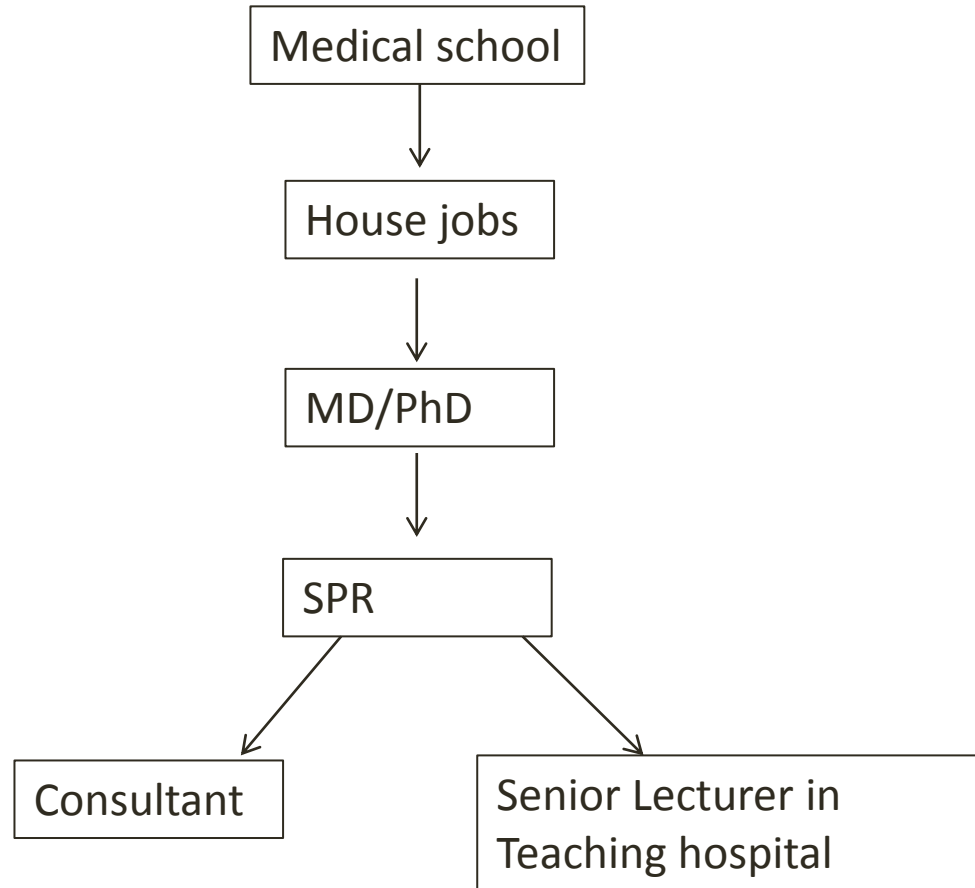


Basic and Translational Research

Kenny Rankin

Basic science term 2013

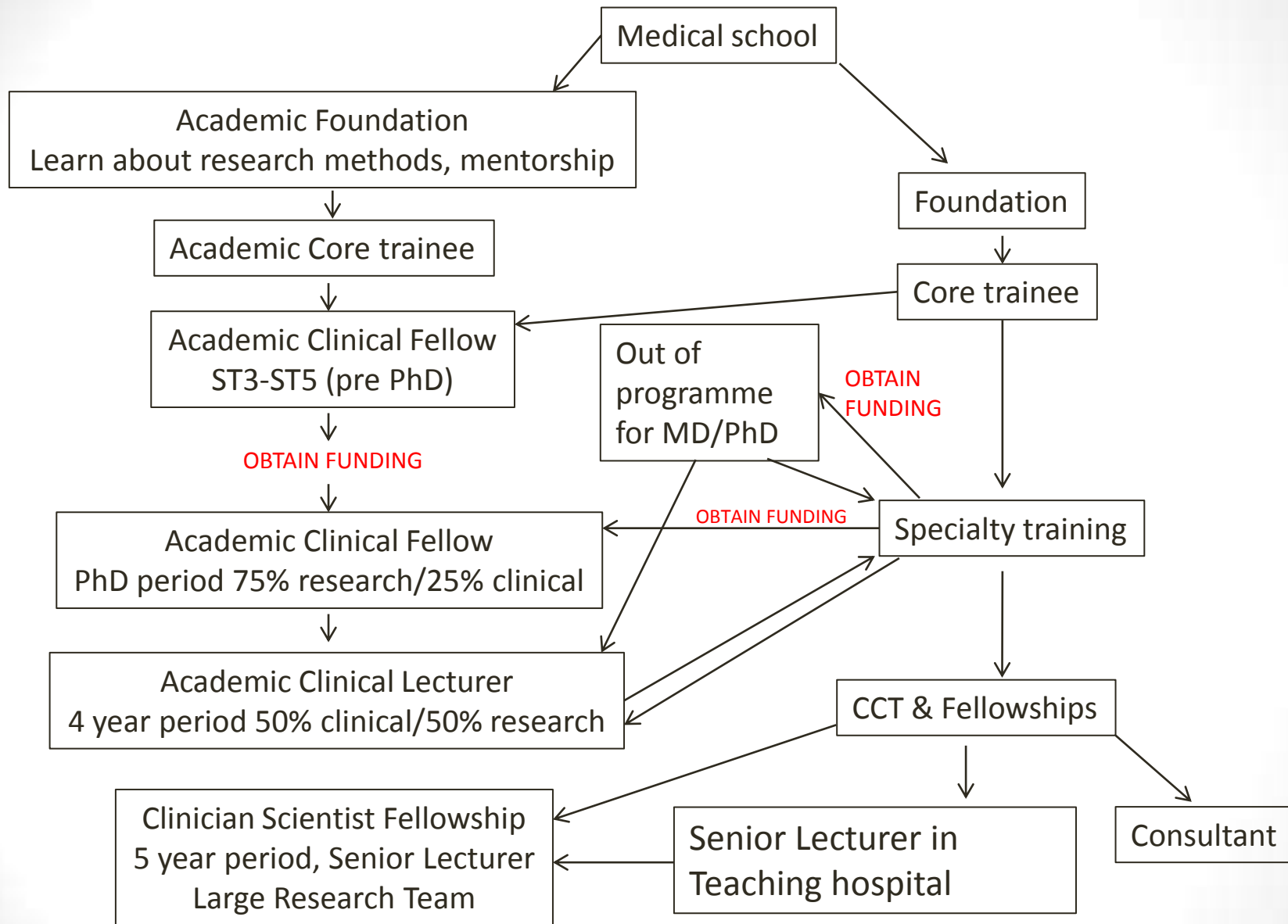
Old style academic training



Academic training

- Walport report 2006
- Requirement for structure to academic training
- National Institute for Health Research (NIHR) funding for academic posts from foundation training stage

ACADEMIC VERSUS STANDARD TRAINING



Basic versus translational science

- Basic= laboratory studies
 - *In vitro*: cell culture
 - *In vivo*: animal models



- Translational= laboratory studies with expected clinical impact in the short term
 - Fostering interaction between basic scientists, clinicians and industry

Newcastle University

- Main institutes
 - Institute of Cellular Medicine
 - Northern Institute for Cancer Research
 - Institute of Genetic Medicine
 - Institute of Health and Society
 - School of Engineering

Musculoskeletal Research



- MRG in ICM
 - Founded by Tim Cawston & Drew Rowan (Non clinical)
 - Matrix cartilage biology
 - John Isaacs (Clinical), John Robinson & Cat Hilkens
 - Immunology of rheumatic diseases
 - Orthopaedic group lead by Prof McCaskie, Craig Gerrand and Mark Birch
 - Fearon, Aldridge, Sprowson, Rankin, Johnson-Lynn, Spalding
 - Recently joined by John Loughlin (OA genetics)

My Research

- MD in breast cancer bone metastases 2005-2007
 - Learned laboratory techniques
 - Experience of the NHS-university interface
- ACL in 2009
 - Osteosarcoma research
 - CD64 infection marker for arthroplasty
 - OA genetics

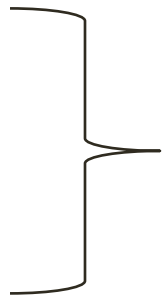
Osteosarcoma research

- 2009/10: building collaborations and research ideas
- 2011: full year in the lab to collect pilot data and submit grant applications
 - Ultimately successful with 2x grants from local charities £86,000
- 2012: Back in clinical training full time
 - Appointed 2x post docs

Why Membrane Type-1 Matrix Metalloproteinase?

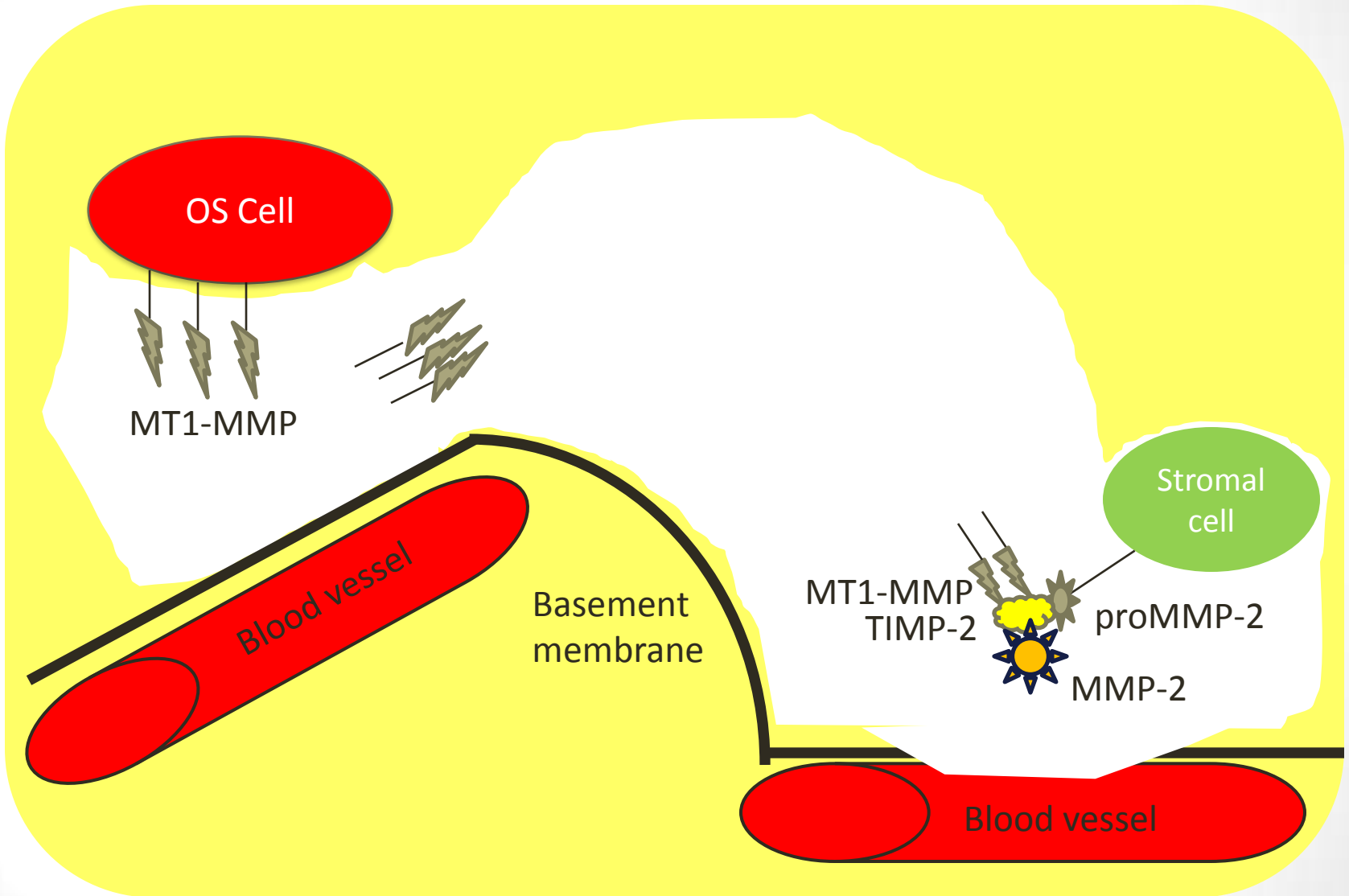
- MT1-MMP demonstrated in several solid common cancers to play important roles in

- Invasion
- Migration
- Angiogenesis
- Metastasis

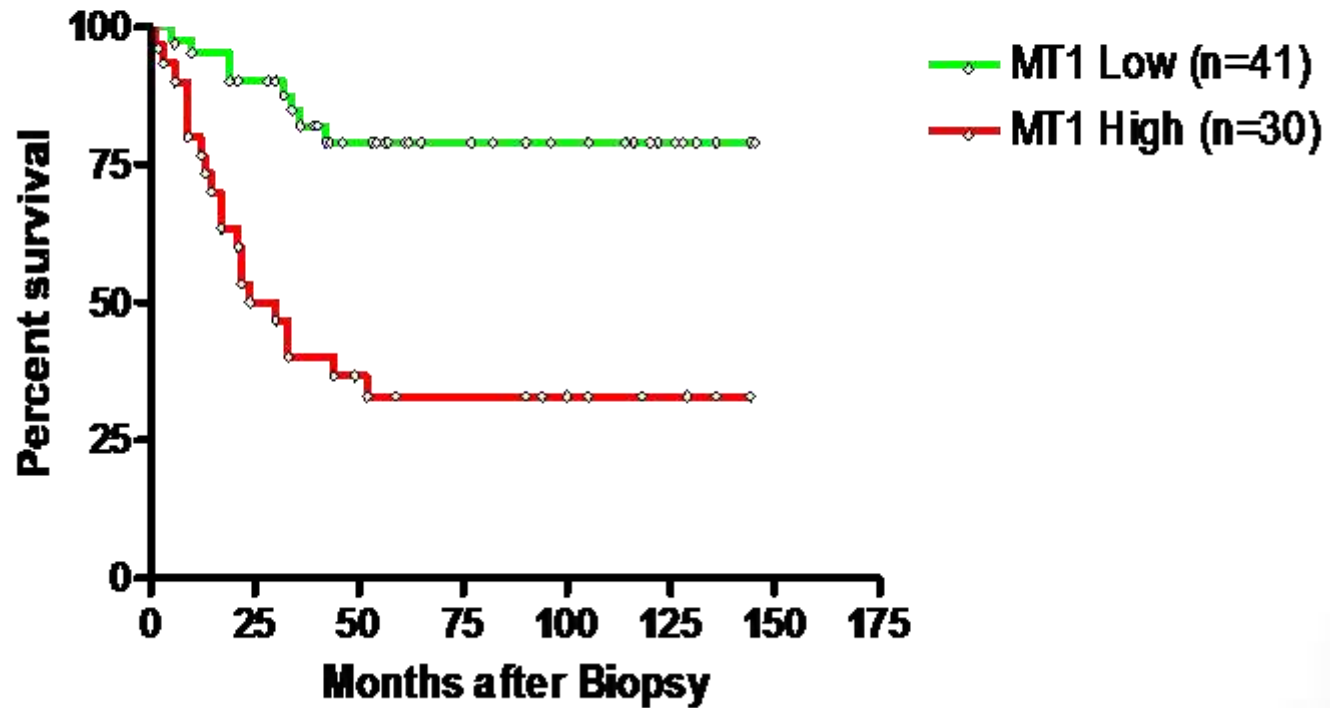


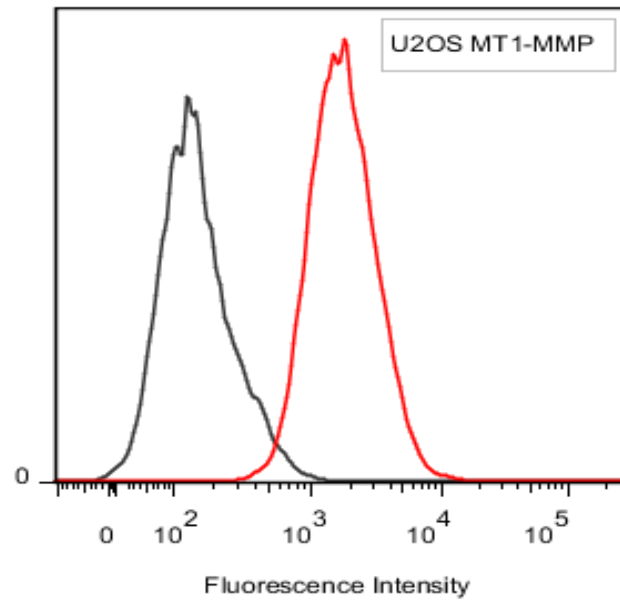
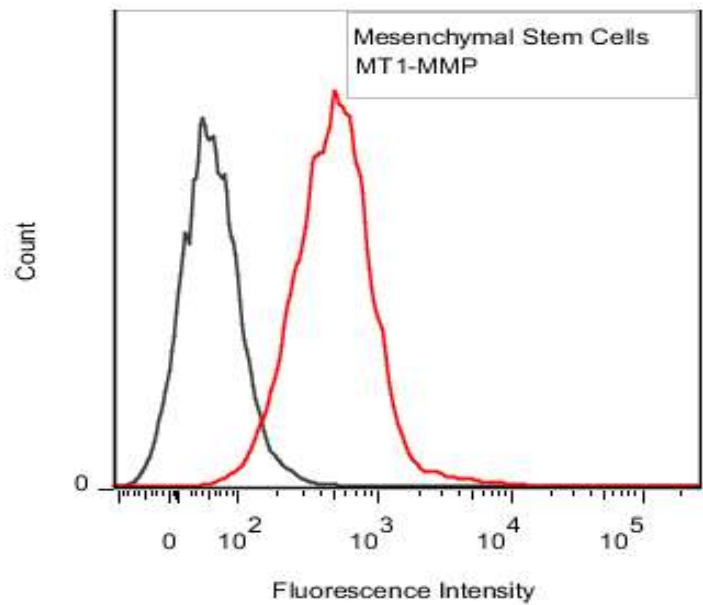
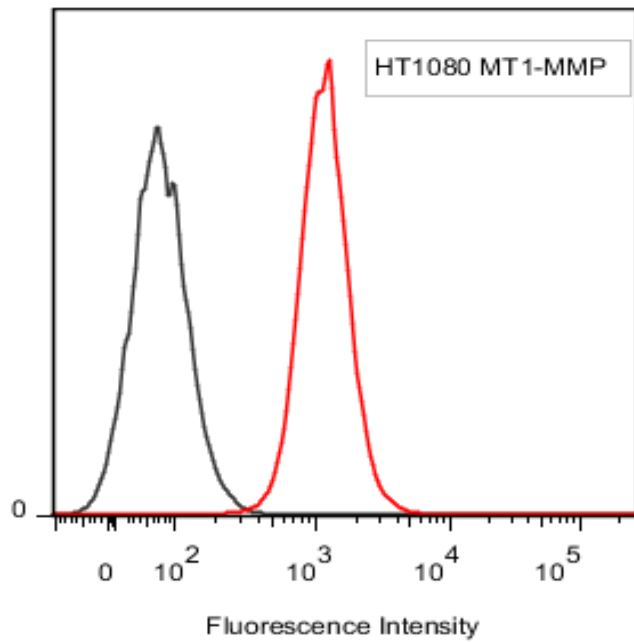
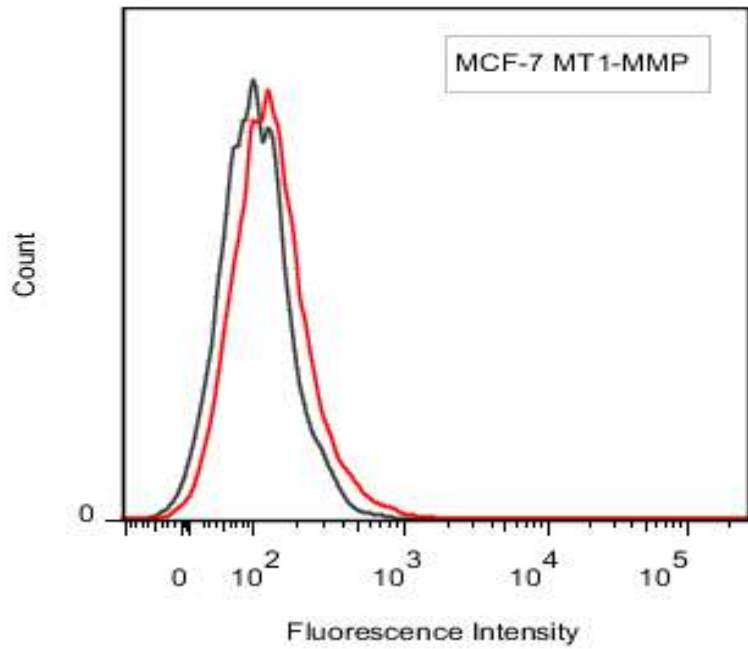
All key features of osteosarcoma,
Particularly haematogenous metastasis

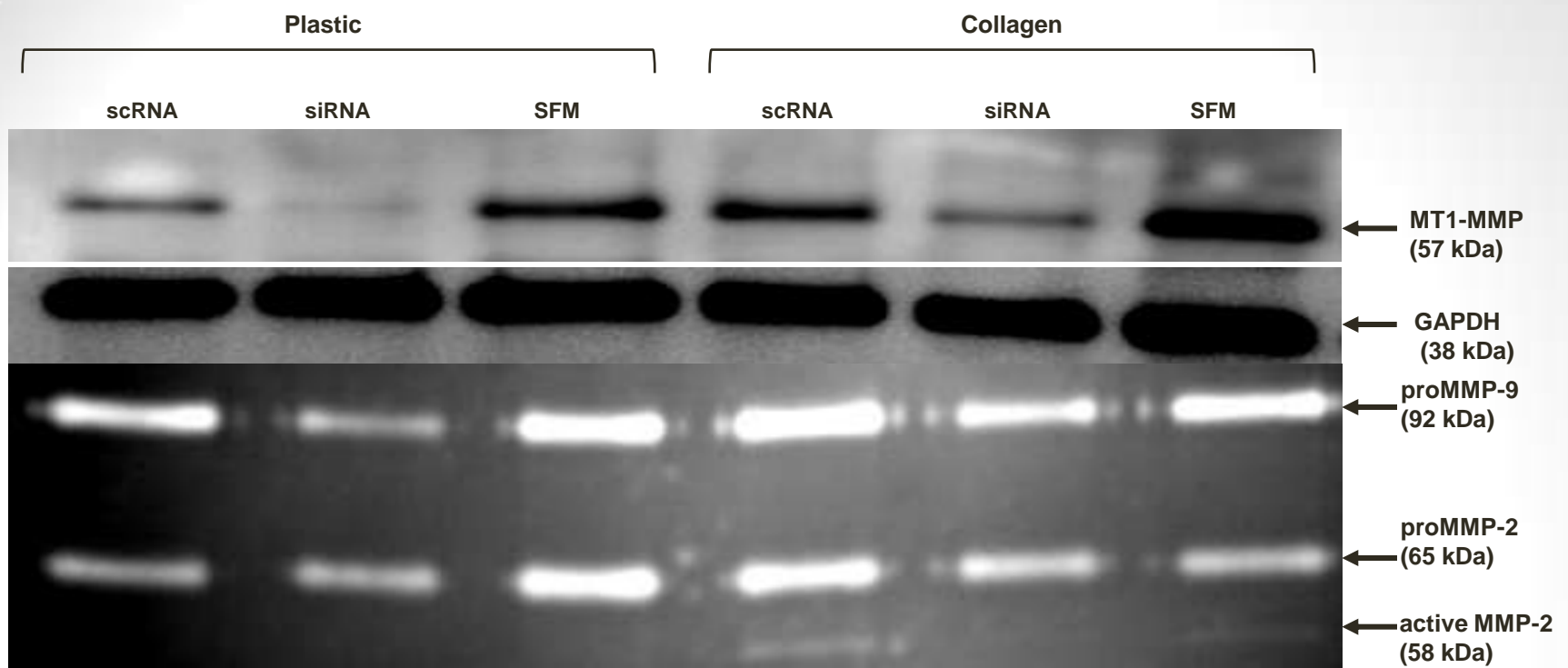
- The HT1080 fibrosarcoma line is the most widely used cell line for the study of MT1-MMP
- ↑MT1-MMP expression in OS tumour samples correlates with poor survival (Uchibori et al, Int J Oncol 2006)



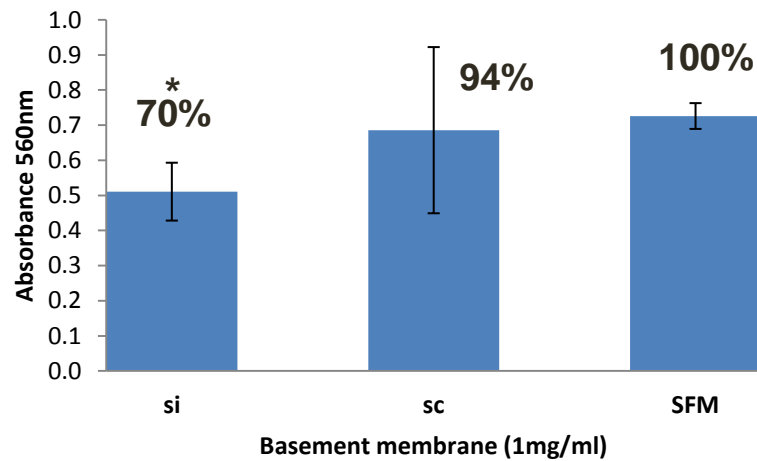
Survival curves of MT1-MMP expression status in osteosarcoma patients diagnosed in Newcastle from 1999-2010







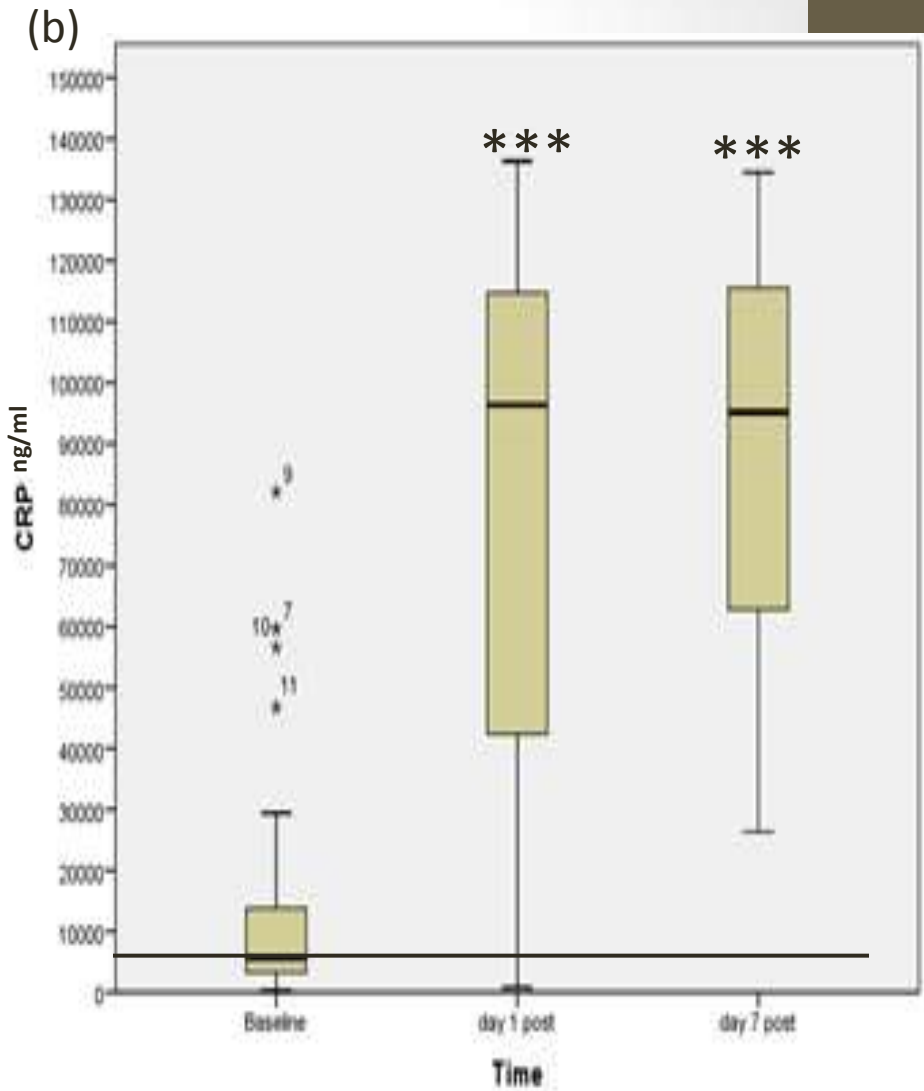
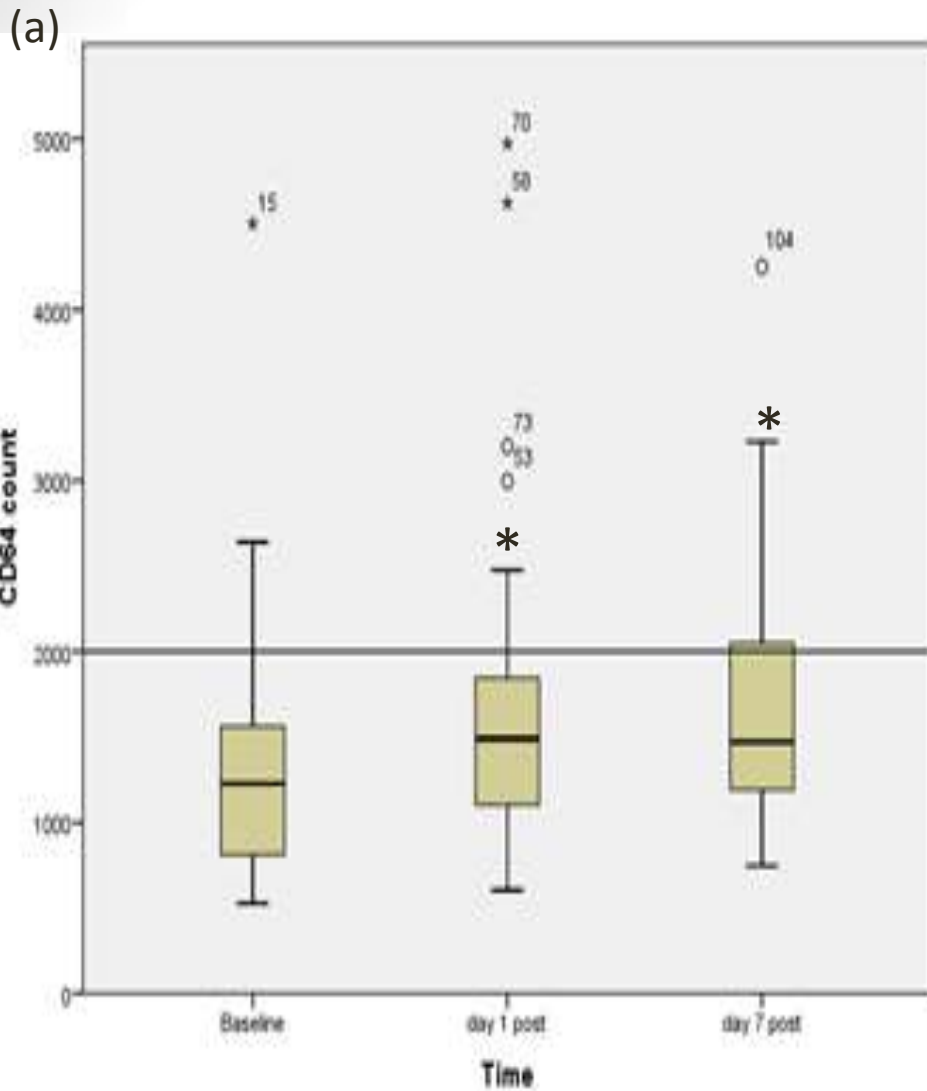
Matrigel Invasion



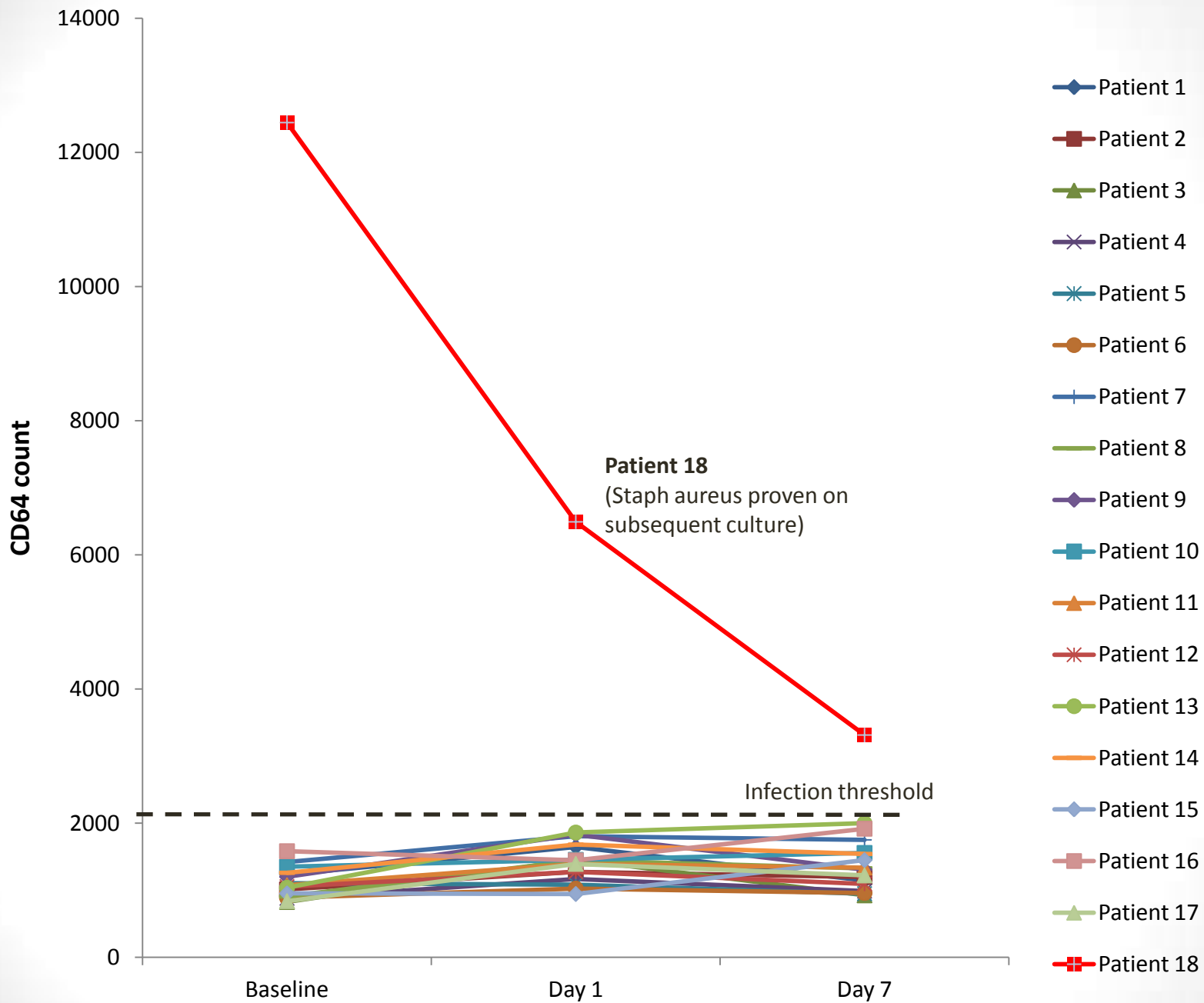
* $P=0.075$

Neutrophil CD64 (Translational)

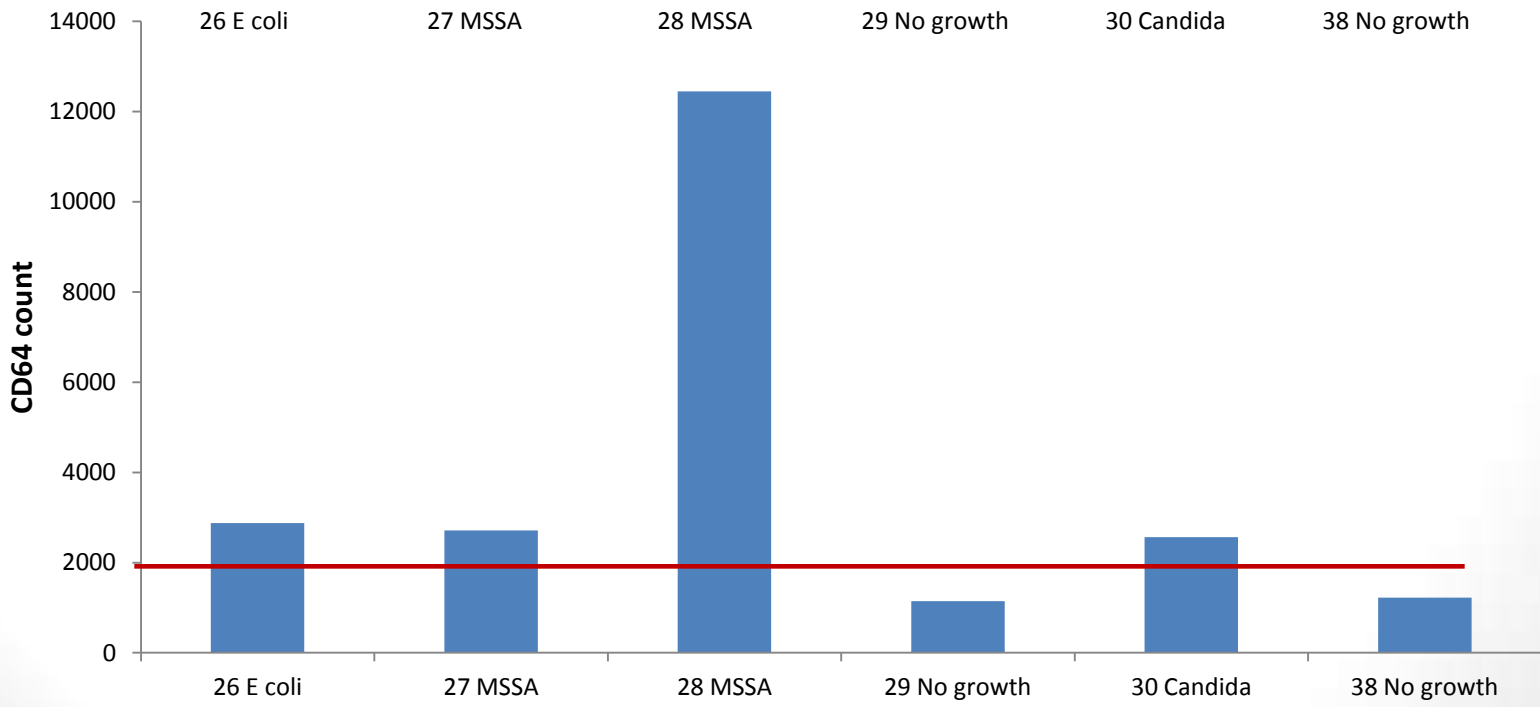
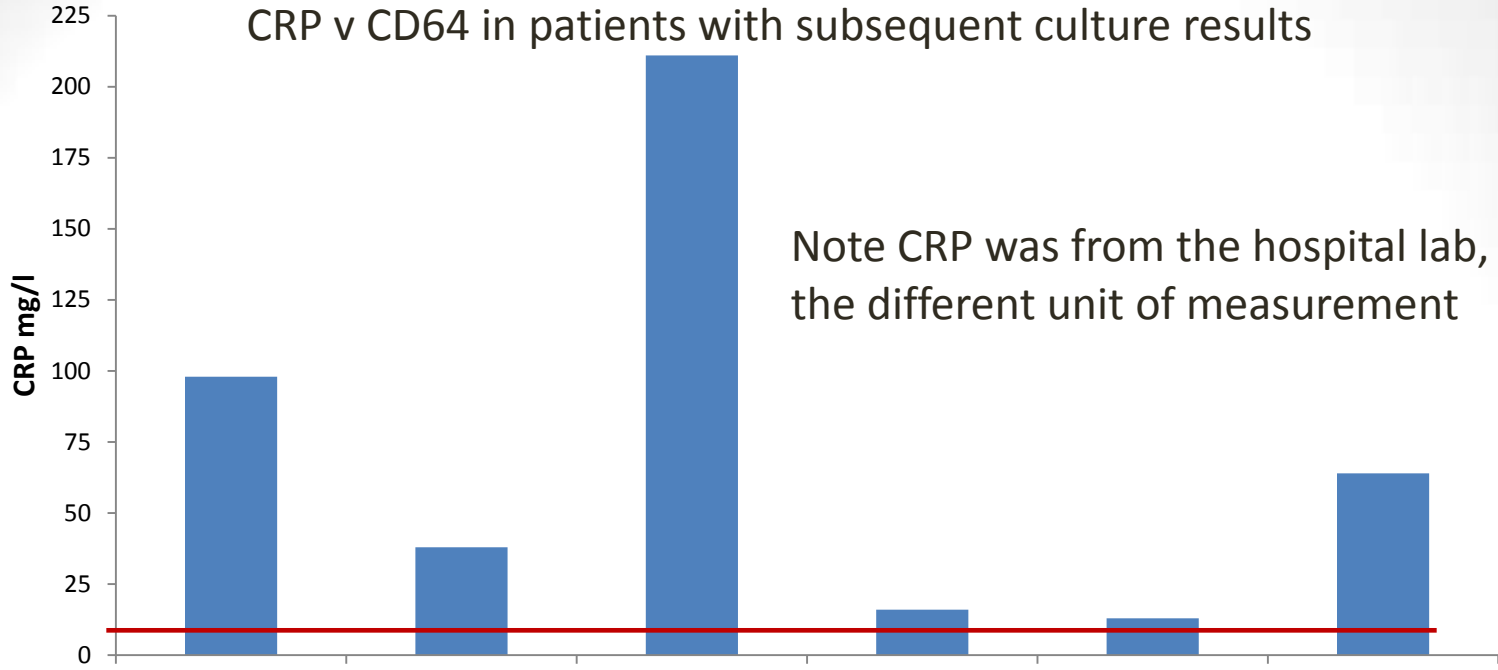
- Mike Reed, Andrew Sprowson meeting 2009
- IRAS to apply for ethical approval
- Started pilot study 2011
- Msc student 2013
- Ramsay grant from Orthopaedic Research UK
£59k
- Developing NIHR EME application



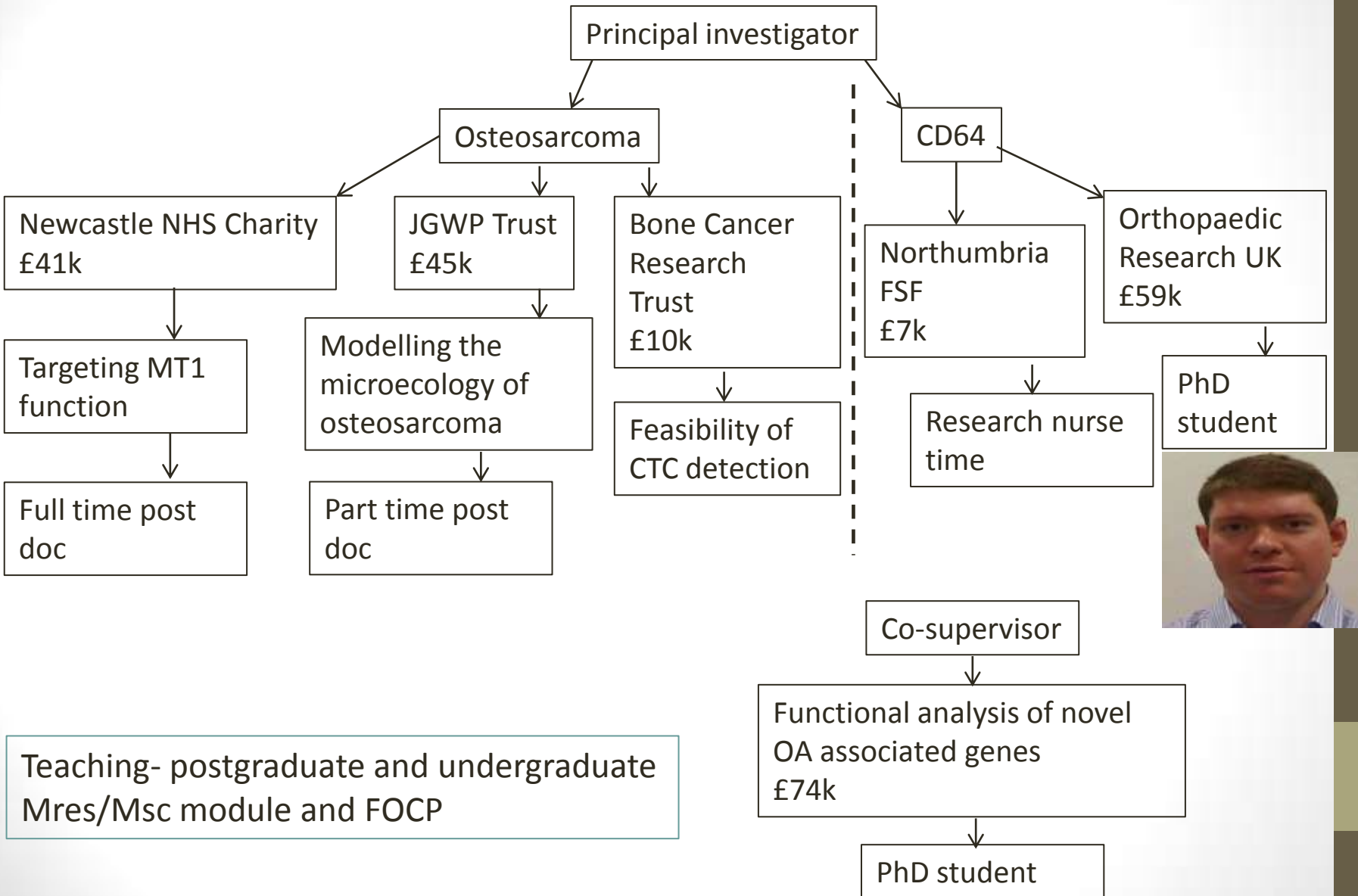
CD64 v CRP in 45 routine patients at pre-op (baseline), day 1 and day 7 post-op.
 (a) There is a significant increase in CD64 at day 1 and day 7 * $p=0.011$ compared to baseline, with one outlier above the infection threshold of 2,000 at day 7.
 (b) The increase in CRP at day 1 and 7 compared to baseline is highly significant *** $p<0.001$, with all values at day 1 and 7 above the infection threshold of 5,000 ng/ml.



CRP v CD64 in patients with subsequent culture results



Current situation



Research Opportunities

- MRG and NICR for laboratory based projects
- Tom Joyce/Dave Langton for Engineering
- Prof Deehan
- Andy Gray for Trauma
- Steve Aldridge for Trauma/Upper limb
- Prof Rangan for Clinical studies
- CORNET
- Building interlinks with University Research Design Service to develop NIHR applications

Funding bodies

National

Local



**National Institute for
Health Research**

NIHR: translational & clinical only

orthopaedic
research UK

basic science,
translational
& clinical



**Arthritis
Research UK**

basic science, translational &
clinical



**British
Orthopaedic
Association**



THE ROYAL COLLEGE
OF SURGEONS OF
EDINBURGH



RCSEng:
Shears Northern
Research Fellowship

Northern Orthopaedic
Research: Pump priming

**The Newcastle
Healthcare Charity**

JGW Patterson
Foundation

Summary

- Orthopaedic research is being heavily promoted by BOA
- Increasing opportunities to gain MD/PhD during 'standard' training
- Opportunities to transfer into Academic stream
- It is enjoyable and does not decrease your ability to operate!