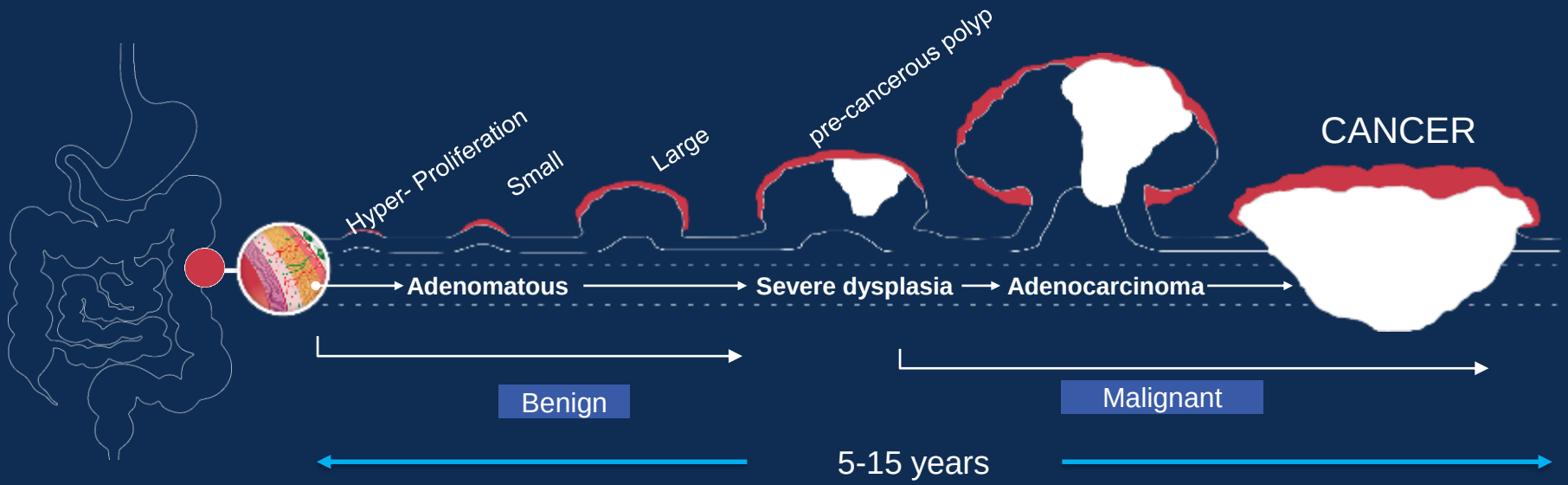
Prospective Clinical Study of Circulating Tumor Cells For Colorectal Cancer Screening

Results From a Multi-Year 620-Sample Study

Presented by: Wen-Sy Tsai, MD, Ph.D

CRC: SLOW GROWING, PREVENTABLE

POLYP TO CANCER CAN TAKE 5 TO 15 YEARS



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Unfortunately, Most CRC Is Diagnosed Late

When Diagnosed	5 Year Survival Rates*
Localized	91%
Regional Disease	71%
Distant disease	14%

61% of Diagnosis**

(57% in Taiwan)

*Siegel RL, Miller KD, Jemal A. Cancer Statistics. 2017. CA Cancer J Clin 2017
**https://www.cancer.net/cancer-types/colorectal-cancer/statistics

Guideline-Recommended Screening Tests

Test	Sample Type
Colonoscopy	Invasive (needs bowel prep)
gFOBT (requires 3 samples)	Stool (3 samples)
FIT	Stool
DNA + FIT*	Stool

- NCCRT Goal For Screening Compliance “80% by 2018”
- 1/3rd of Americans have never been screened[1]
- 87% of non-compliant individuals preferred blood- tests to stool based testing[2]

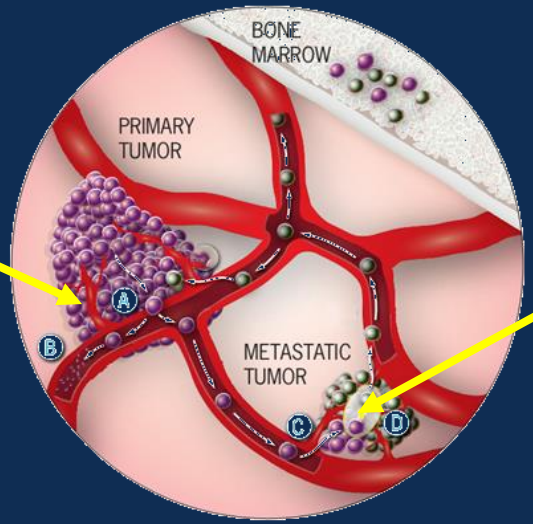
In Taiwan:
About 40.7 % FIT screen cover rate of people over age 50
Over 70% FIT positive people showed normal colonoscopic findings
About 30% FIT positive do not receive colonoscopy.

*Exact Sciences FDA Molecular and Clinical Genetics Panel, March 27, 2014

1 Colorectal Cancer Facts & Figures 2017-2019
2. BMC Gastroenterology 2014

CTCs: Shed Early But Extremely Rare

CTCs: Cells that leave the primary tumor & enter bloodstream



- CTCs may leave the bloodstream to form new metastatic lesions
- Metastatic lesions evolve over time & release CTCs

1

PER BILLION BLOOD CELLS

Pre-Cancer

10s

PER BILLION BLOOD CELLS

Early Stage Cancer

100s

PER BILLION BLOOD CELLS

Late Stage Cancer

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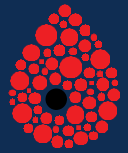
CMx™ CTC PLATFORM: US PATENTED

CellMax Life

05. **ISOLATED CTC**
binding of target cells to the membrane

06. **RELEASING THE CTC**
Air-foam enabled cell release, maintaining cell viability for further analysis

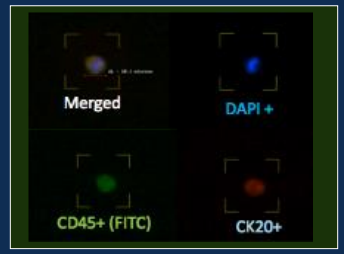
03. **BIOMIMETIC SURFACE COATING**
maximizes clustering of cells



CTC

Air

binding event in the chip



01. Blood

Patented microfluidic chip

07. Staining & Enumerate

02. **AFFINITY BASED MICROFLUIDICS**
reduces non-specific adsorption

04. **Gentle buffer** flow flushes out non-specific binding blood cells in microfluidic channel to further improve the purity of captured CTC

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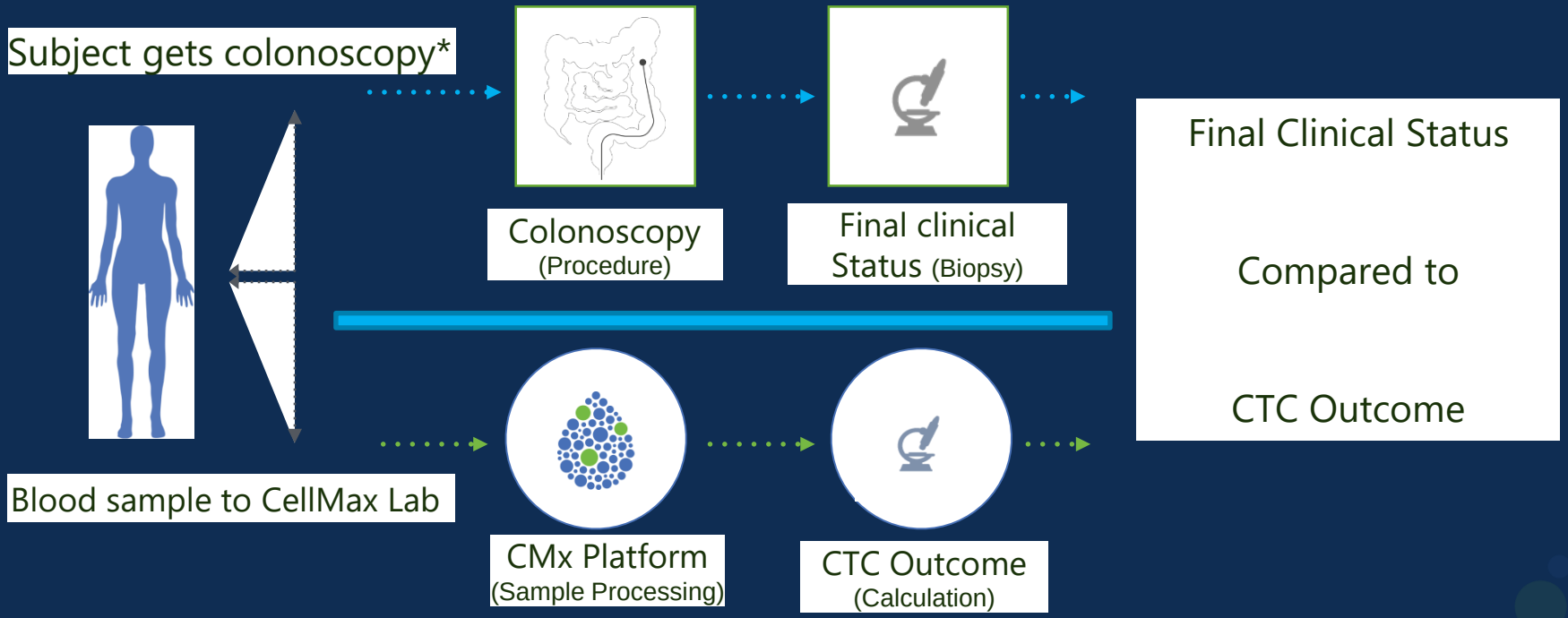
Study Overview

- Evaluate the performance of a routine blood-draw based CTC assay for early detection
- Prospective & multi-year study
- Assay uses CMx platform to capture & enumerate CTCs confirmed by CK20
- 620 samples tested

Prospective Study Design



* Some control samples were from self-declared healthy subjects

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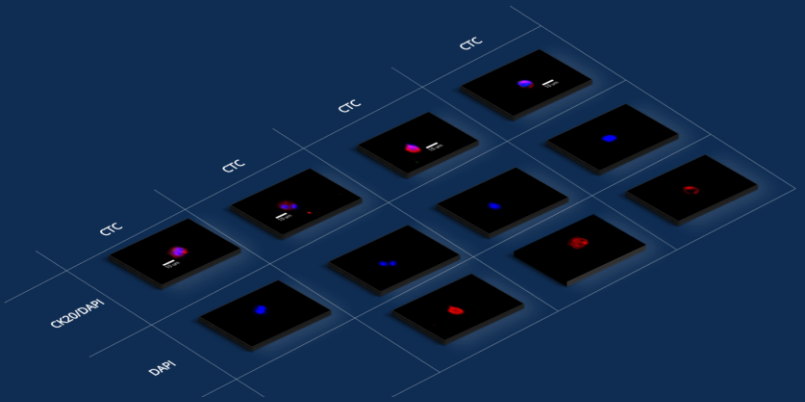
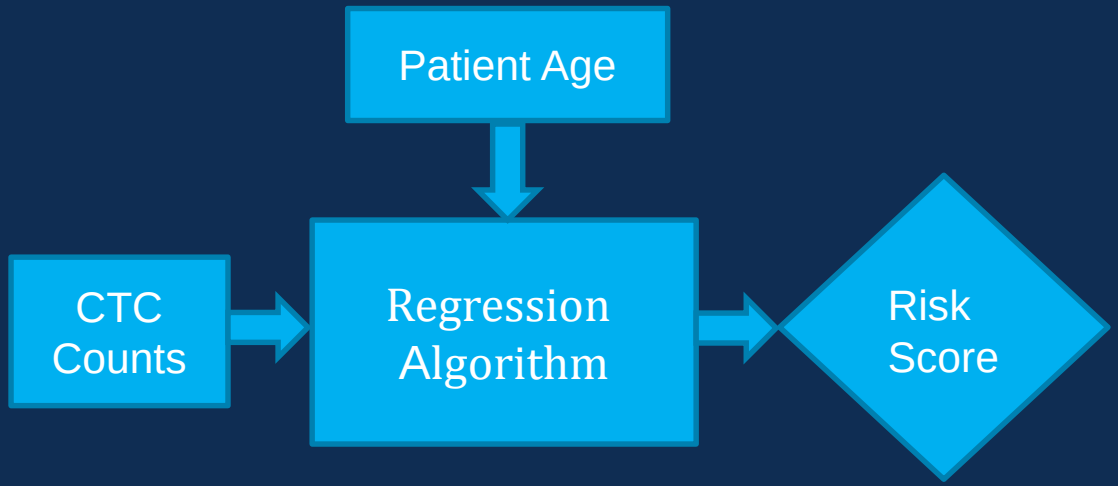
CMx Test & Algorithm

CTC:
Intact, nucleated cells
CK20+ & CD45-

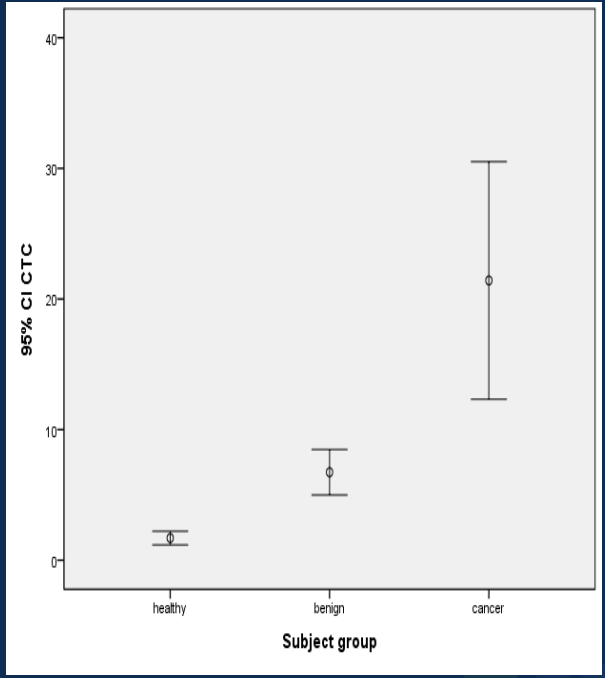




Patient Disposition

CellMax Life

Total Samples = 620	Number	Age
Control (Healthy)	182	20~80
Pre-Cancer (Adenoma/Advanced Adenoma/Stage 0)	111	20~81
Cancer	327	31~87
Stage 1	**56**	
Stage 2	**84**	
Stage 3	**118**	
Stage 4	**43**	
Un-staged	**26**	
Total Diseased	**438**	



Linear association
(P < 0.01, R = 0.144)

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CTC Test Groups Individuals As High or Low Risk

Predicted Risk Factor	Healthy	Pre-cancer	Cancer (327)					
			Total	Un-staged	Stage I	Stage II	Stage III	Stage IV
High Risk	6	84	285	23	50	72	100	40
Low Risk	176	27	42	3	6	12	18	3
Total	182	111	327	26	56	84	118	43

(Risk score = Logistic regression (CTC number and age)

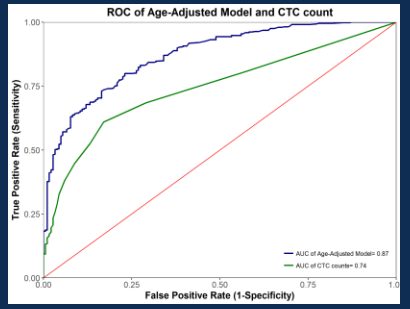
Test Performance

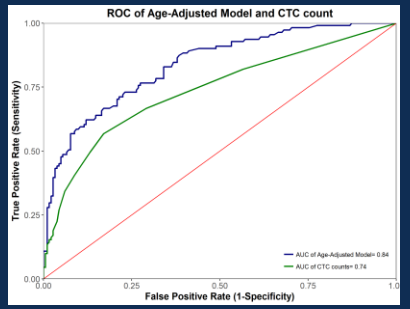
	Diseased			Healthy	Total
	Cancer	Pre-Cancer	Total		
Test +ve	285	84	369 (True Positive)	6 (False Positive)	375
Test -ve	42	27	69 (False Negative)	176 (True Negative)	245
Total	327	111	438	182	620

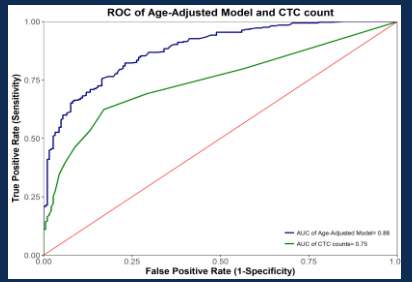
Accuracy = 87.9%
False positive rate of healthy group = 3.3 %
False negative rate of diseased group = 15.8%

Results

Tested Population	Sensitivity	Specificity	AUC
All (620)	84.0%	97.3%	0.87
Pre-cancerous lesions (111)	76.6%	97.3%	0.84
Cancer (327)	86.9%	97.3%	0.88







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Guideline-Recommended Screening Tests

Test	Sensitivity for CRC	Sensitivity for Pre-cancer
CMx™	87%	**77%**
gFOBT [1]	62-79%	**2-10%**
FIT[2]	73-88%	**23.8%**
Stool DNA + FIT[2]	92%	**42%**
Colonoscopy[1]	75-93%	76-94%

1. USPTF Final Recommendation for Colorectal Cancer Screening, National Cancer Insitute: https://cisnet.cancer.gov/projections/colorectal/screening.php
2 Exact Sciences FDA Molecular and Clinical Genetics Panel, March 27, 2014

Conclusions/Next Step

- CRC screening is a Group A recommendation by USPTF
- CMx CTC assay is capable of detecting both early stage cancer with low false positives
- Blood Test → Higher Compliance → Better Outcomes
- Selecting Collaborators for extended Study to US populations
- CTC is fundamental mechanism of metastasis: Ongoing studies extend to other solid tumor cancers e.g., Prostate, Breast, Lung…