Innovations for Treatment of Gastric Cancer

Jimmy B.Y. So
Associate Professor of Surgery
National University of Singapore
Head, Upper Gastrointestinal Cancer Group
National University Cancer Institute,
National University Hospital
Singapore
Singapore Gastric Cancer Consortium

IMPROVING OUTCOMES FOR OUR PATIENTS

Lead PI: Khay Guan Yeoh
A National Translational & Clinical Research Flagship Programme
Outline

SGCC’s contribution on patient outcomes
- Early detection and Biomarker discovery
- Better treatment for Gastric Cancer
Why Study Gastric Cancer?

• Common & important
  2nd leading cause of cancer death worldwide

• 5th cancer in men in Singapore

• Asian disease
Competitive Advantages of SGCC

**Scientists**

State of Art Facilities for
- Genome mapping
- Biomarker discovery and validation
- Proteomics
- Imaging
- Animal models
- Testing new devices
- Clinical trials
- Experimental therapeutics

**Clinicians**

**Comprehensive Team**
- Translational scientists
- Genomics scientists
- Bio-engineers
- Gastroenterologists
- Oncologists
- Surgeons

**Answering Important Questions**

**Planning Unique Clinical Studies**

**State of Art Facilities for**
- Genome mapping
- Biomarker discovery and validation
- Proteomics
- Imaging
- Animal models
- Testing new devices
- Clinical trials
- Experimental therapeutics
Signature Programmes

Unique Clinical Studies

Gastric Cancer Epidemiology Programme (GCEP)
- cohort study of 4000 susceptible subjects at high risk of gastric cancer, comprehensive clinical data gastric tissue, blood specimens and DNA/RNA

Gastric Cancer Discovery (GASCAD)
- newly diagnosed gastric cancer, tissue, blood and gastric juice specimens
What population should we target for endoscopic screening?
Prospective surveillance of a “High-risk” cohort (Chinese, age >50) for 5 years (n=3000)

Scientific Aims
- Predictive Risk Factors
- Screening Algorithm
- Premalignant lesions (IM, SPEM)

Interim results (Jan 2012)
- Completed recruitment 3000.
- 15 patients with early GC (Stage 0/1).
- First time screen-detected GCs diagnosed in SG.
- Tissue Bank: 2,600 sera and DNA 36,000 tissue specimens

Next Steps 2012-17
- Completion of 5 years surveillance.
- Validate Risk Prediction Tool.
- Propose a cost-effective screening algorithm for Singapore population.
- Genomic and epigenetic profiling of early gastric cancers.
Gastric Cancer Epidemiology Programme (GCEP)

GCEP Platform supporting other scientific studies & Health Svc research

- Imaging studies: Raman, Confocal
- Path, Microbial & Biomarkers: Pathology, *H. pylori*, Biomarker, Serology, Proteomics

- Health Services Research
- Cost-effectiveness of screening
Highlights & Achievements:

15 Early Gastric Cancers (Stage 0 or 1) resected with cure. Major surgery avoided. Life-years saved, Quality of life, Cost-effectiveness.

Cancers prevented by treatment of risk factors
3000 patients in GCEP screened for gastric cancer and risk factors such as *Helicobacter pylori* treated.

Patients benefitted from receiving novel therapies free-of-charge from 2 clinical trials (3G and Dovitinib)
Scientific Achievements

New genomic classification of gastric cancer


- Prognostically relevant for patients' survival, predictive of response to chemotherapy

- A completely new way of classifying gastric cancer, prognostically superior to the classic Lauren classification and diagnostically more robust

“A reliable classification of biological and clinical significance.”

*P Correa, Faculty of 1000*
Gastric Cancer is a heterogeneous disease

Tay et al., Cancer Research 2003
Genomic Profiling of GEMINI Lines Reveals Two Distinct Subclasses

Singapore/Australia/UK/Hong Kong/S Korea/MD Anderson Cohort (~550 patients)
G-INT and G-DIF Cell Lines Respond Differently to Platinum Treatment

Tan et al., 2011, *Gastroenterology*
Genomic-Guided therapy for advanced Gastric cancer - 3G Trial

Treatment naïve Advanced Gastric Cancer (primary in situ)

OGD guided Bx ➔ Expression profile ➔ Ascertain G1/G2

~ 5-7 working days

NCI Trial Number **NCT01100801**

Multi-center
(NCIS, NCCS, Yonsei CC, Korea)

G1 : S1/ oxaliplatin

G2 : S1/ cisplatin
Novel Target Therapy for Gastric Cancer

Deng N et al., Gut 2012
Robot Endoscope- *made in Singapore*!

- First in the world flexible endoscopic robot
- First Singapore robot entering human trials
- Natural Orifices Transluminal Endoscopic Surgery (NOTES) on human patients
- Singapore is a world leader
- IP held by EndoMaster Pte Ltd, Oct 2011

International Media Coverage

A/Prof Louis PHEE
NTU

Prof Lawrence HO
NUHS

Singapore Gastric Cancer Consortium
Translation into Clinical Trials

**RAMAN endoscopy** – real-time in vivo diagnostics of precancer and cancer with high sensitivity (94.6%) and specificity (97.8%)  *Bergholt, Int. J. Cancer 2010*

Outer diameter ≈1.8 mm

Zhi-Wei HUANG, BioEngineering, NUS

IP recently filed
Endoscopic Raman Spectroscopy

- Identify cancer by detection the laser light scattering of molecules
- Provides specific biomolecular fingerprinting related to tissue pathology
Raman Spectroscopy for diagnosis of gastric cancer

In vivo diagnosis:
Sensitivity of 94.6\%(122/129)
Specificity of 94.7\% (884/934)

M Bergholt, J So et al., Int J Cancer 2010
Translational Research at NUHS

Zang et al., 2011 *Cancer Research*

Hillmer et al., 2011 *Genome Research*

Drug Screening and Therapeutic Discovery

Tao et al., 2011 *Science Translational Medicine*

Palanisamy et al., 2010 *Nature Medicine*

Tan et al., 2011 *Gastroenterology*
Summary

• SGCC established a platform for translational research through close collaboration between clinicians and scientists

• We focus on improvement of patient’s outcome by early diagnosis, better treatment and understanding of cancer biology
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<td>Axel HILLMER</td>
<td>GIS</td>
<td>Celestial YAP</td>
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Funding agencies
National Medical Research Council
National Research Foundation
Thank you
## THEME 2 – THERAPEUTICS

### Peptide Vaccine Program

1. Early phase clinical trial of HLA-A2401 restricted peptide vaccine cocktail

2. Development of HLA-A1101/3303 restricted peptide vaccine

**Proposal:**

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Promising clinical response in advanced cancer

Antigen specific tumor kill by HLA restricted CTL clone

Wei-Peng YONG, Med Oncology, NUHS

A/Prof Koji Kono
Dept of Surgery, NUS