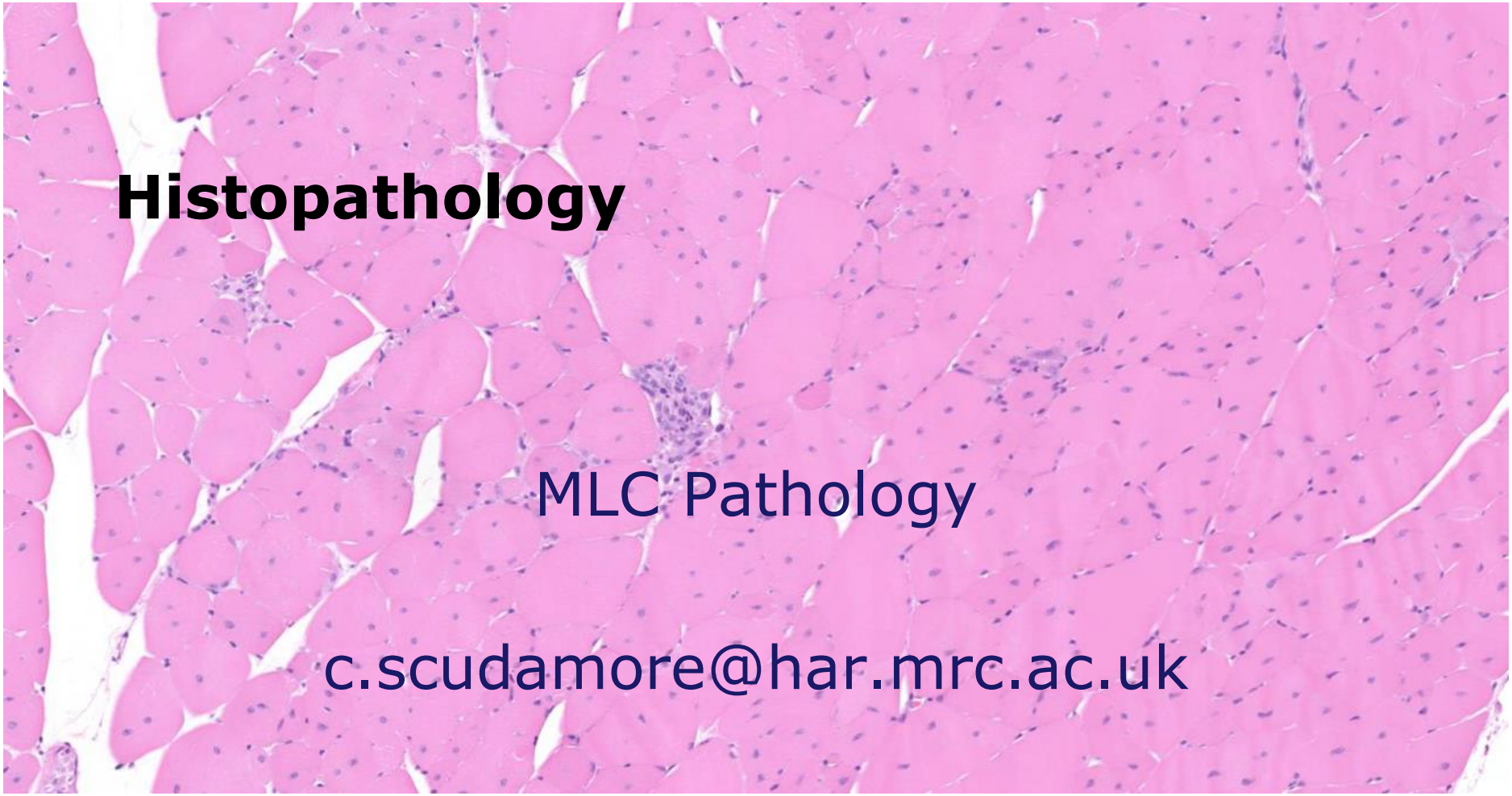

Histopathology

MLC Pathology

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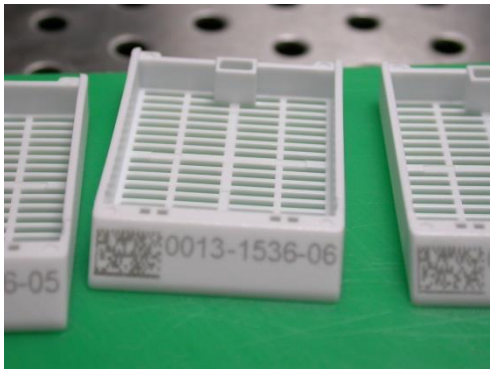
Phase 1 pathology

- IMPC Phase 1
  - Funding only to collect biobank tissues from all lines into fixative
  - Harwell - Currently tissues from most lines have been processed and embedded in wax
  - ~60 lines have been examined for histopathology
    - Lines of interest because of in vivo observations
    - Lines chosen to correlate with other tests eg clinical chemistry/NMR pilot and FACs



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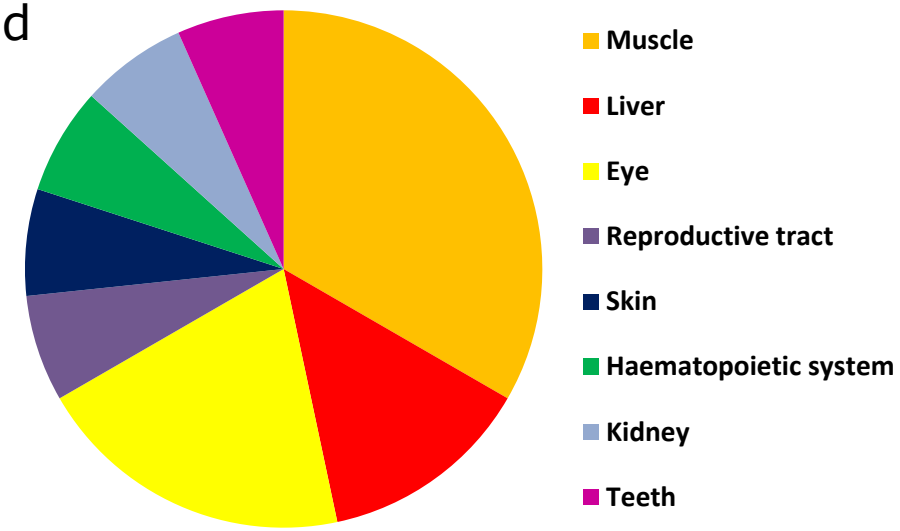
Phase 1 pathology results

- 57 lines examined
  - 14 lines with pathology and in vivo observations
  - 22 lines no pathology but in vivo observations recorded
    - *In vivo observations with no correlation mainly behavioural/gait*
  - 21 lines no pathology and no in vivo observations
    - *ie pathology did not detect any unexpected phenotypes*
- Tissues affected



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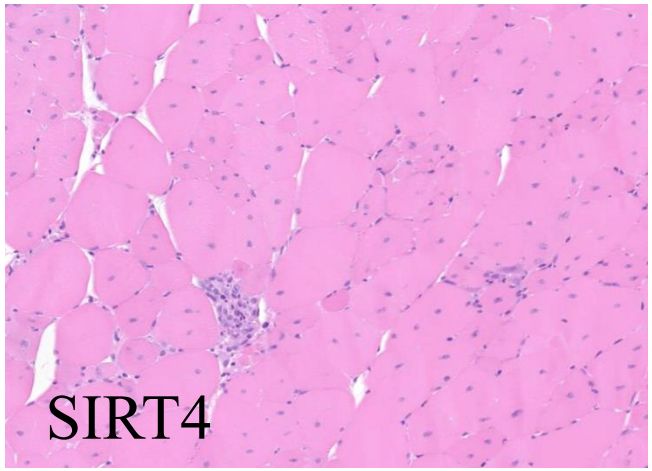
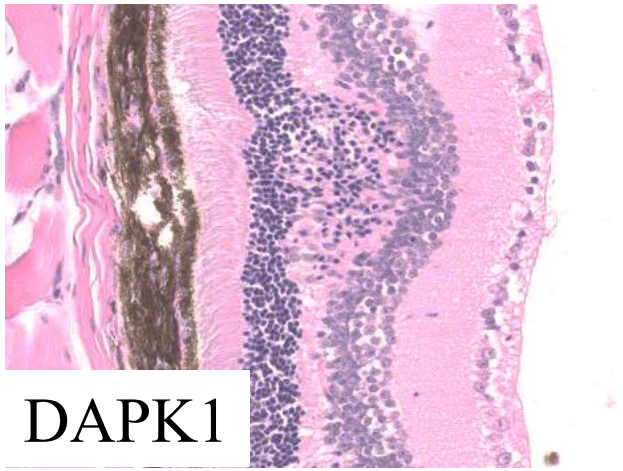
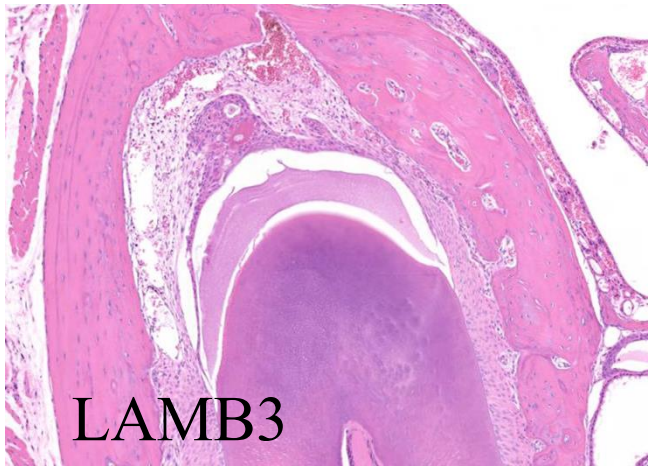
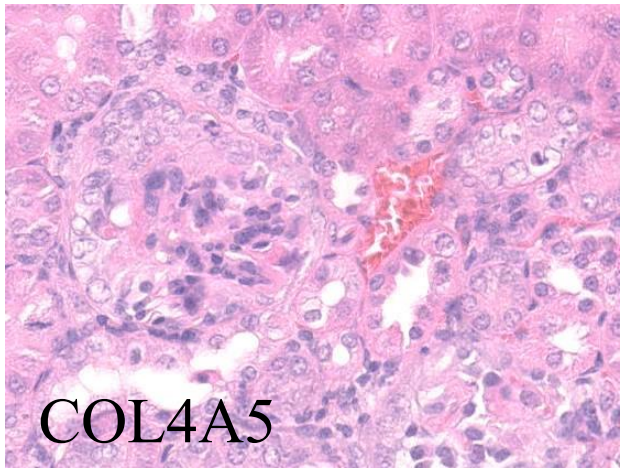
Examples









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Conclusions from phase 1

- Histopathology provides confirmation of in vivo phenotypes – less frequently detects novel phenotypes
- Data gained allows direct comparison/correlation with human disease syndromes
- In (relatively) young adult mice pathology is only likely to detect lesions in organs which are not vital for life or have significant reserve eg muscle, eyes, liver
- Light microscopy is generally not sufficiently sensitive to detect most CNS lesions ie poor correlation with behavioural tests

Possible approaches for Phase 2 pathology

- Include pathology on triaged lines as part of the work package
  - To provide confirmation of phenotype and additional information
  - For nominated lines of interest for networks

- Consider the inclusion of pathology for:
  - Investigation of early neonatal mortality
  - Placental/embryonic pathology in support of imaging data in lethal phenotypes