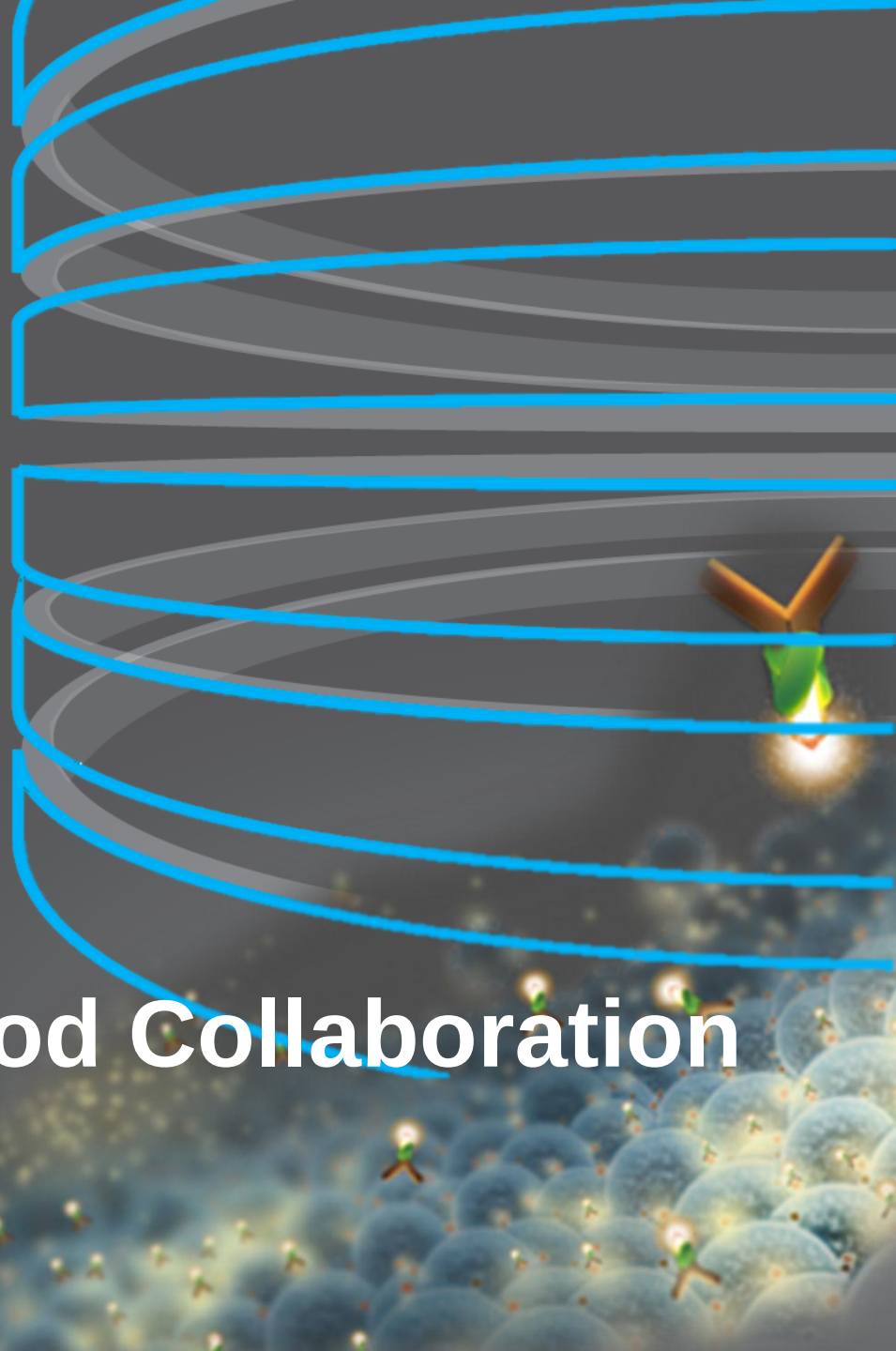
ImaginAb

Molecular Imaging

Recipe For A Good Collaboration

Shuwen Koh



recipe [rɛsɪpi]

- a set of instructions for preparing a particular dish, including a list of the ingredients required
- something which is likely to lead to a *particular outcome*

No-bake?

collaboration [kəlabəˈreɪʃn]

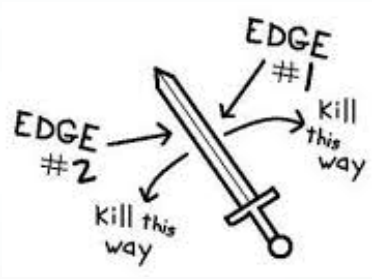
- the action of working with someone to produce something
- traitorous cooperation with an enemy

ImaginAb

Ingredients for Success

- Knowing *when* and *whom* to partner
- Internal champion/point-of-contact (preferably based locally)
- Skin in the game
- Tenacity & resourcefulness
- Constructive skepticism
- Project management
- Transparency & good faith…

Leave your ego at the door



ImaginAb

… for Disaster (worst case trajectory)

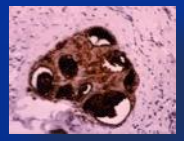
- A paradoxical fear of success
- A paradoxical funding situation

ImaginAb

Diagnostic Imaging – *in vivo* and real-time

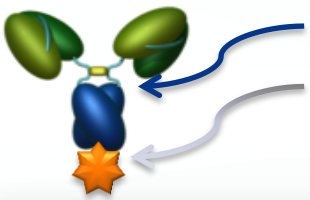
OLD WORLD

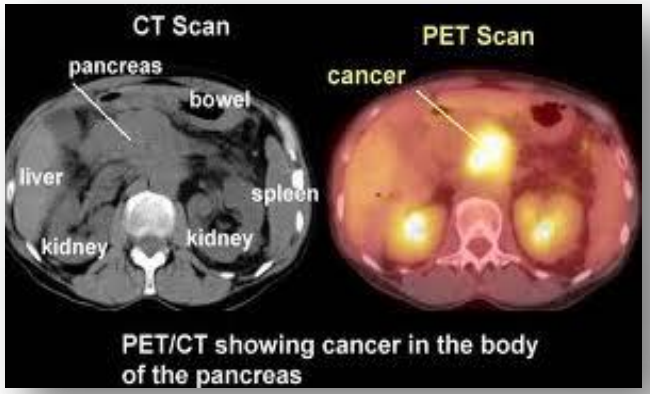
Antibodies are used to detect / charac important targets in tissue and blood specimens *ex-vivo*



A pancreatic cancer biopsy specimen "stained" with an antibody

NEW WORLD





From antibodies and ***in vitro*** immunohistochemistry …

… to radiolabeled mAb fragments and ***in vivo*** diagnostic imaging with **P**ositron **E**mission **T**omography (PET)

ImaginAb

Centre for Translational Molecular Imaging

@ DUKE NUS GRADUATE MEDICAL SCHOOL SINGAPORE

- CTMI serves as a platform to generate high quality *in vivo* data research capabilities in Singapore universities and research institutes. This facility opens up *in vivo* targeted molecular imaging opportunities for scientists in Singapore.

- The laboratory is accessible to industry and academic collaborators with the objective of developing precision medicine strategies to impact healthcare.

ImaginAb

CTMI @ DUKE NUS GRADUATE MEDICAL SCHOOL SINGAPORE

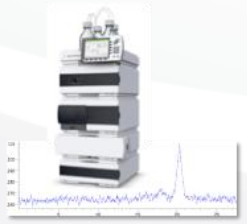
- CTMI supports drug development processes using i*n vivo* imaging to evaluate:

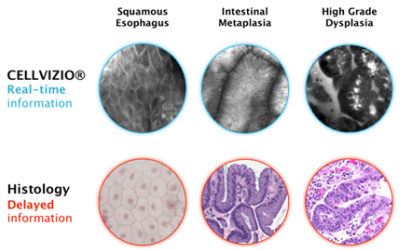
- *In vivo* biodistribution studies
  - Receptor occupancy / distribution / density studies
  - Drug pharmacokinetics
  - Therapy efficacy (longitudinal intra-animal)
  - Biosynthesis / Metabolism / Stability
- Novel tracer evaluation
- *In vivo* disease model characterisation

ImaginAb

Capabilities

- *In vitro* assay development (FACS; Radio-immunoassay)
- Imaging probe development and analysis (Chemistry and HPLC)
- *In vivo* model development (cell banking/tumour growth kinetics)
- *In vivo* PK/biodistribution and imaging (Gamma Counter; PET/X-Ray; CellVizio; IVIS Xenogen)





ImaginAb

Case study:

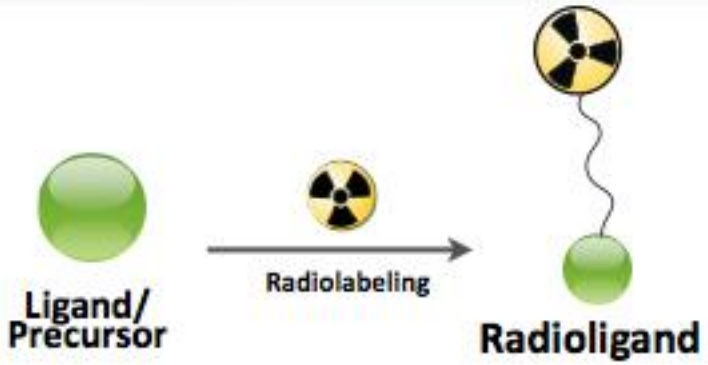
In Vivo Validation of Antibody Fragments against Receptor X using Multi-Modality Imaging

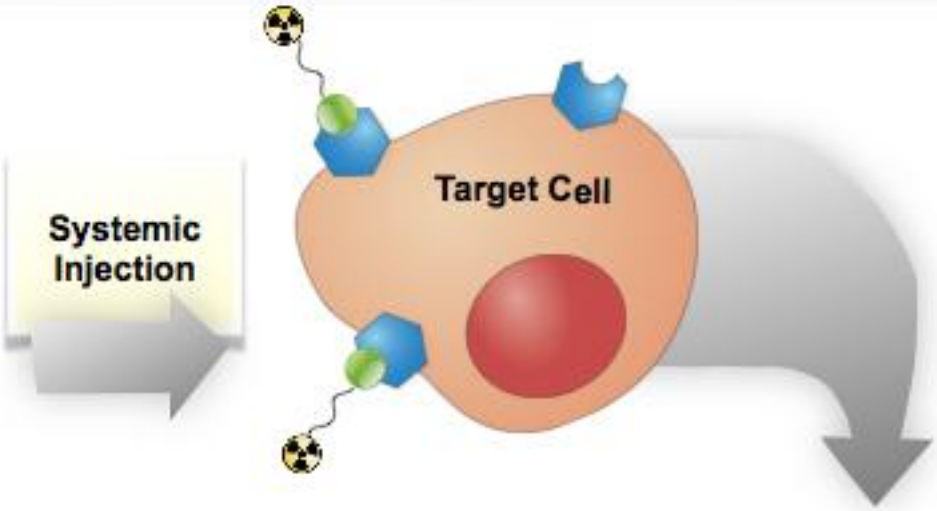
- *In vitro* target validation – biological relevance and clinical acceptance
  - Characterisation and selection of cell lines (controls!) for binding assays
  - Selection/Generation of antibodies
  - Development of imaging probes

- Selection/Generation of antibodies
- *In vivo* validation
  - Development, characterisation and selection of relevant mouse models (controls!)
  - Selection of imaging modality
  - Generation of antibody fragment (repeat *in vitro* validation of binding)

ImaginAb

Work Flow





Small Animal
PET/SPECT Imaging

Clinical
Nuclear Imaging
Probe
Distribution

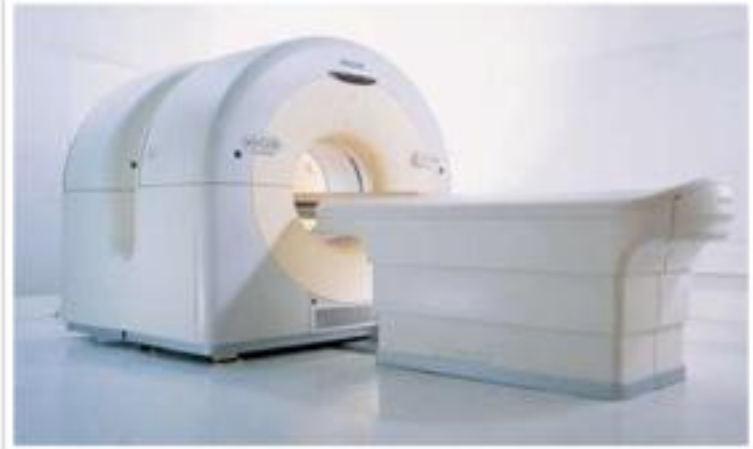


Image courtesy of Dr. Ann-Marie Chacko

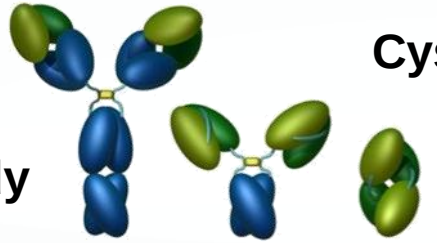
ImaginAb

About ImaginAb

- UCLA / City of Hope spin-out (October 2007)
- Primary focus: cancer & immunology
- ~50 employees – Los Angeles, Singapore, Tokyo
- 30 collaborations with global pharma
- Clinical stage: Phase II
- Early revenues
- Significant IP
- ~S$60 million raised to date

ImaginAb Core Technology

Engineered Antibodies for Accelerated Kinetics

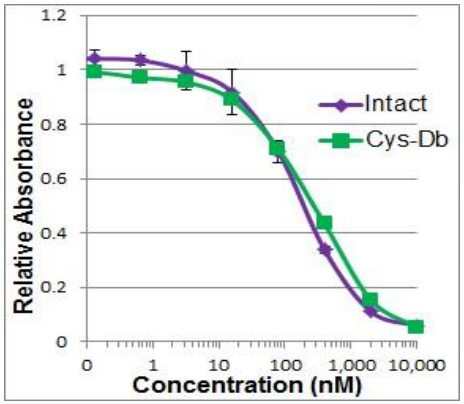


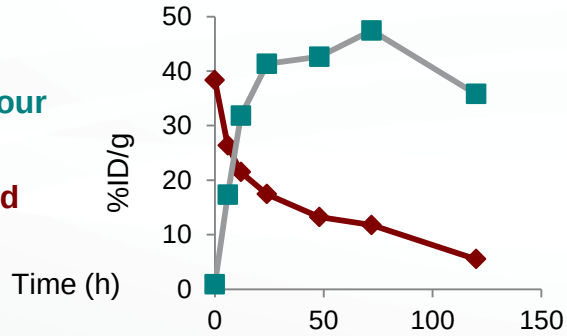
Intact Antibody
150 kDa

Cys-Diabody
55 kDa

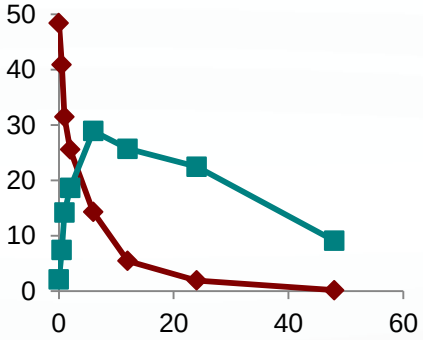
Minibody
80 kDa

Preserving Affinity…

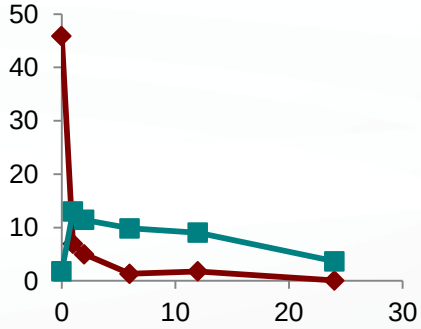




- 7-10+ days for adequate blood clearance to see small signal
- Hepatic clearance (masks disease until fully cleared)

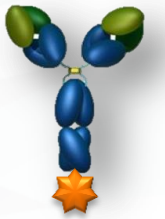


- Same or next day imaging / targeting
- Hepatic clearance

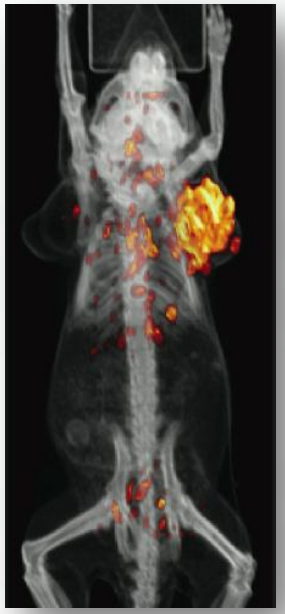


- Imaging at 2-4 hrs post injection
- Renal clearance: keeps upper abdomen clear

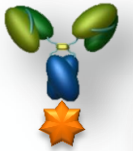
ImaginAb



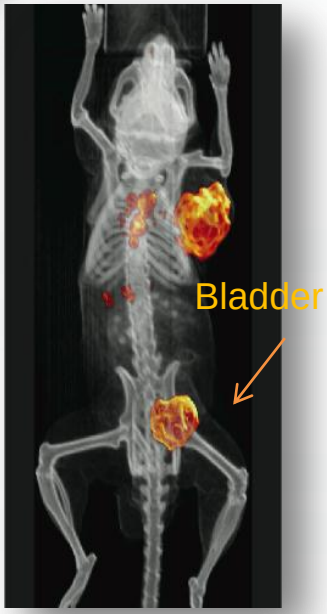
Intact Ab



168 hours

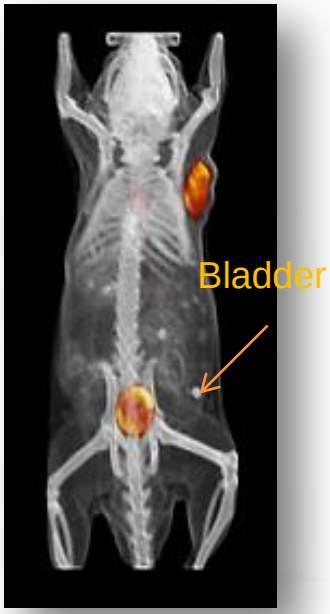


Minibody



20 hours

Cys-Diabody



3 hours

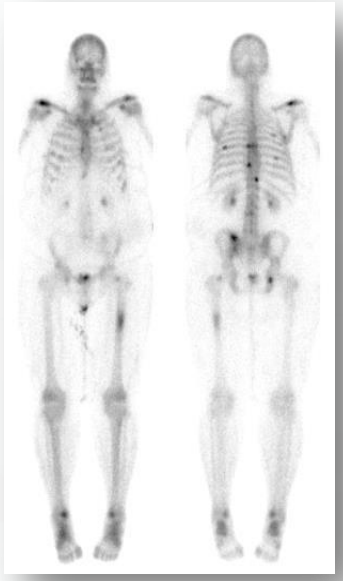
Knowles and Wu J. Clin. Oncol. 2012

ImaginAb

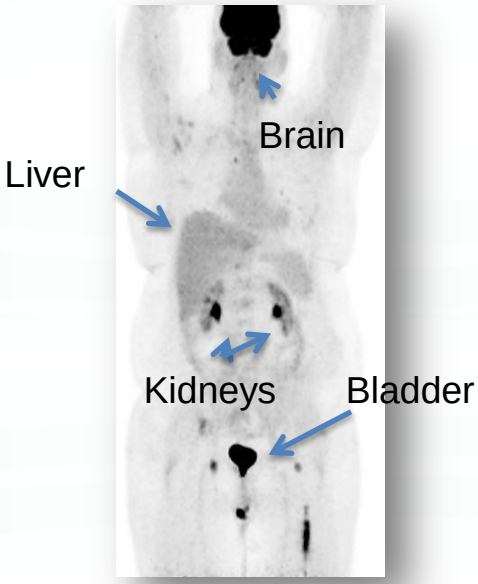
ImaginAb's PSMA PET Scan

- **The new Standard for Imaging of Prostate Cancer**

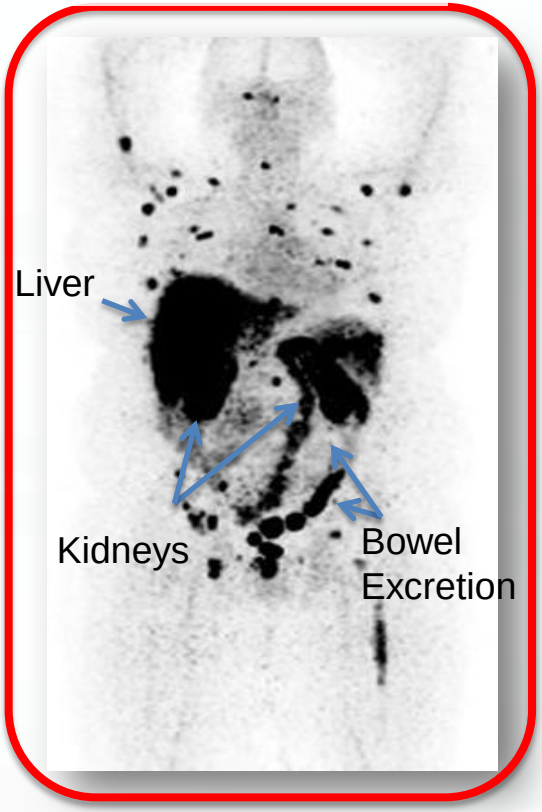
Bone Scan



FDG PET scan



PSMA PET Scan



If we can *see* cancer,
we can manage it better…

In conjunction with Memorial Sloan Kettering Cancer Center

ImaginAb

*Same patient for all scans in the same week