

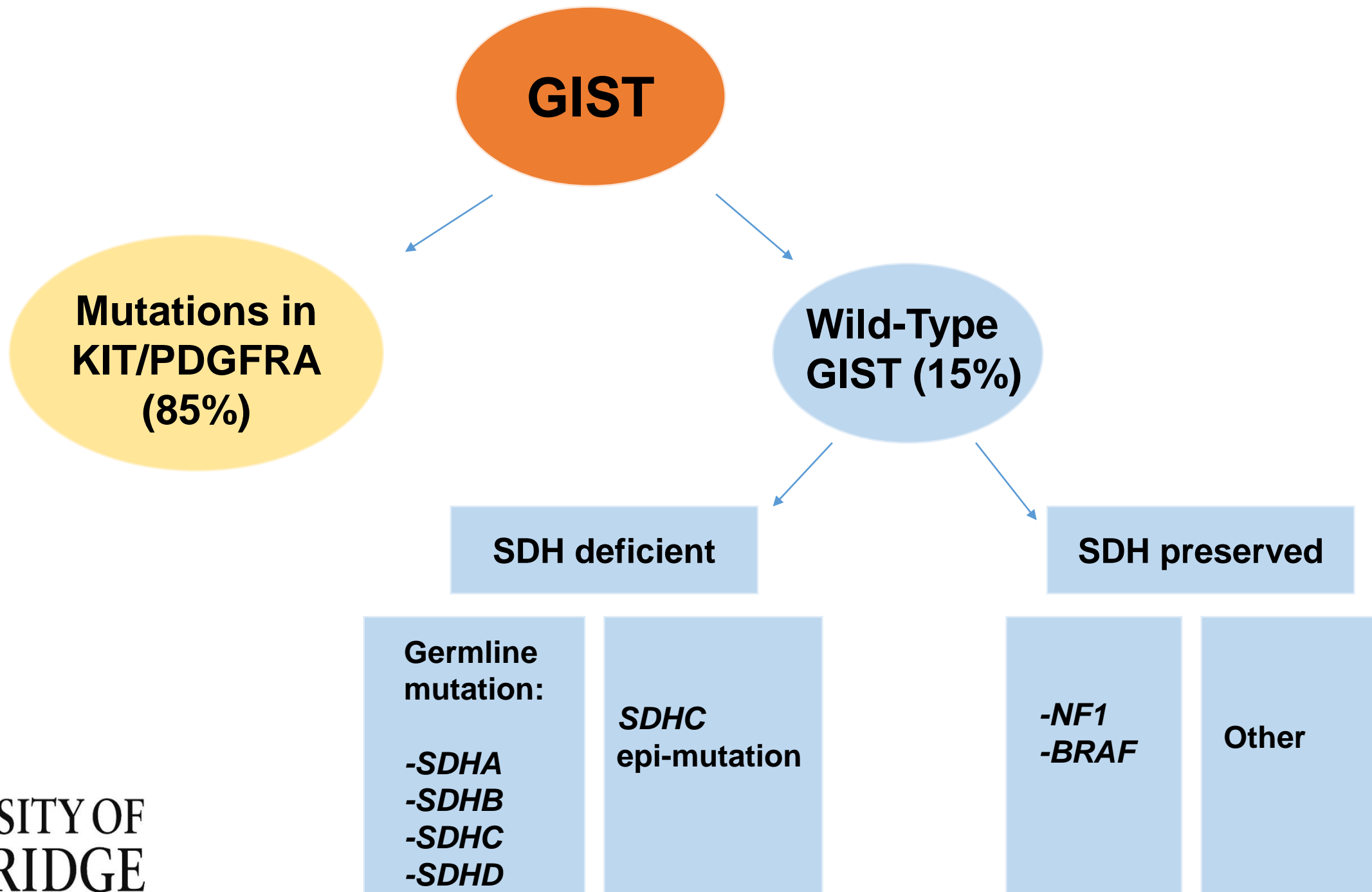
Current Research Findings from the UK Paws GIST Clinic

Dr Ruth Casey

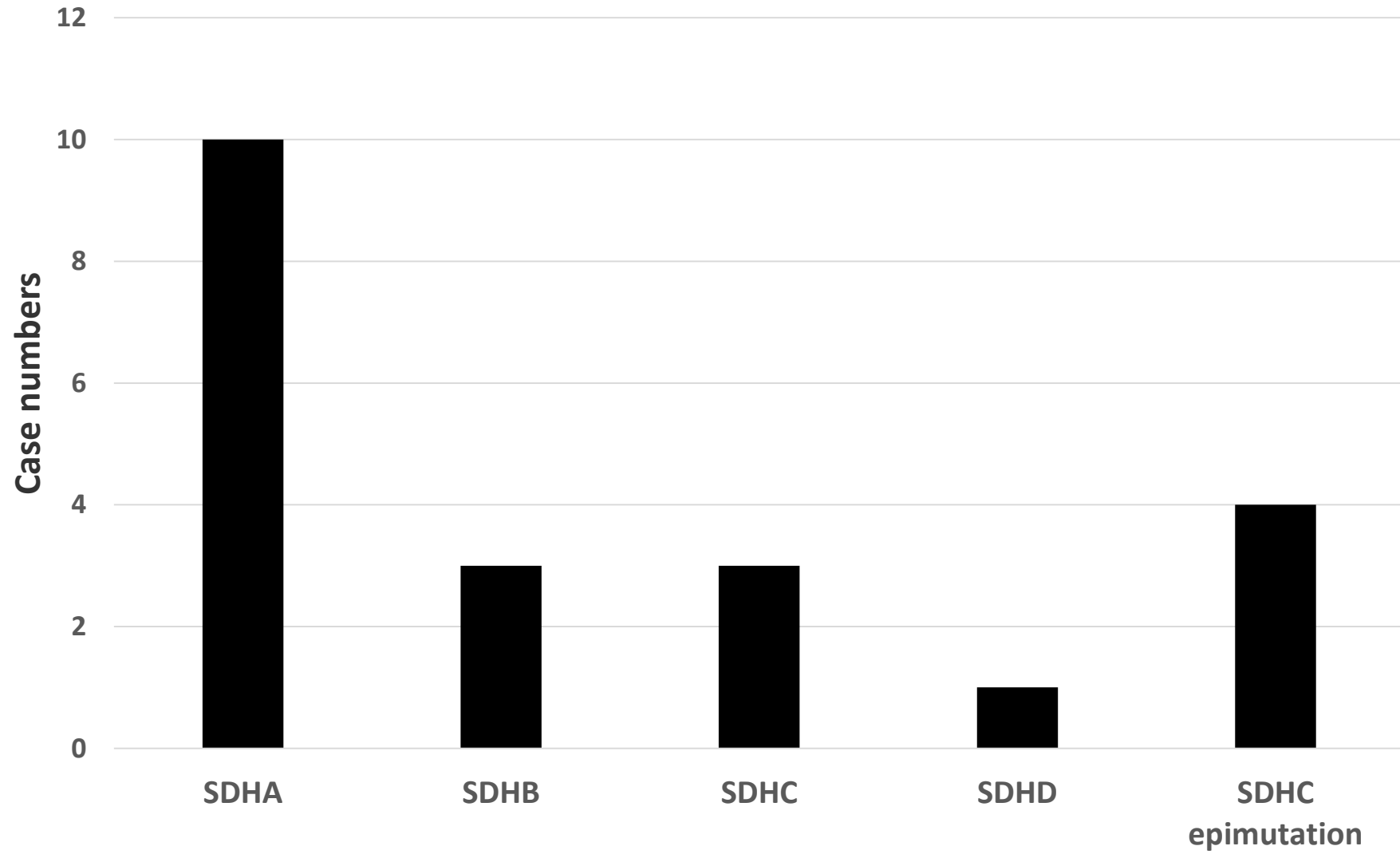
(rc674@medschl.cam.ac.uk)

Clinical research fellow
Cambridge University , UK

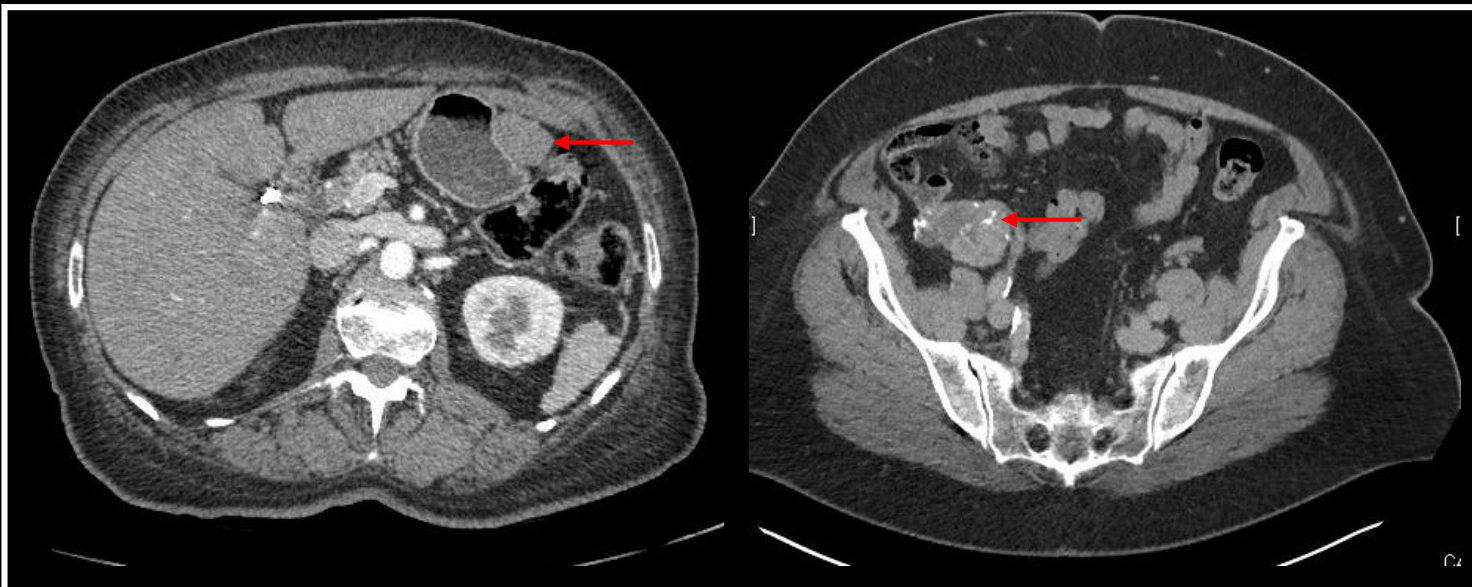
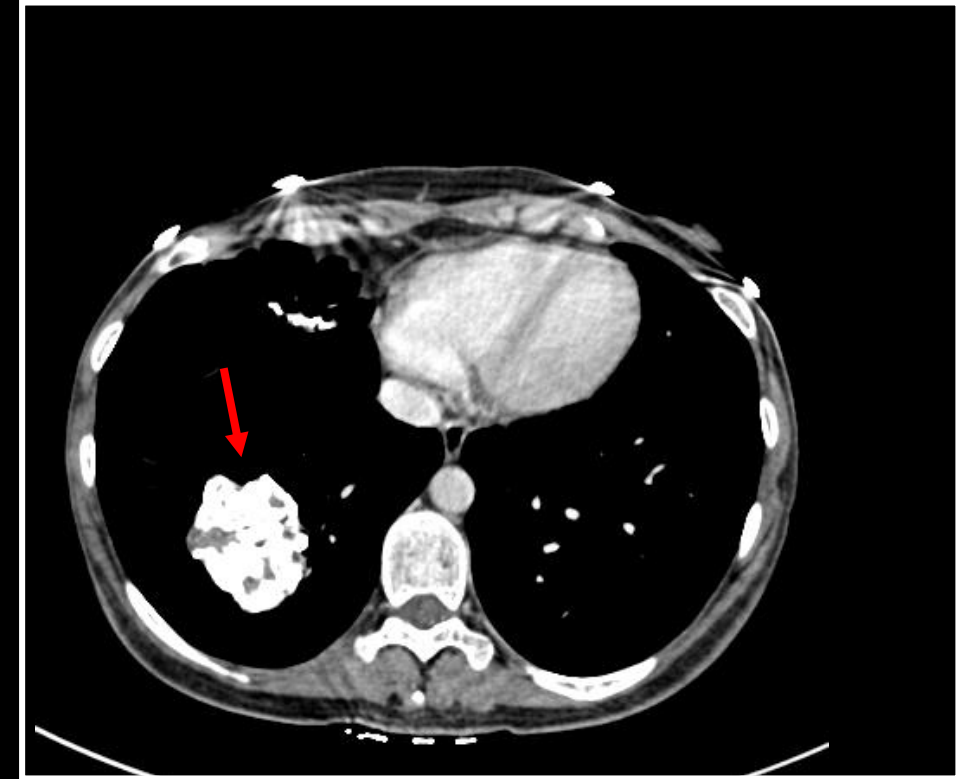
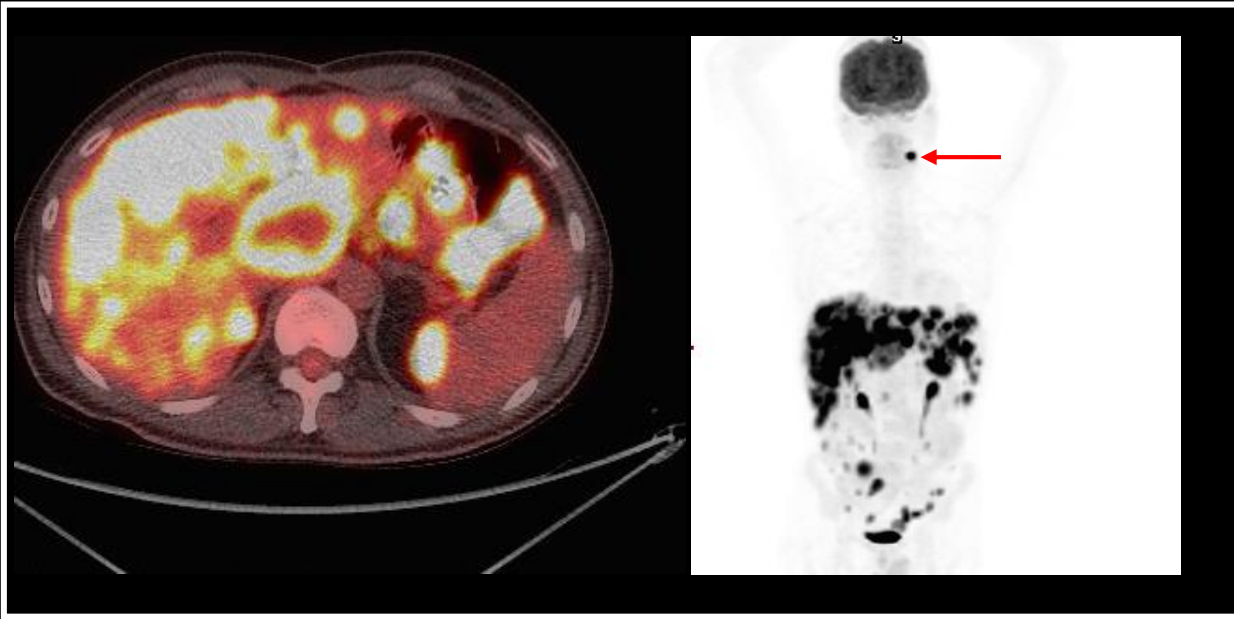




Genotype of SDH deficient UK PAWS GIST WT GIST cohort

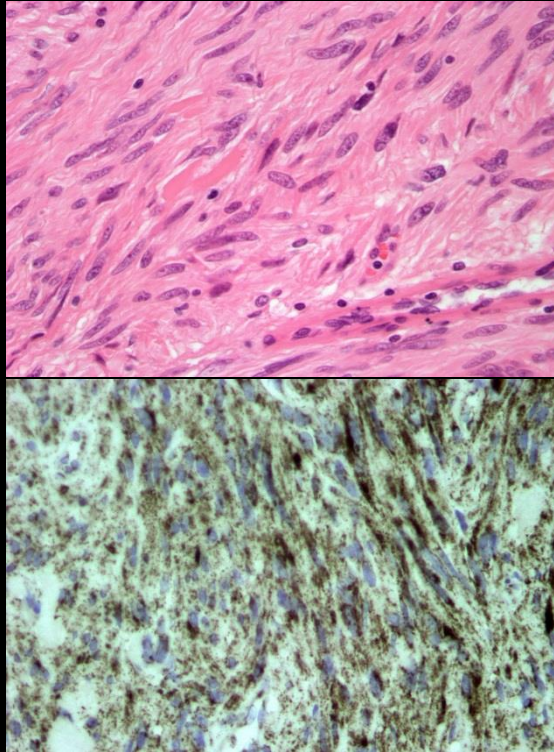


Synchronous tumours with SDH deficient GIST



26% of SDH deficient GIST cohort had synchronous tumors

Histological characteristics of wt GIST

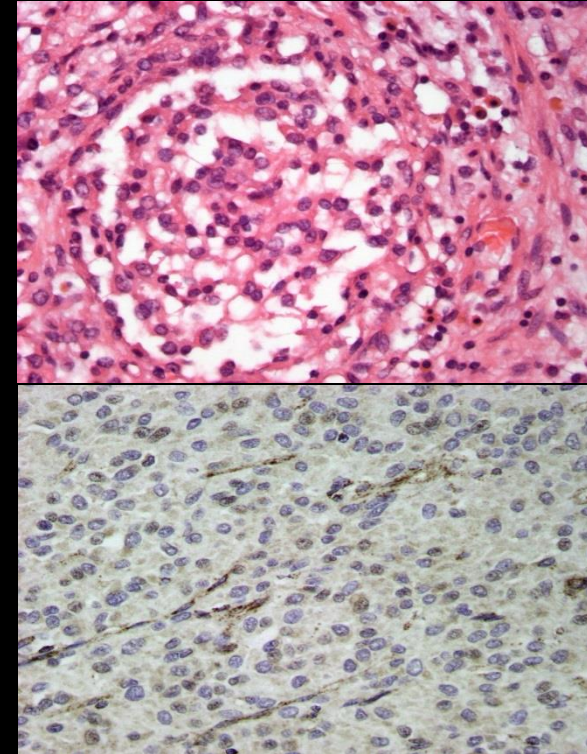


SDH preserved

- Spindle cell histology from small bowel GIST
- Typically small bowel



- Gross specimen of gastric wt GIST



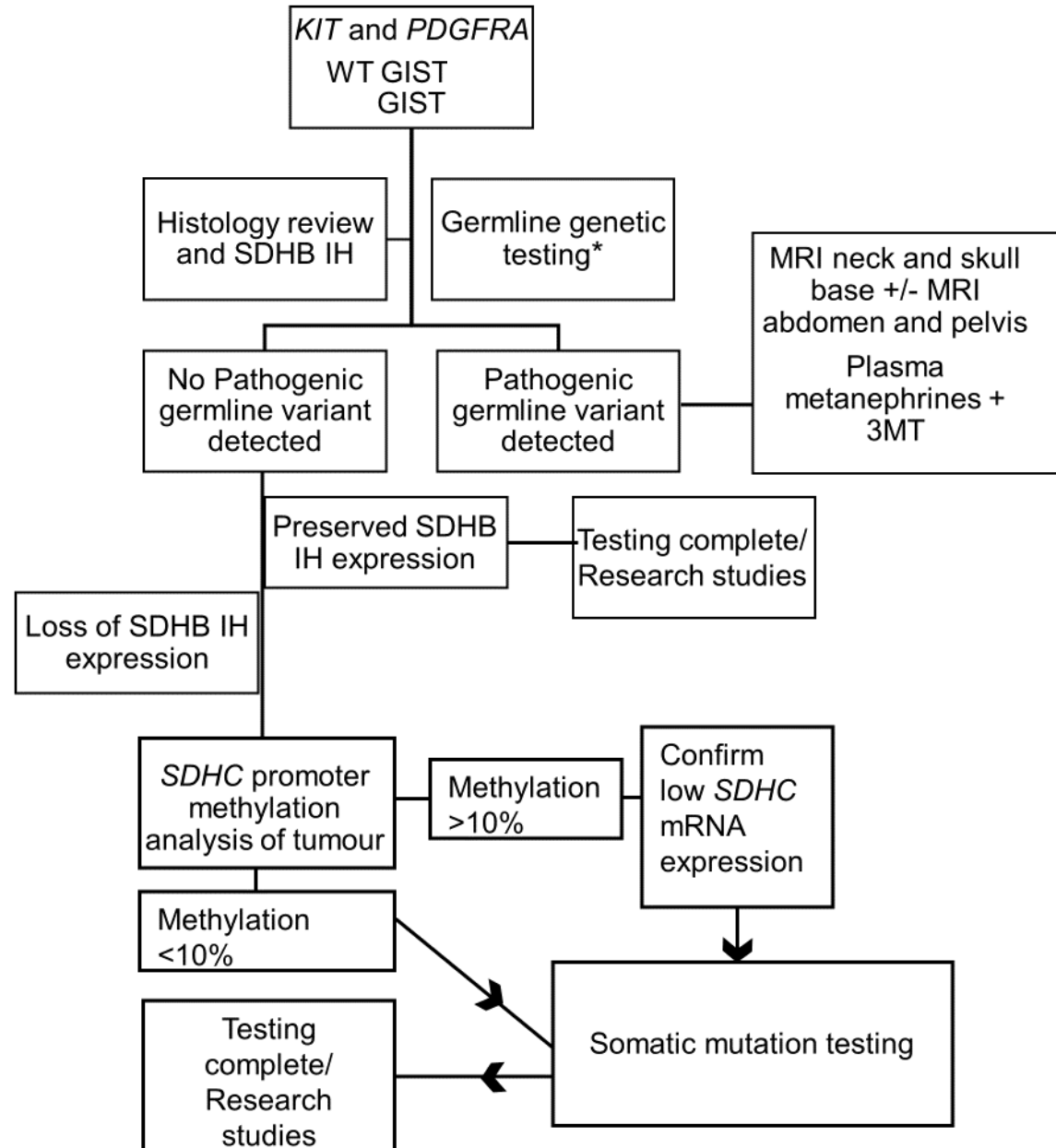
SDH deficient

- Mixed epithelioid histology from gastric GIST
- Typically gastric

SDH deficient GIST

- Young age at presentation
- Primary tumour is typically gastric in location
- Histology is epithelioid or mixed epithelioid
- High rates of metastases
- *SDHA* is the most common *SDHx* gene implicated in SDH deficient GIST
- Most common variant is *SDHA* c.91C>T p.(Arg31Ter)
- Important to remember genetics may not always be the answer in wt GIST, high frequency of *SDHC* epi-mutations in this cohort

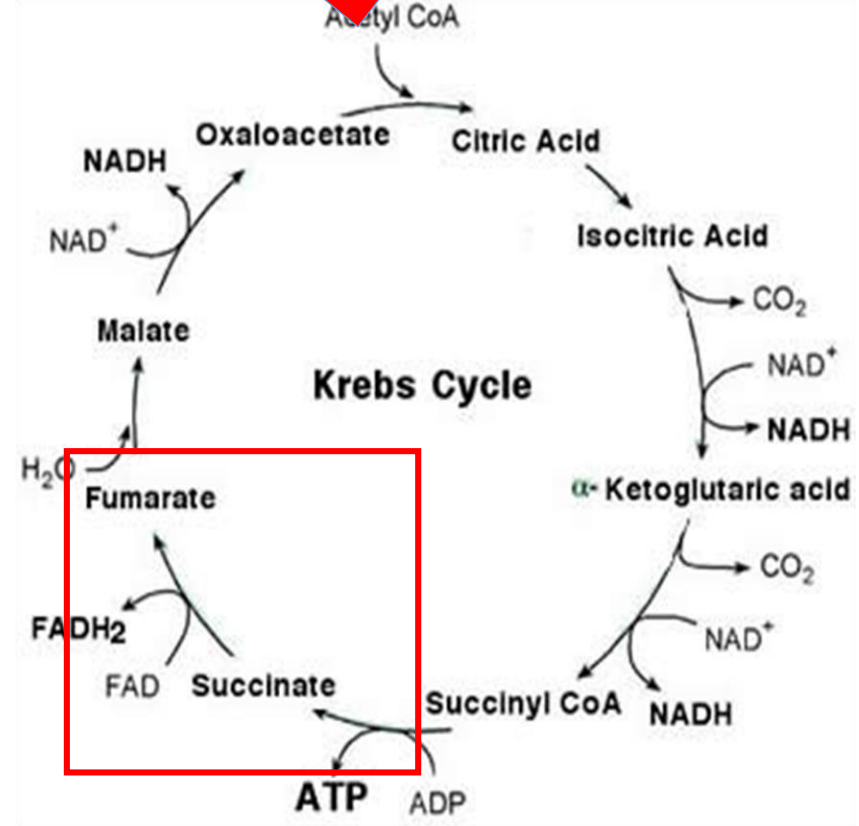
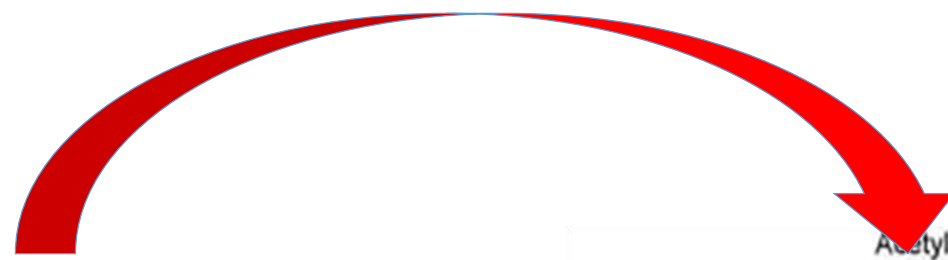
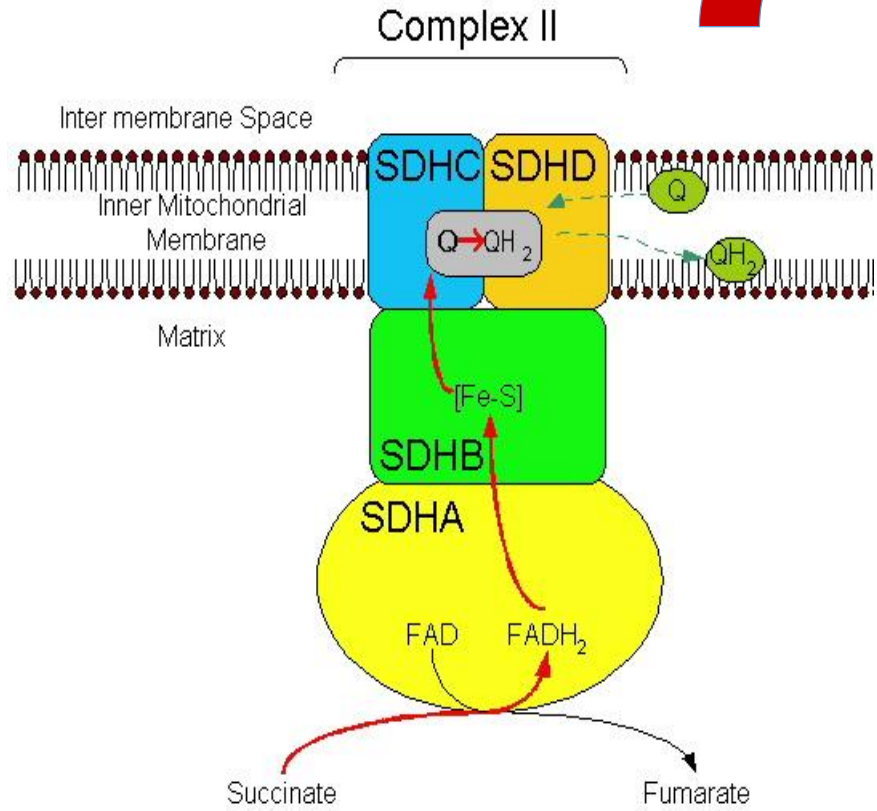
Diagnostic algorithm for SDH deficient wt GIST:



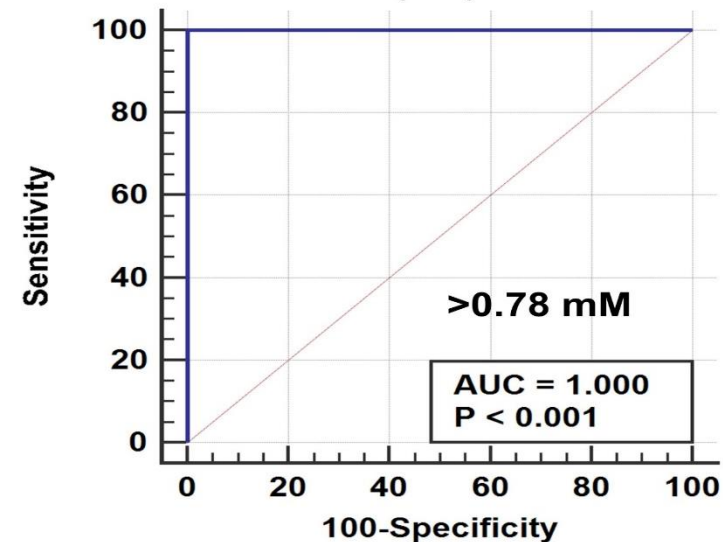
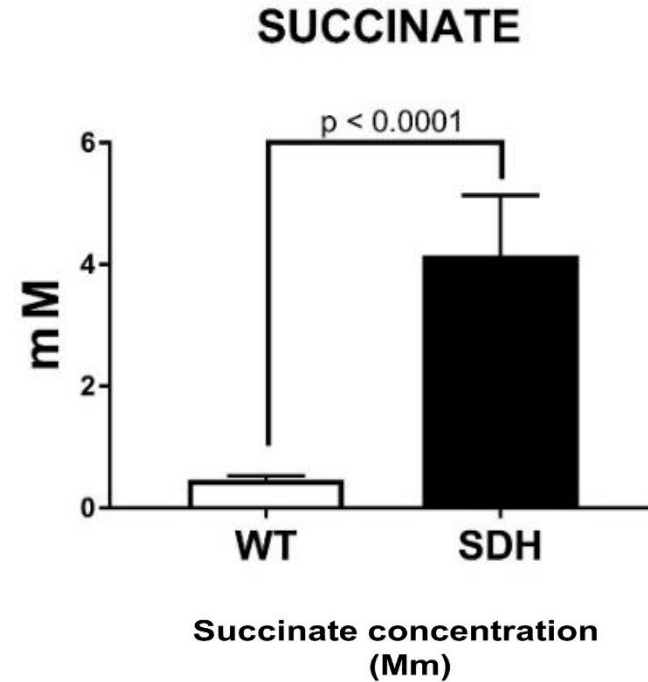
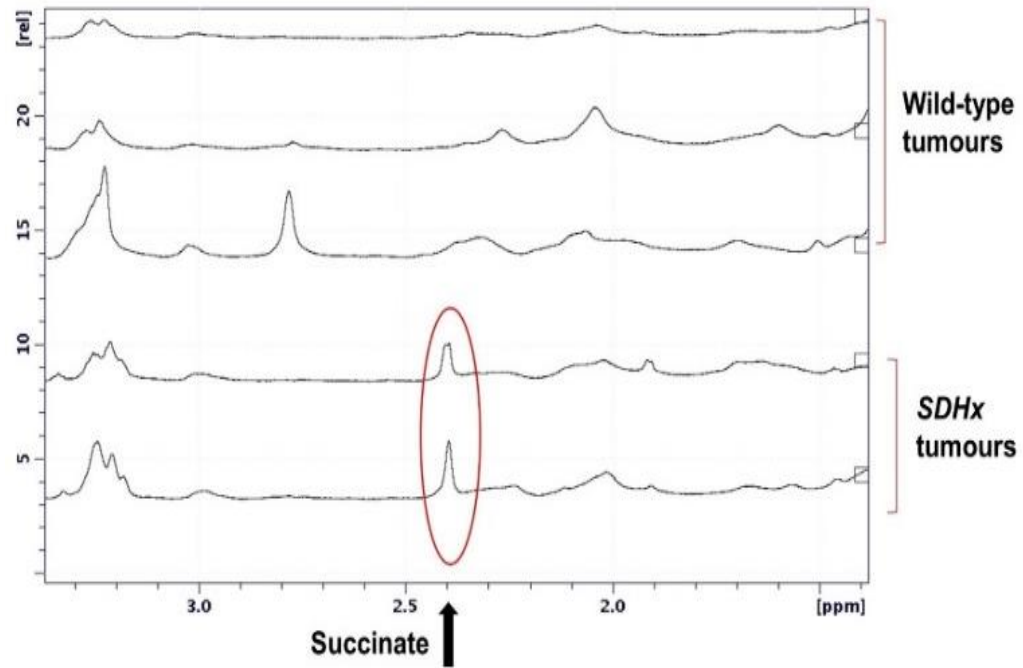
*=
*SDHA, SDHB, SDHB,
SDHD, SDHAF2,
NF1, MAX,
TMEM127,
KIT, PDGFRA, VHL*

Identify new functional assessment tools to identify SDH deficiency

- Ex-vivo metabolomics

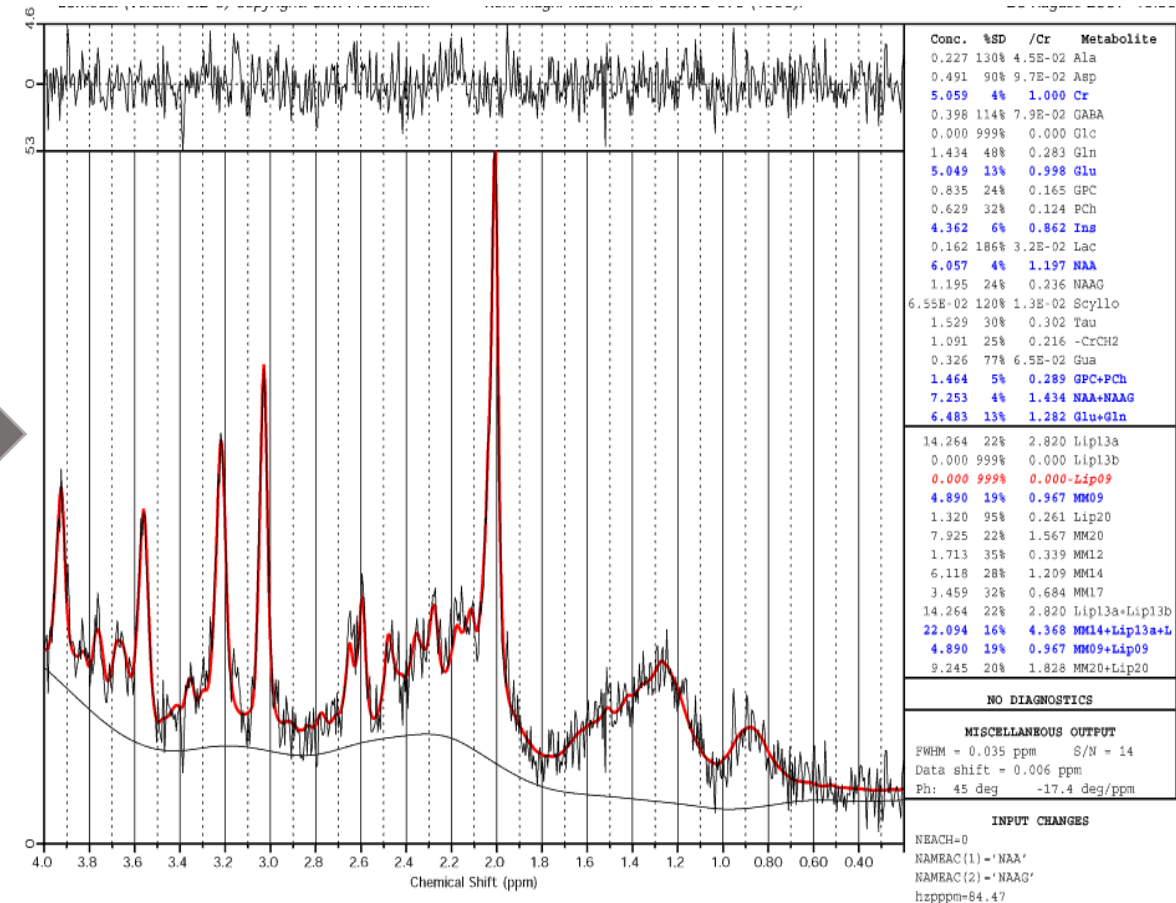
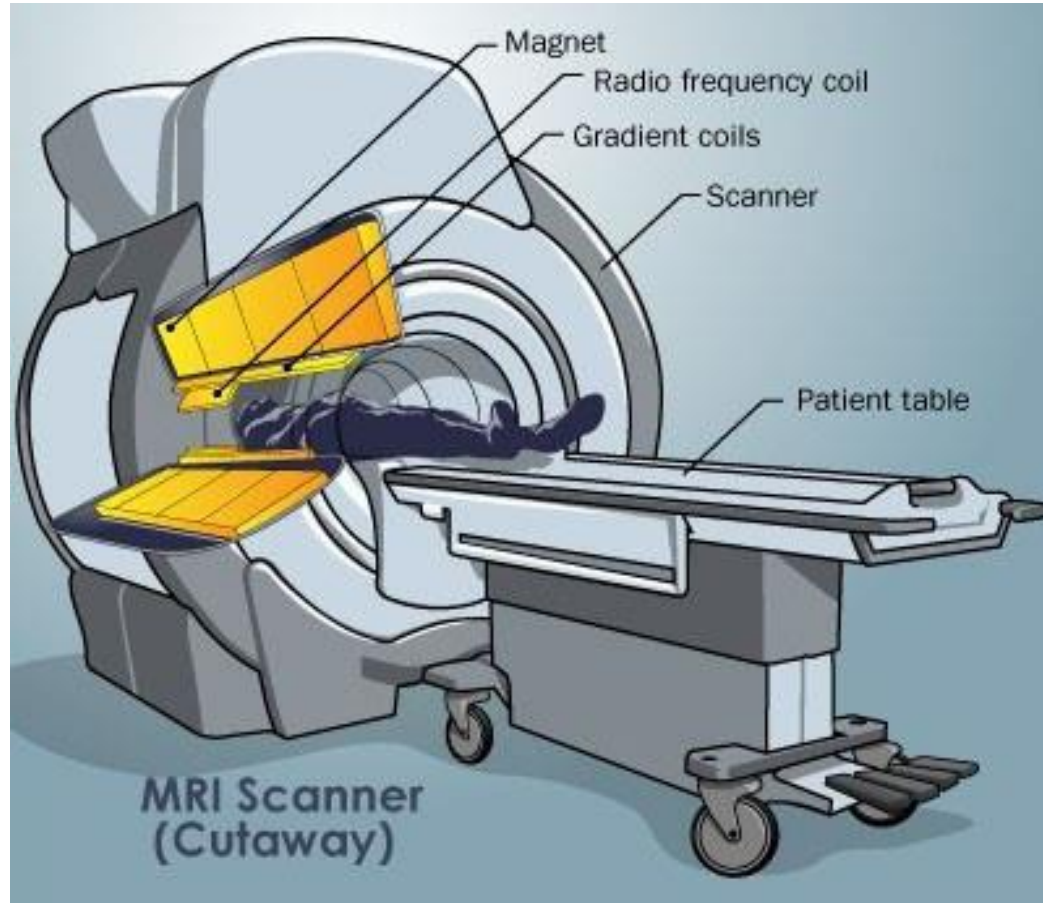


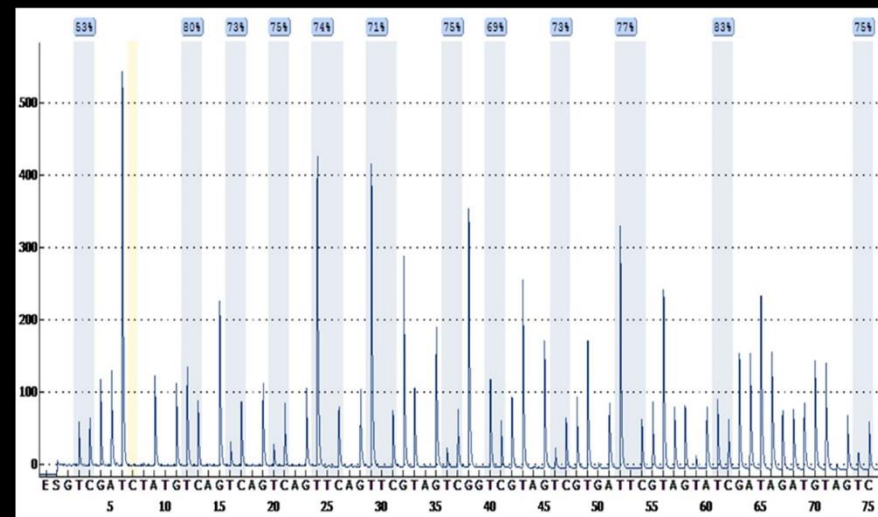
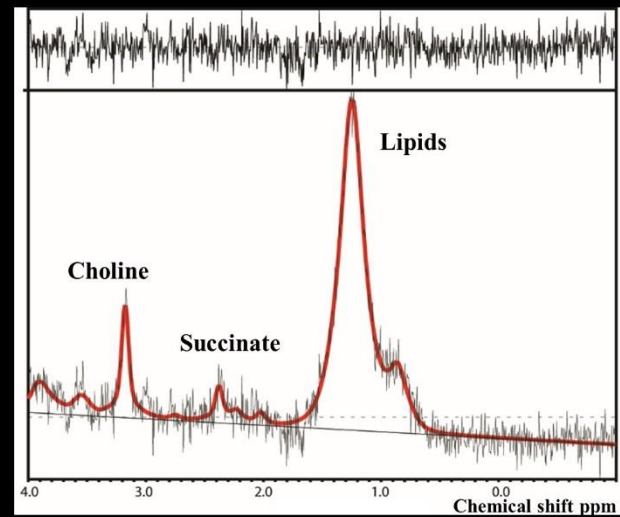
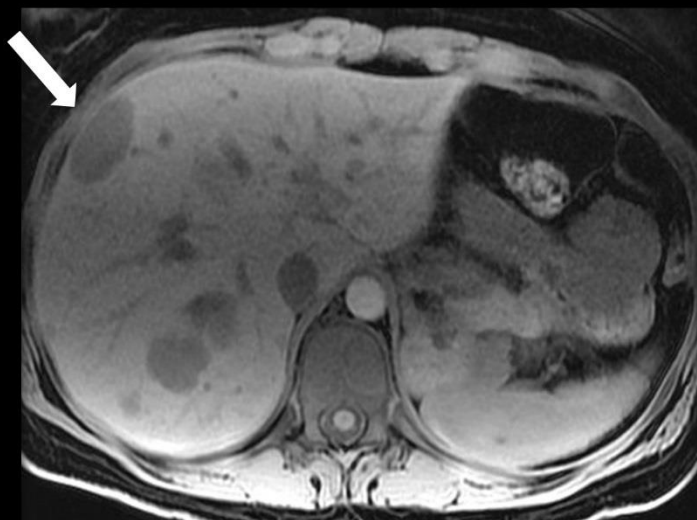
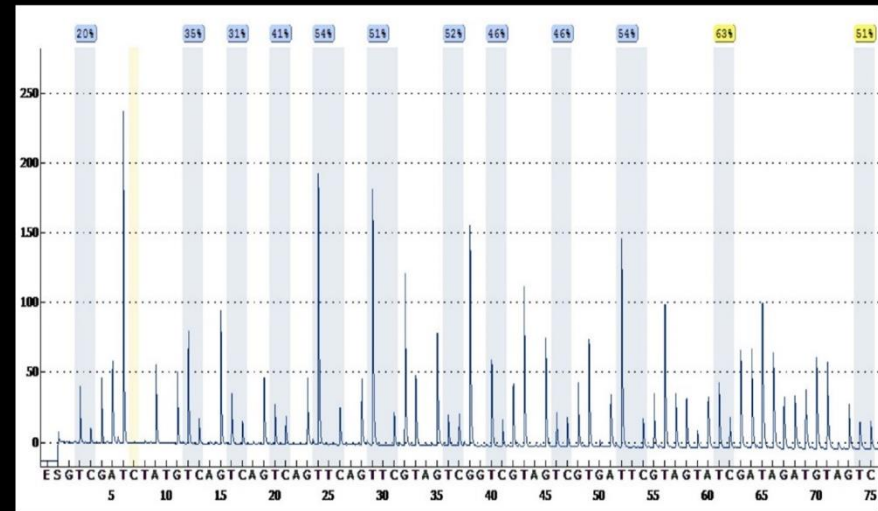
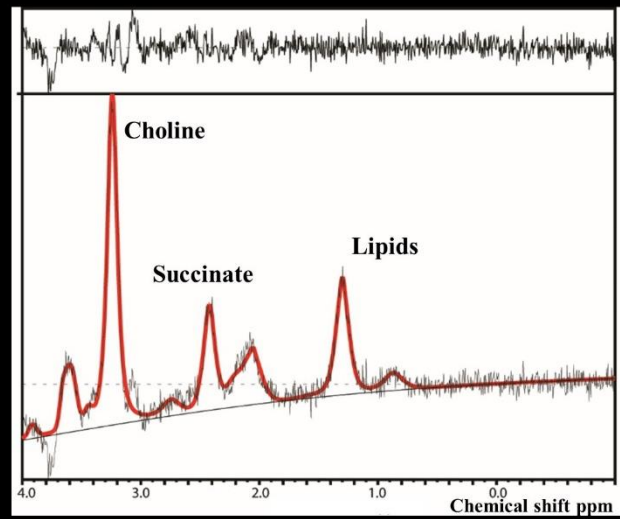
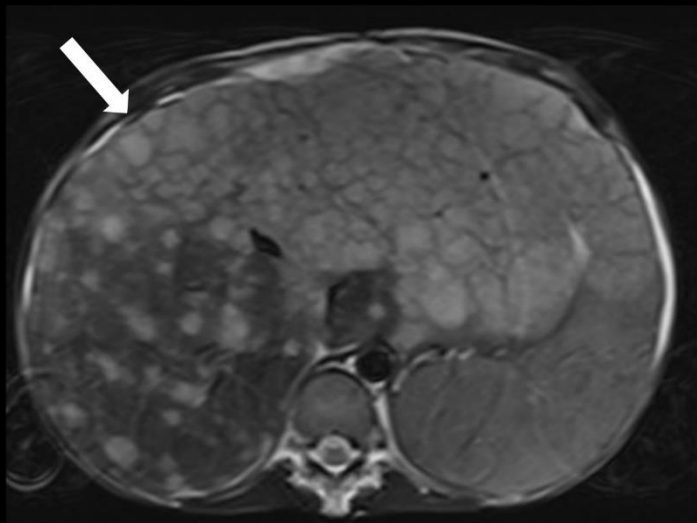
Targeted metabolomics profiling for succinate



2. Evaluate new translational biomarkers for diagnosis, surveillance and to monitor response to therapeutic intervention in SDH deficient disease.

In-vivo metabolomics using MRI spectroscopy (H^1 -MRS)





Monitoring biological response to treatment

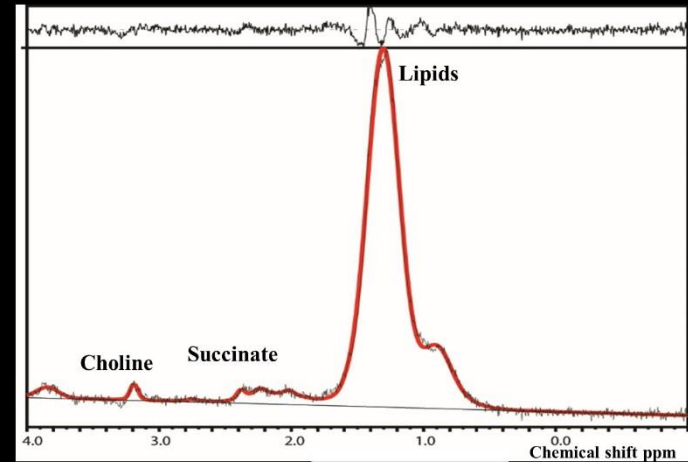
37 year old female

Metastatic PPGL, *SDHB c.268C>T*

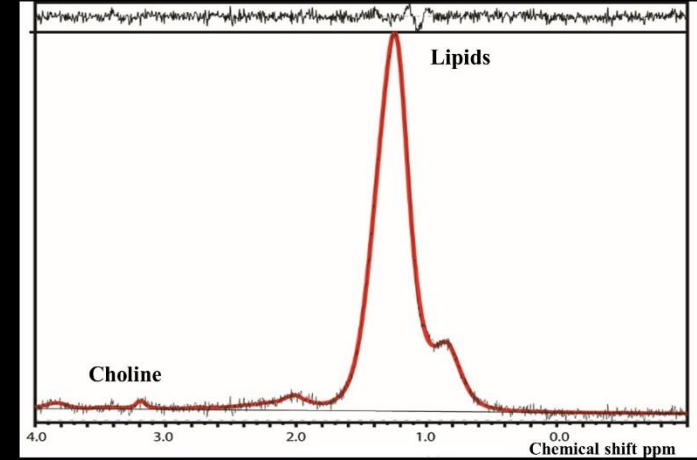
Treatment with Lu¹⁷⁷ PRRT



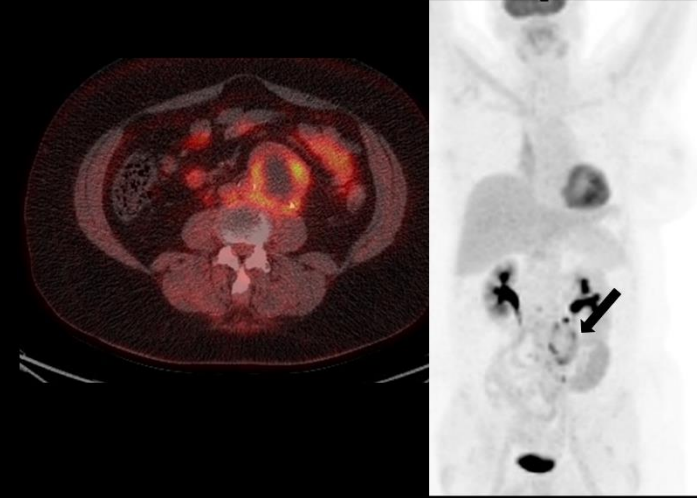
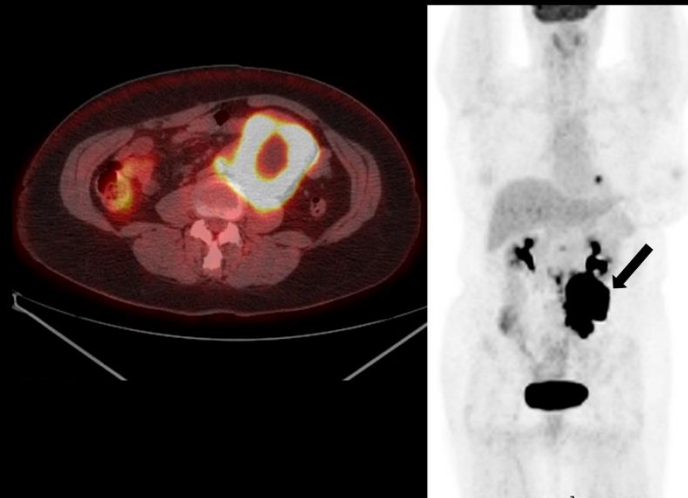
Pre-treatment with Lu¹⁷⁷ PRRT



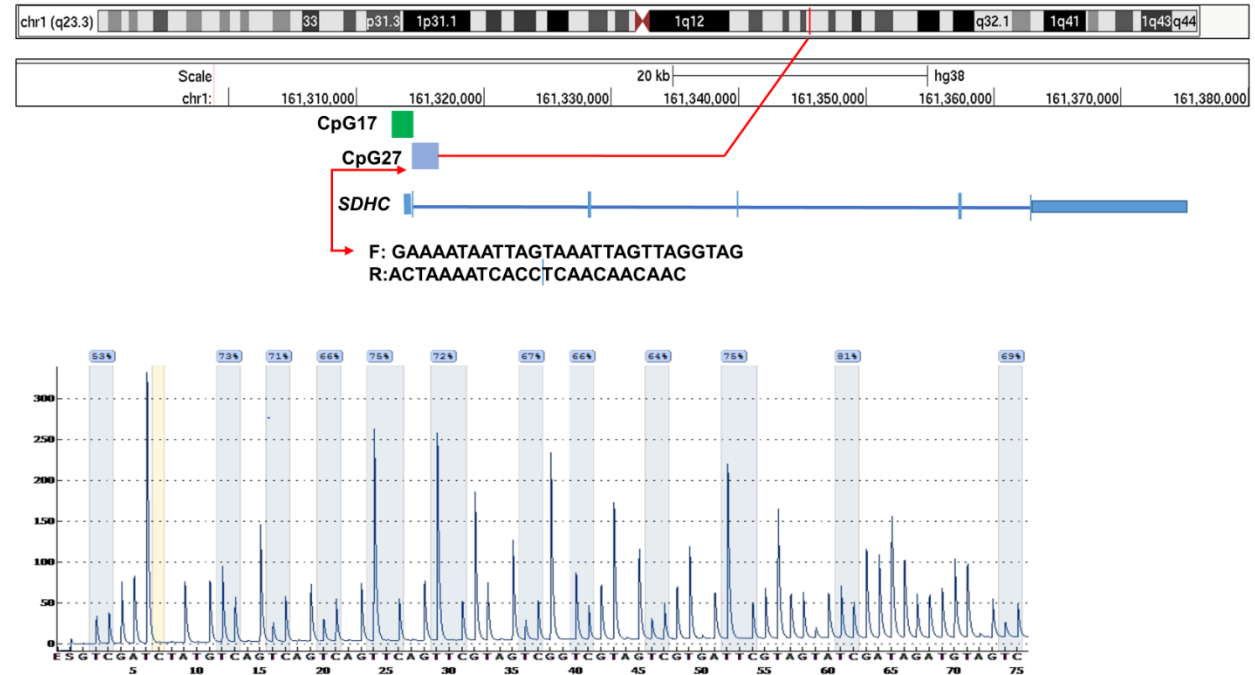
Post 4 cycles of Lu¹⁷⁷ PRRT



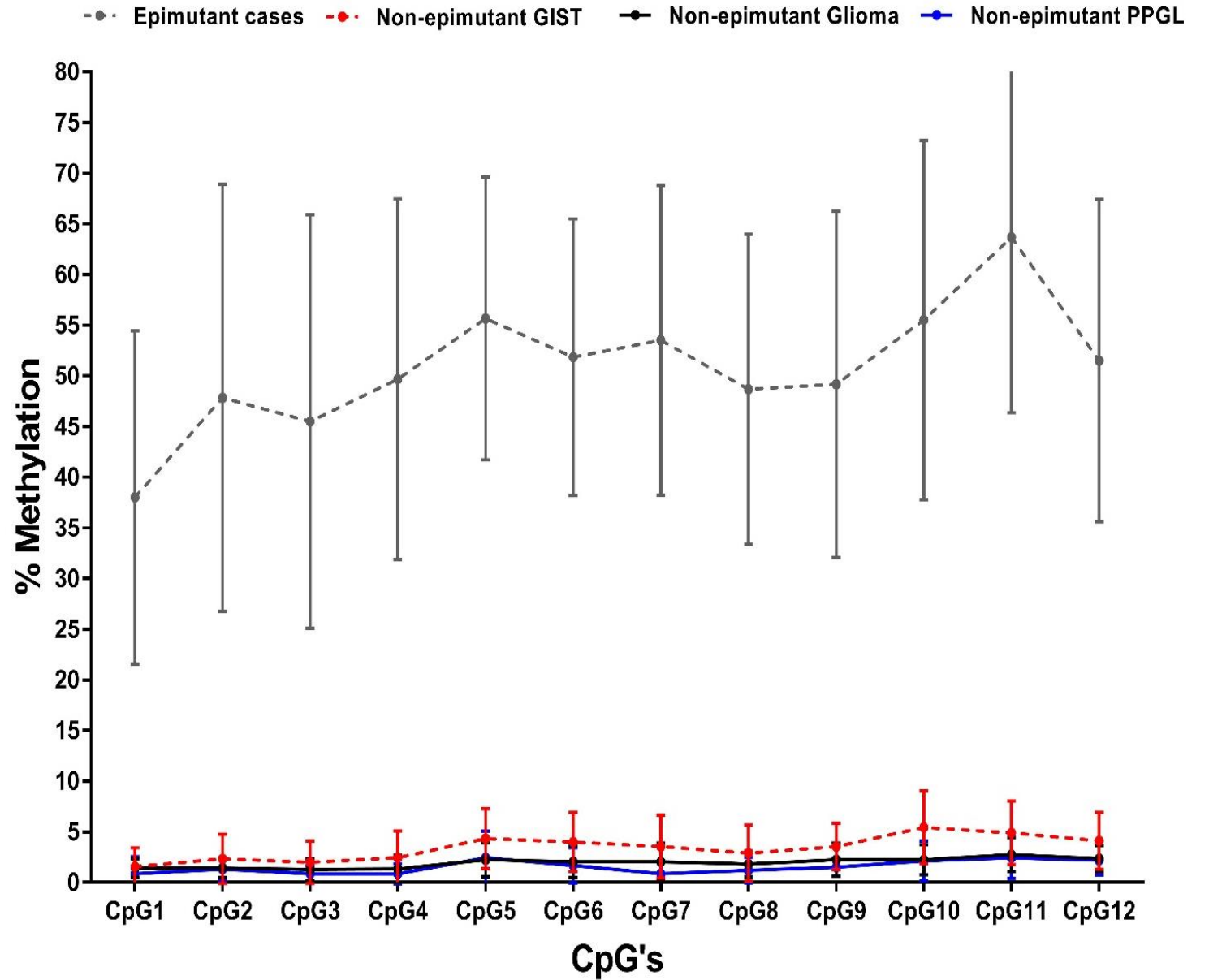
	Pre-treatment	Post-treatment	Reference range
Plasma normetadrenaline	1861	1193	<1000 pmol/l
Plasma metadrenaline	<180	<180	<600 pmol/l
Plasma methoxytyramine	2910	1193	<180 pmol/l



3. Developing diagnostic tests for clinical utility to identify potential therapeutic targets



- **Technique which can be applied to paraffin embedded samples**
- **Cost effective and time efficient**
- **Pyrosequencing technique**



Acknowledgements

Supervisor

Prof Eamonn Maher

Collaborators

Dr Ferdia Gallagher

Dr Mary McLean

Dr Olivier Giger

Dr Madhu Basetti

Dr Alison Marker

Dr Rogier ten Hoopen

Dr David Asher

Dr Anne Warren

Clinical team

Dr Ramesh Bulusu

Dr Ben Challis

Dr Soo-Mi Park

Funding bodies

GIST Support UK

HRB Ireland

PAWS GIST

PATIENTS





PAWS-GIST CANCER CLINIC

<http://www.pawsgistclinic.org.uk>

PAWS = Paediatric Adolescent Wild-type Syndrome
GIST = Gastro-Intestinal Stromal Tumour

WILD-TYPE & PAEDIATRIC GIST CANCER CLINIC

<p>What we are</p> <ul style="list-style-type: none"> - A national clinic and network of experts-GIST cancer specialists 	<p>What we aim to do</p> <ul style="list-style-type: none"> - Improve knowledge of this rare cancer - Develop new and innovative therapies - Stimulate research - Ultimately to find a CURB!
<p>Where we are</p> <ul style="list-style-type: none"> - Addenbrooke Hospital, Cambridge 	

How to apply
 Register at www.pawsgistclinic.org.uk

PAWS-GIST is rare, but you are not alone!


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