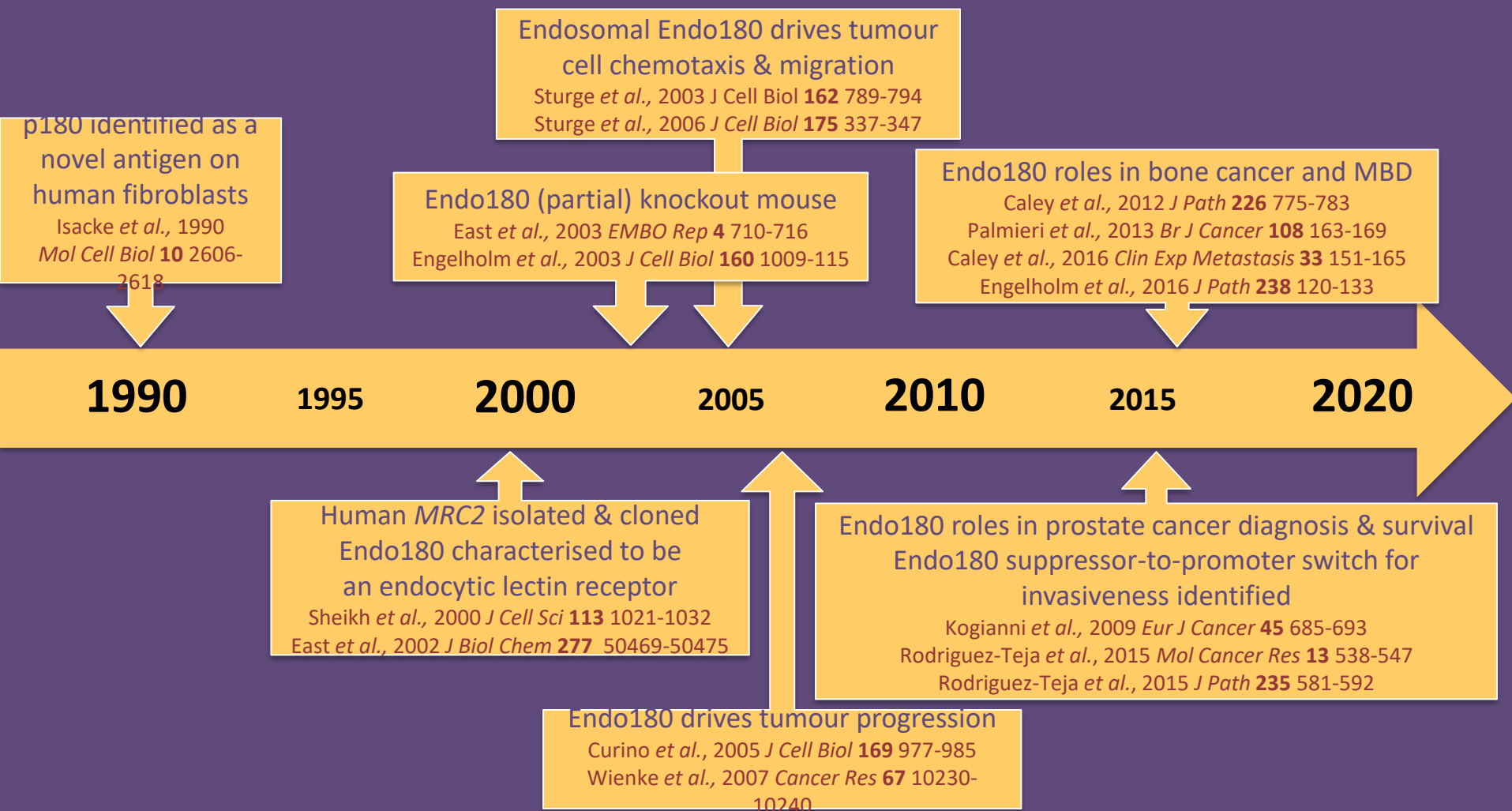


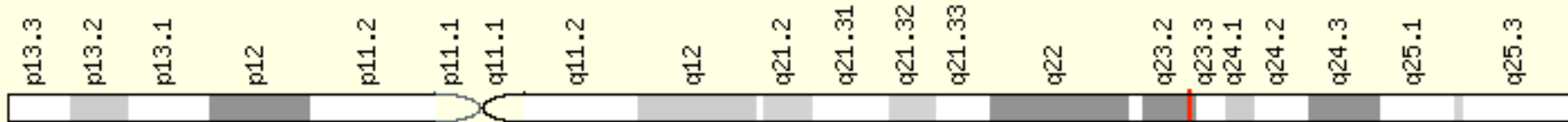


[j.sturge@hull.ac.uk](mailto:j.sturge@hull.ac.uk)

# Endo180: Road To Cancer Discovery



Chr 17



# Cancer Evolution & Progression

## ENDOLEVELS

### **PECs and PTCs *in vitro***

- Acini
- Human ECM
- Bone cell co-cultures

*MIGRATION, INVASION, EMT  
MECHANOTRANSDUCTION  
ECM REMODELLING*

## ENDOGLOWS

### **Pre-clinical models**

- Orthotopic
- Intracardiac
- Intratibial

*METASTATIC DISSEMINATION  
PRE-METASTATIC NICHE  
BONE REMODELLING*

## ENDOMETES

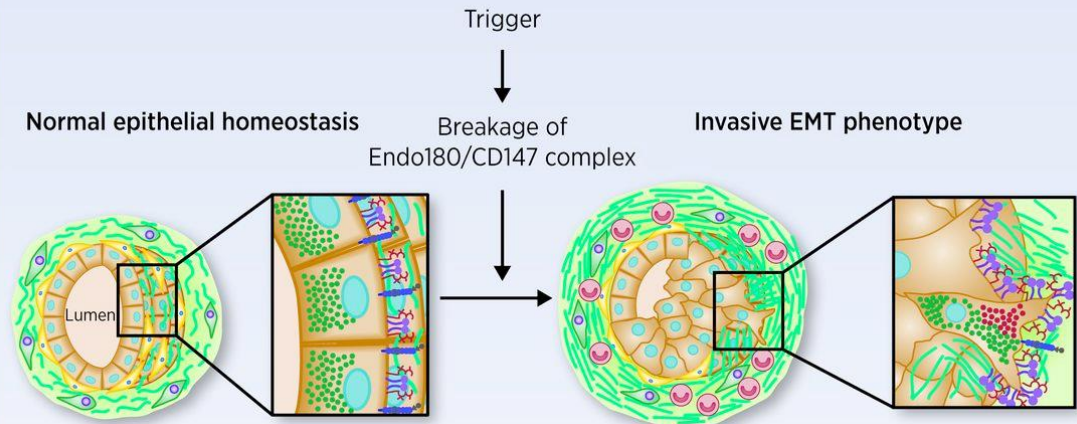
### **Patient studies**

- Diagnostic tools
- Surgical tools
- New treatments

*MONITORING METASTASIS  
PRECISION SURGERY  
TARGETED DRUG DELIVERY*

# Endo180 Switch Drives Early Invasive Cancer

## Breaking up Endo180 and CD147 triggers EMT to reduce prostate cancer survival

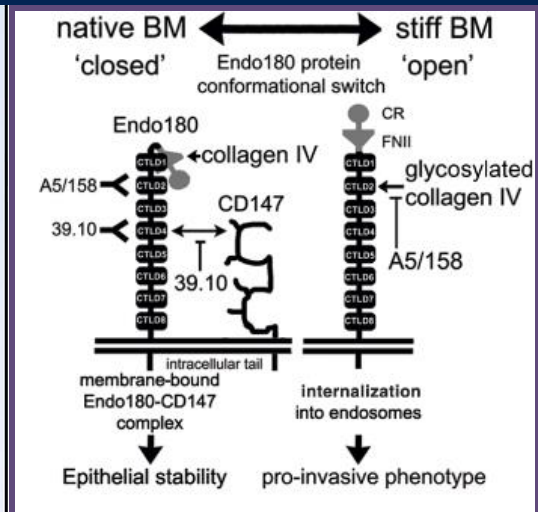


■ Luminal epithelial cell    ■ Basal epithelial cell    ■ Fibroblast    ■ Inflammatory cell    ■ Integrins  
~ Compliant ECM    ~ Stiff ECM    ~ Highly glycosylated CD147    ■ Transformed epithelial cell  
■ Membrane bound Endo180 (C-type Lectin Domain 4/CTLD4 in gray)    ■ Endosomal Endo180 (clathrin-dependent endocytosis)    ■ Low glycosylated CD147 (clathrin-independent endocytosis)

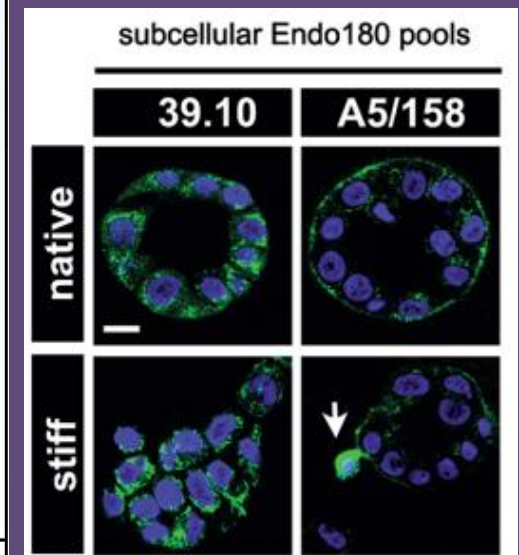
- |  |  |
|--|--|
| <ul style="list-style-type: none"> <li>• Endo180-CTLD4/CD147 complex intact</li> <li>• Endo180/CD147 at basolateral plasma membrane</li> <li>• Highly glycosylated CD147</li> <li>• E-cadherin high</li> <li>• Intact adherens junctions</li> <li>• Polarized epithelial cells</li> <li>• Invasiveness suppressed</li> </ul> | <ul style="list-style-type: none"> <li>• Endo180-CTLD4/CD147 complex disrupted</li> <li>• Endo180/CD147 internalized</li> <li>• Loss of CD147 glycosylation</li> <li>• Rho GTPase spatiotemporally activated</li> <li>• Decreased E-cadherin</li> <li>• Disrupted adherens junctions</li> <li>• Scattered epithelial cells</li> <li>• Enhanced invasive potential</li> </ul> |
|--|--|

**Implications:**  
 This study identifies the interaction between CTLD4 in Endo180 and CD147 as an EMT suppressor and indicates that stabilization of this molecular complex improves prostate cancer survival rates.

© 2014 American Association for Cancer Research

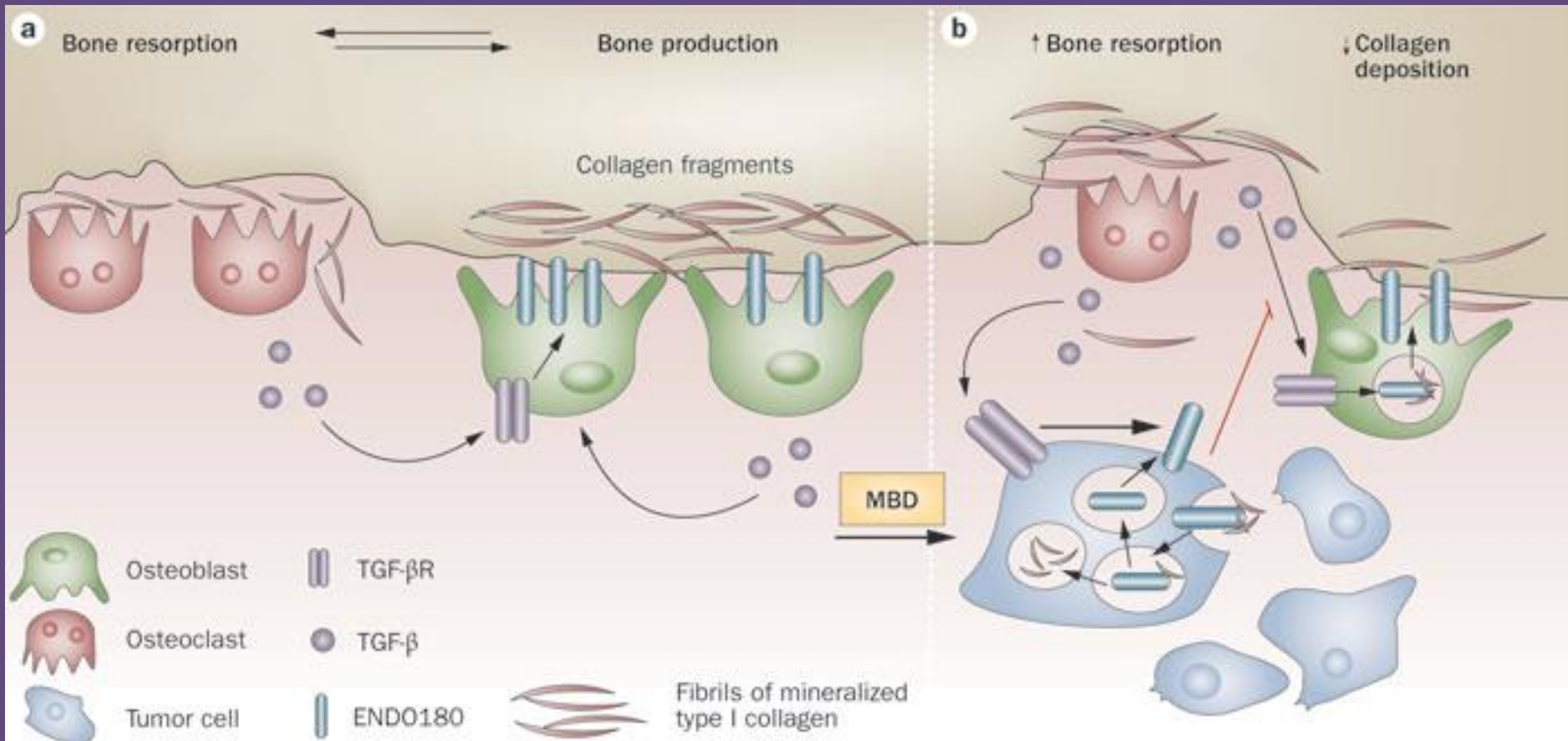


39.10 detects Endo180 inside cells; A5/158 detects basolateral Endo180 and on surface of invasive cells!

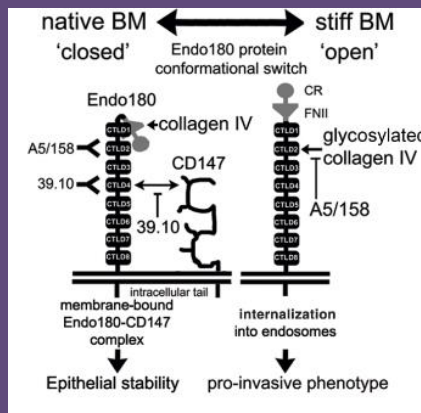
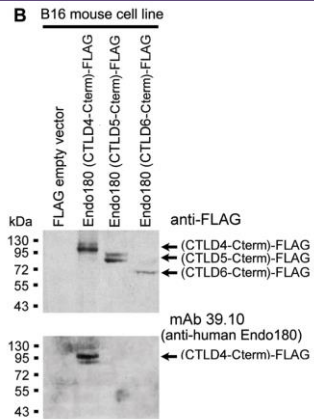
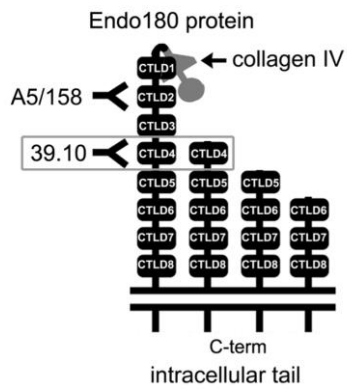


J Path 2015  
 JOVE 2016

# Endo180 Dysfunction Drives Metastatic Bone Cancer



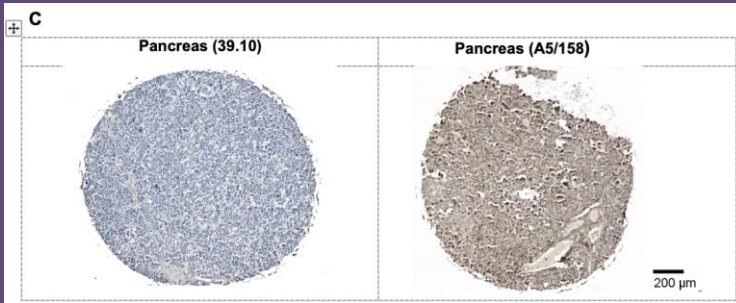
Therapeutic target in osteosarcoma – antibody therapy



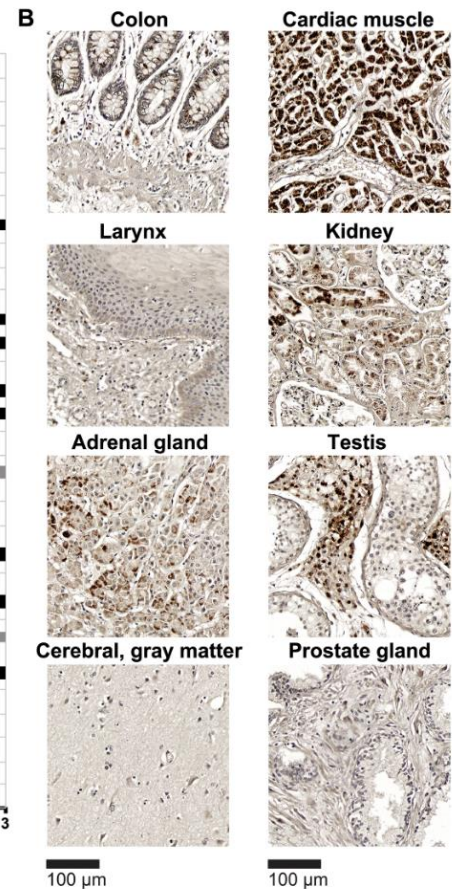
39.10 does not detect Endo180 when in suppressor complex; whereas A5/158 does!

Julian Gronau, PhD thesis

### Epitope mapping



FDA approved normal tissue TMA



## **Hyperglycaemia: Co-morbidity and risk factor....**

Diabetes currently affects around 537 million people worldwide and this figure is predicted to increase rapidly to 643 million in 2030 and 783 million in 2045.

Type 2 diabetes is responsible for 90-95% of diabetes diagnoses and is considered a modern preventable pandemic.

In the UK, 3.5 million people have diabetes, 549,000 are living with undiagnosed diabetes and 7 million are pre-diabetic [Diabetes UK].

Pre-diabetes increases cancer risk by 15% [1] and diabetes **doubles** liver, **pancreatic** and endometrial cancer risk; and increases colorectal, breast and bladder cancer risk by 20-30% [2].

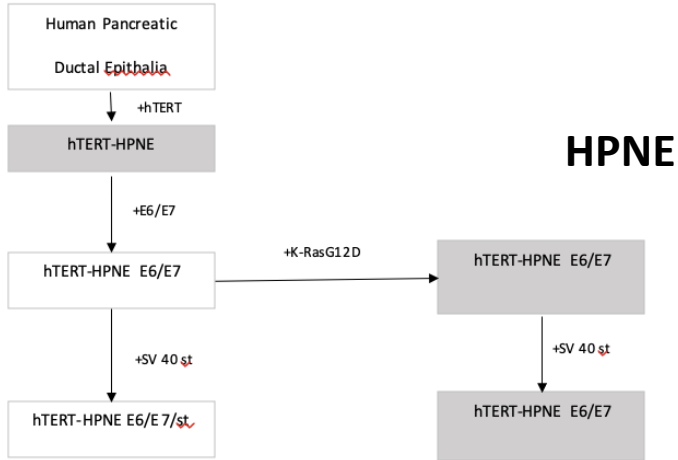
In contrast, diabetes reduces localised and intermediate-grade prostate cancer risk by 18% and 23% respectively but increases mortality by 29% [3].

[1] Diabetologia 2014 57 2261-9

[2] J Res Med Sci 2019 24 94.

[3] Br J Cancer 2020 123 657–665

# Effect of hyperglycaemic microenvironment on Endo180 cell surface levels

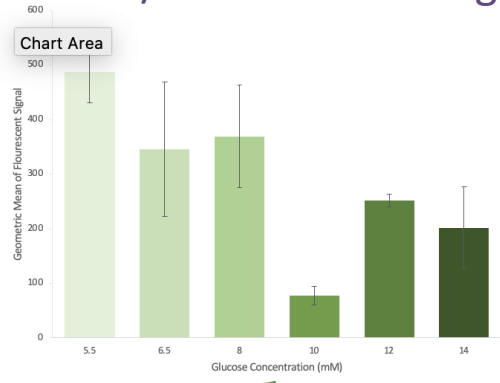


**HPNE**

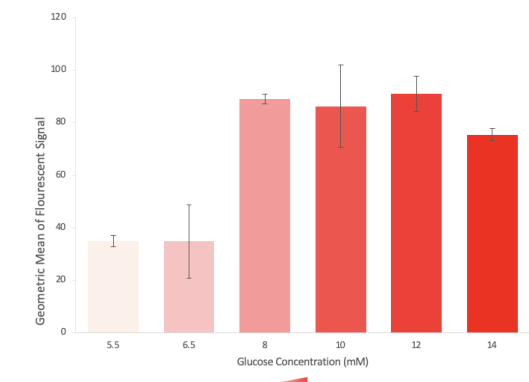
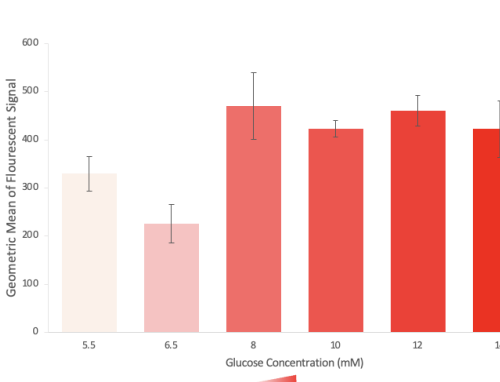
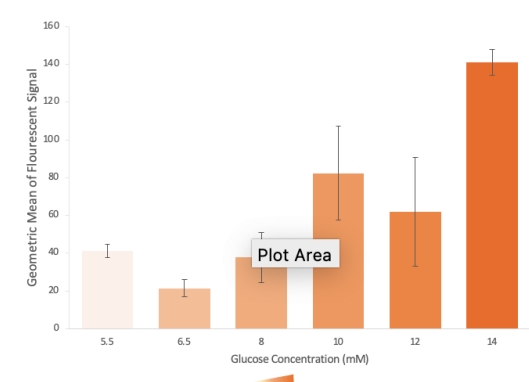
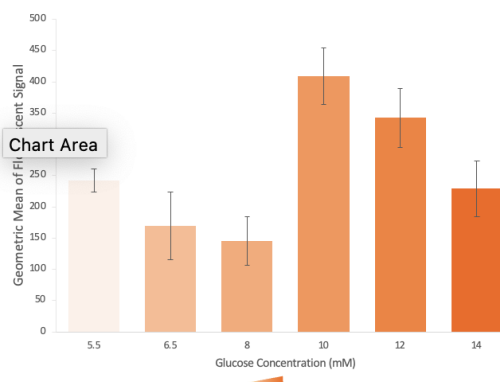
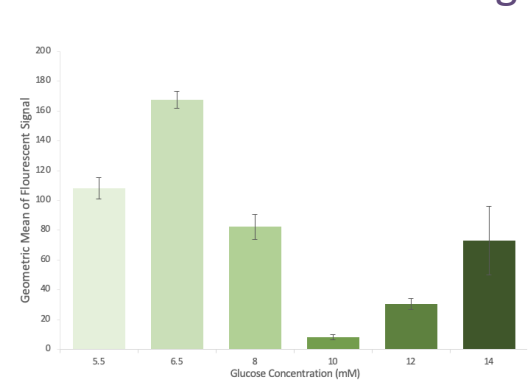
**HPNE-I**

**HPNE-M**

A5/158 mAb staining

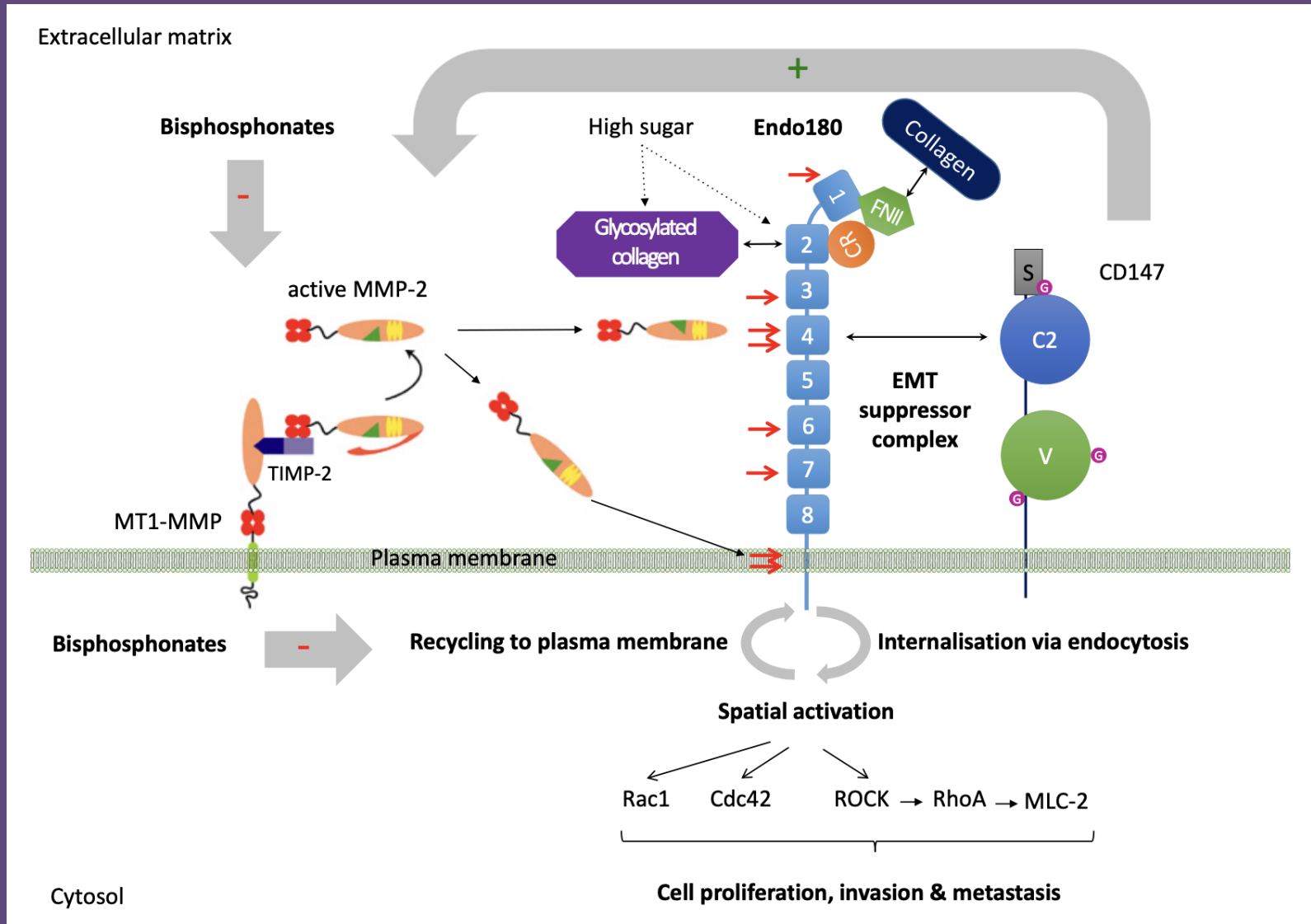


39.10 mAb staining





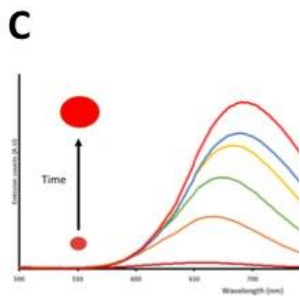
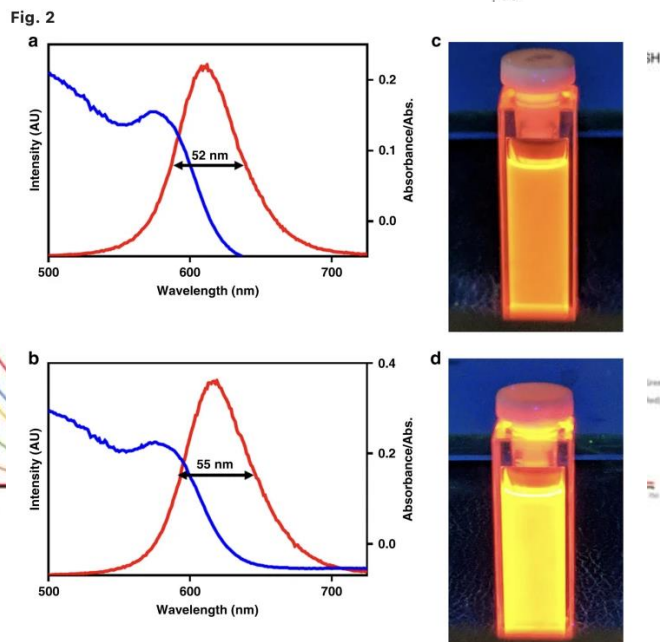
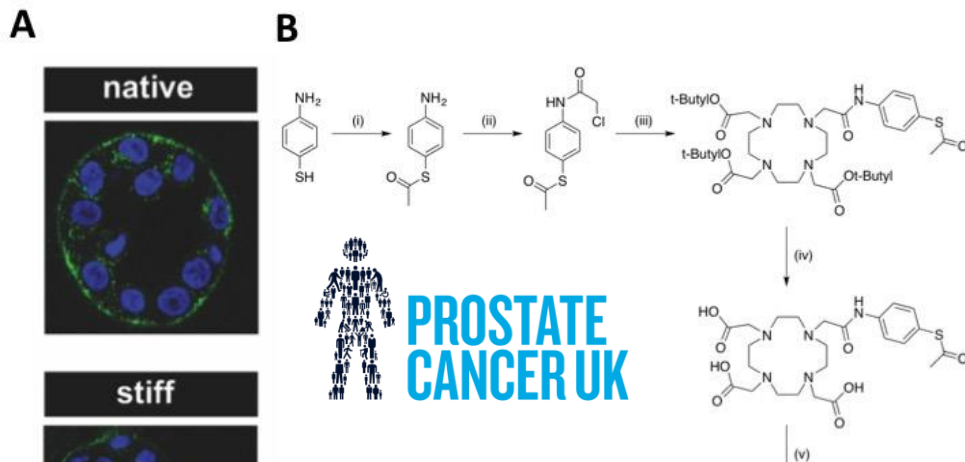
# Patient Studies – ENDOLEVELS – Breast, Prostate, Pancreas



What is the biological function of soluble Endo180?

# MRI/PET – ENDOGLOWS – IMAGE GUIDED SURGERY

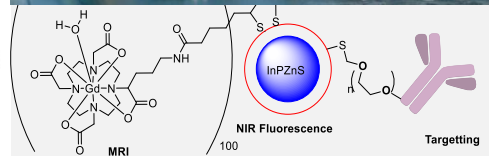
## ENDOGLOWS: BIOIMAGING OF NEWLY METASTATIC CANCER



**E**



+ HC Photophysical properties of InP/ZnS(1) and InP/ZnS(2). **a, b** Absorption (red) and emission spectra (blue), along with the full width at half maximum InP/ZnS(1) (**a**) and InP/ZnS(2) (**b**). **c, d** Photographs showing the obtained luminescence of both InP/ZnS(1) (**c**) and InP/ZnS(2) (**d**) under ultraviolet light (365 nm)

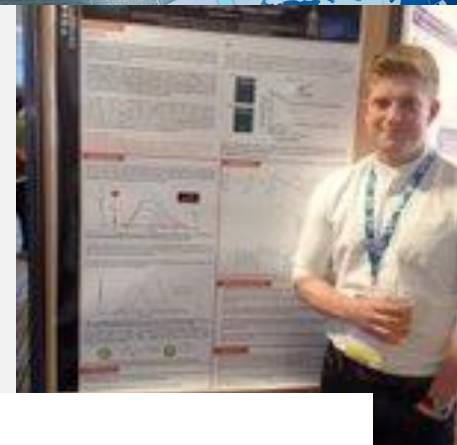


**Dr Graeme Stasiuk**

University of Hull

**Mitchell Clarke**, Prostate

Cancer UK Ph.D. Studentship



**COMMUNICATIONS CHEMISTRY**

ARTICLE

<https://doi.org/10.1038/s42004-019-0138-z>

OPEN

Synthesis of super bright indium phosphide colloidal quantum dots through thermal diffusion

Mitchell T. Clarke<sup>1</sup>, Francesco Narda Viscomi<sup>2</sup>, Thomas W. Chamberlain<sup>3</sup>, Nicole Hondow<sup>4</sup>, Ali M. Adawi<sup>2,5</sup>, Justin Sturge<sup>1</sup>, Steven C. Erwin<sup>6</sup>, Jean-Sebastien G. Bouillard<sup>2,5</sup>, Sudarsan Tamang<sup>7</sup> & Graeme J. Stasiuk<sup>1</sup>

- Multi-modal bio-imaging probes targeting Endo180
- Proof-of-principle application for bio-imaging Endo180 status in cancer
- Application in diagnosis, prognosis, personalised treatment planning, image-guided surgery

# TARGETED THERAPY – ENDOMETETS – DRUGS ON DEMAND

- Exploit Endo180 ligand uptake into endosomes
- Engineer drug accumulation in target region of tumour cells (Endo180<sup>+</sup> perinuclear endosomes)
- Targeting ligands (Endo180 antibodies) on vehicle surface to facilitate binding to Endo180<sup>+</sup> tumour cells
- Acoustic activation + microbubbles
- Magnetic nanoparticles + magnetic field

## Ultrasound sensitive release

- thermally sensitive carriers (heat)
- physically disrupt carriers (bubbles)

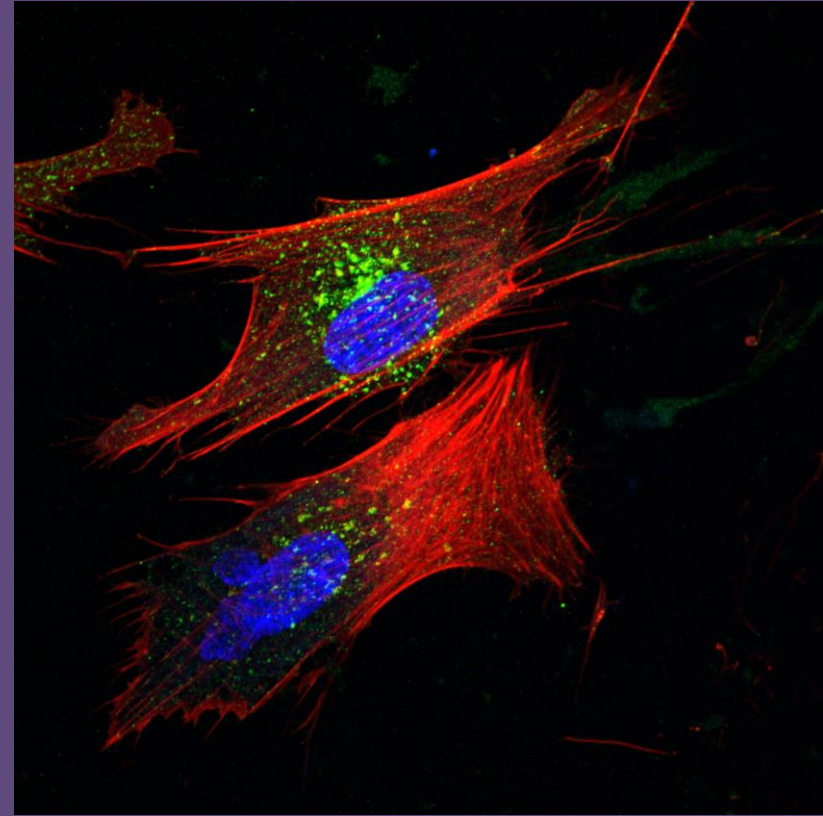
## Photosensitive release

- incorporate gold nanoparticles

## Charge sensitive release

## Stimuli responsive components

- monitor drug delivery
- incorporate ENDOGLOWS (diagnostic)



### Imperial College London

Professor Jonathan Waxman  
Dr Francesco Mauri  
Professor Justin Cobb

### Breakthrough Breast Cancer

Professor Clare Isacke  
Dr Afshan McCarthy  
Dr Dirk Wienke

### Institute of Cancer Research

Professor Chris Marshall

### University of Copenhagen

Dr Janine Erler  
Dr Thomas Cox

### Newcastle University

Professor Craig Robson  
Dr Luke Gaughan

### Cardiff University

Dr Catherine Hogan

### University of Liverpool

Professor Carlo Palmieri

### University of York

Professor Norman Maitland  
Dr Fiona Frame

### University of Hull / HYMS

Professor Anthony Maraveyas

Dr Farzana Haque

Dr Camille Ettelaie

Dr Leonid Nikitenko

Professor Thozukat

Sathyapalan

+ many more ...

### University of Hull

Dr Daniel Diaz-Garcia (Charles, UANL/Texas)

Dr Rajeev Kumar (Guiyang, Ghizhou)

Dr Conan Wang (CSC, Breast Cancer Campaign)

Dr Mitchell Clarke (Prostate Cancer UK)

Mr Kamil Talar (M.Res.)

Mr George Firth (M.Res.)

Mr Matthew Walker (M.Res.)

### Imperial College London

Dr Mercedes Rodriguez-Teja (AICR, British Council)

Dr Matthew Caley (Rosetrees Trust)

Dr Violeta Fonseca (FCT)

Dr Giolanta Kogianni (Tony Gallagher & Lord Harris)

Dr Julian Gronau (Prostate Cancer UK)

Mr Adam Adamarek (Prostate Cancer UK)

Dr Ai Minamidate (TMDU/Imperial Exchange)

Dr Dennis Zhang (UROP Studentship)

Dr Karin Purshouse (Newcastle/Imperial Exchange)

Dr Claudia Breit (École Normale Supérieure de Lyon)

Dr Helen King (M.Res Cancer Studies)

Dr Neel Shah (BSCB Studentship)

Dr Assem Allam



WELLBEING  
OF WOMEN



PROSTATE  
CANCER UK

breast cancer  
now



worldwide  
cancer research

WINNER



in association with  
The Telegraph

