

## HKU Identifies a Subset of Cancer Stem Cells Responsible for Chemoresistance and Recurrence in Liver Cancer



Professor Irene NG Oi-lin  
Dr. Terence LEE Kin-wah

Department of Pathology,  
The University of Hong Kong Li Ka Shing Faculty of Medicine  
State Key Laboratory for Liver Research (HKU)



### Liver cancer in Hong Kong

- 4<sup>th</sup> most common cancer in Hong Kong – more than 1,700 new cases per year
- 2<sup>nd</sup> and 4<sup>th</sup> leading cause of cancer death in males and females respectively; 3<sup>rd</sup> leading cause for both sexes
- In 2008, 1,499 deaths in HK were caused by liver cancer, accounting for 12% of all cancer deaths

Hong Kong Cancer Registry, 2008



## Main causes of liver cancer

- In Hong Kong and the region, hepatitis B virus is the leading cause of liver cancer
- 10% of the population are hepatitis B virus carriers
- Other risk factors include hepatitis C, alcoholism and genetic factors



## Current treatments for liver cancer

### First line treatment

- Liver resection (20%)
- Liver transplantation (<5%)

### Second line treatment

- Chemotherapy (25%)
- Systemic therapy (30%)
- Local ablative therapies (25%)



## The Limitation of liver resection and transplantation

- Majority of patients have unresectable liver cancer because of advanced tumour or poor liver function
- Transplantation is applicable only for early small tumours. Also, its application is limited by the shortage of liver grafts in Hong Kong



## Main hurdles in treating liver cancer

- High chance of tumour recurrence
- Chemoresistance for chemotherapy

Therefore, understanding the mechanism of tumour recurrence and chemoresistance will help improving treatment result.

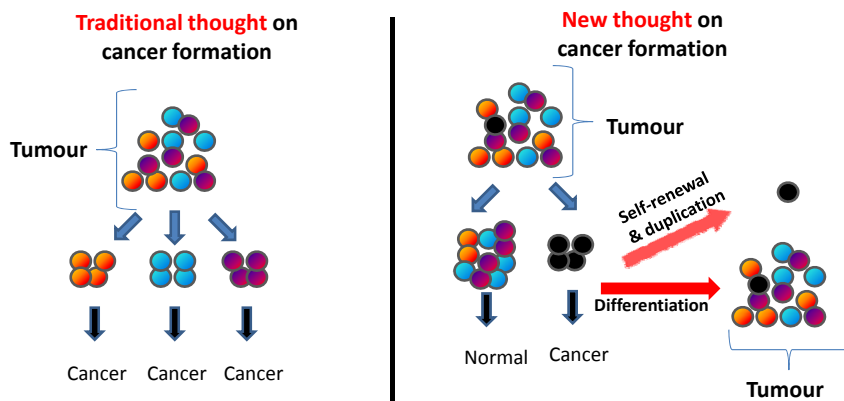


## HKU Discovery

- We have identified a type of cancer stem cells (CSCs) with a surface marker CD24+ responsible for tumour recurrence and chemoresistance
- We have revealed the mechanism on how CD24+ liver cancer cells mediates tumour recurrence and chemoresistance – via STAT3 (a kind of protein) activation



## Cancer Stem cells (CSCs)

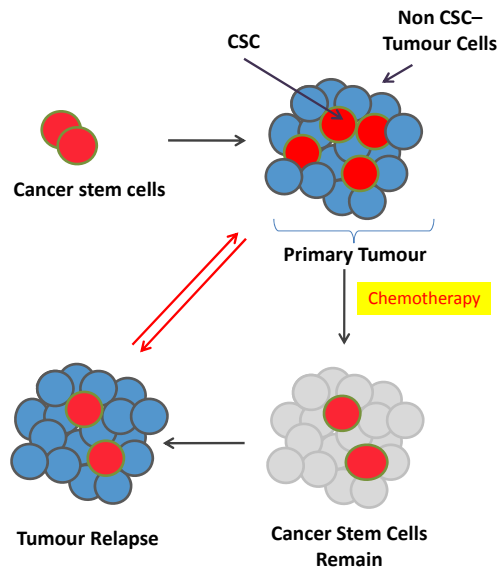


Traditional thought proposes that every tumour cells within the tumour can induce tumour formation

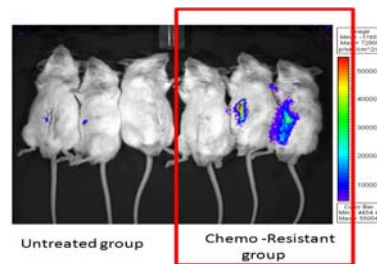
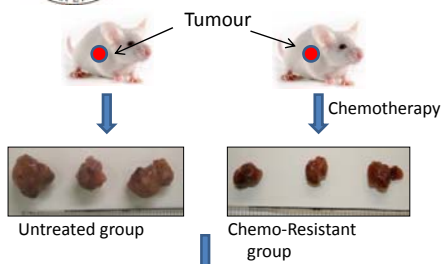
Latest thought proposes that only small subset of tumour cells within the tumour can induce tumour formation. These cells have abilities of self-renewal, differentiation and duplication.



## CSCs and Chemoresistance

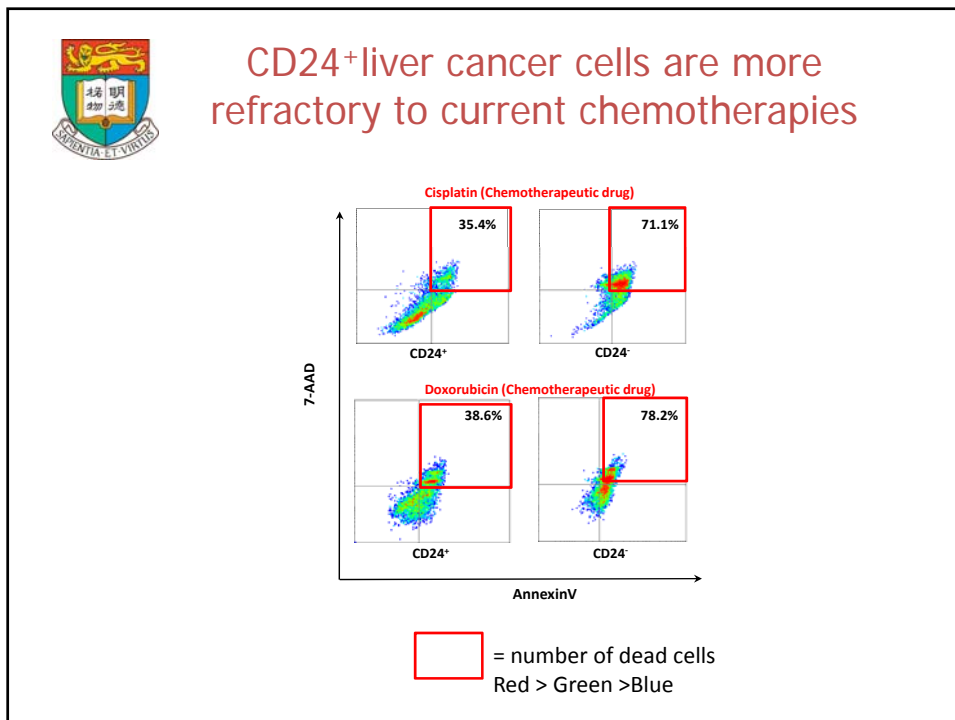
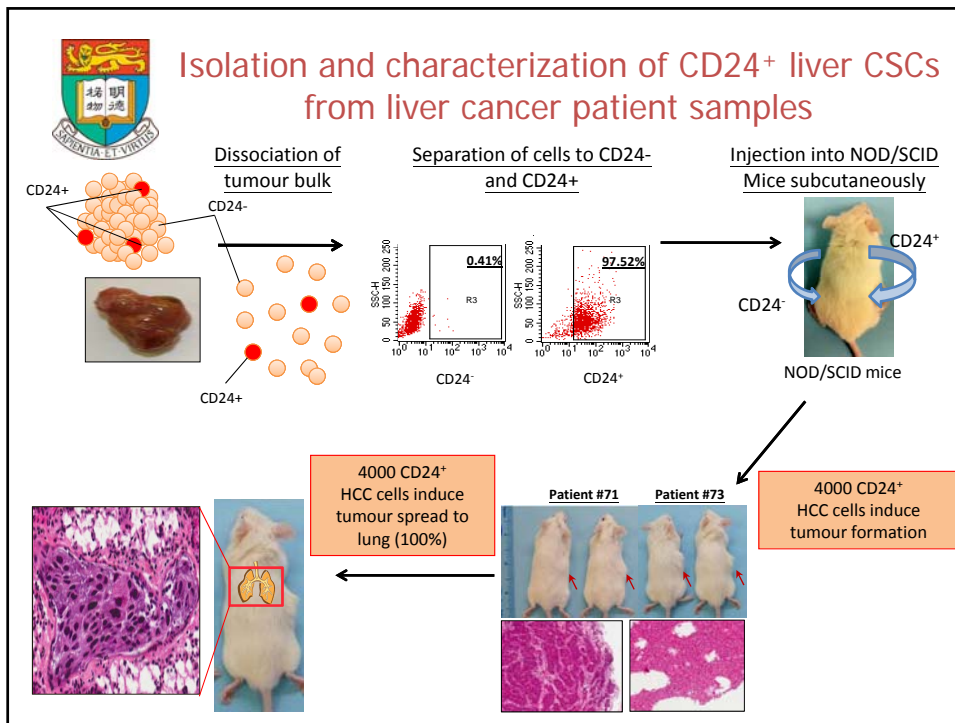


## Identification of CD24+ as a novel CSC marker for Liver Cancer



Analyzing various markers in the two groups, HKU finds that upregulation of CD24 markers in chemo-resistant group is the most prominent

Marker	Fold upregulated
CD24	2.5
CD36	2.1
TP63	2.1



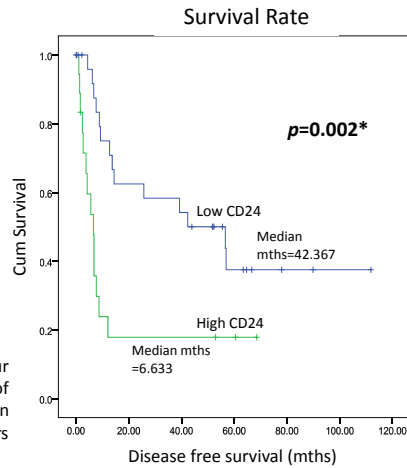


## Clinical significance of CD24+ expression in liver cancer clinical samples

Clinical variables	CD24 expression		p-value
	Low	High	
Recurrence after one year of surgery (N=46)	21%	67%	0.002*
Venous infiltration(N=43) (Important indicator for tumor metastasis)	32%	80%	0.003*

-According to clinical data, liver cancer patients whose tumour had high CD24+ expression had a significantly higher risk of tumour recurrence in the first year after surgery when compared to patients with low CD24+ expression in tumours (67% VS 21%)

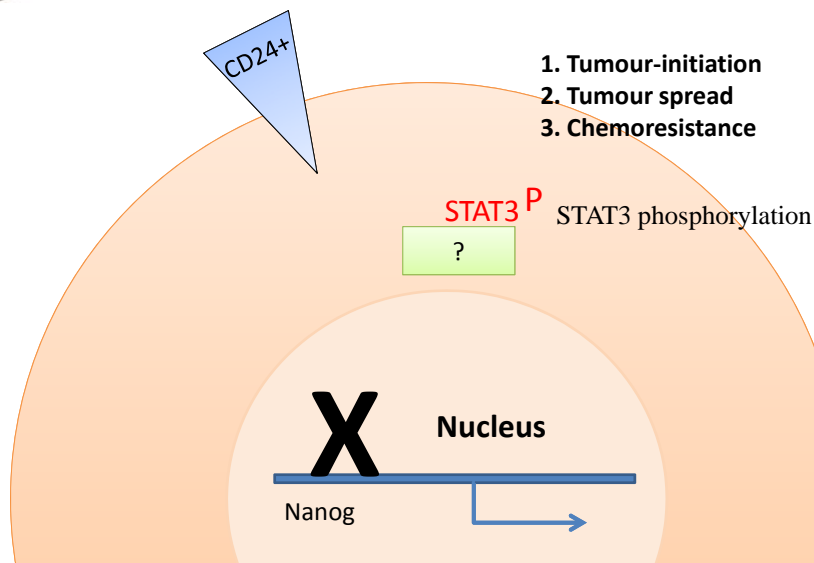
-At the same time, patients whose tumours had high CD24+ expression had a higher chance of tumour metastasis (80% VS 32%)



Liver cancer patients whose tumours had high CD24+ expression had much shorter duration of survival (6.6 months) when compared to patients whose tumours had low expression of CD24+ (42 months)



## The mechanism of how CD24+ leads to tumour development & renewal





## Summary: Clinical implications

- HKU researchers find that CD24+ cancer stem cells are responsible for chemoresistance, metastasis and tumour recurrence in liver cancer. Thus, CD24+ is regarded as a novel biomarker for prediction of tumour recurrence and patients' survival.
- STAT3 phosphorylation is a druggable target for liver cancer therapy.
- HKU will evaluate the therapeutic efficacy of STAT3 phosphorylation inhibitors alone in the suppression of liver cancer recurrence and its combined effect with conventional chemotherapy.
- In long term, the findings facilitate the development of safe, effective and targeted treatment to completely eradicate this deadly disease.



## Questions and Answers