



Department of Pathology
Li Ka Shing Faculty of Medicine
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**HKU Discovers that Antioxidants
Lead to Growth in Liver Cancer Cells**

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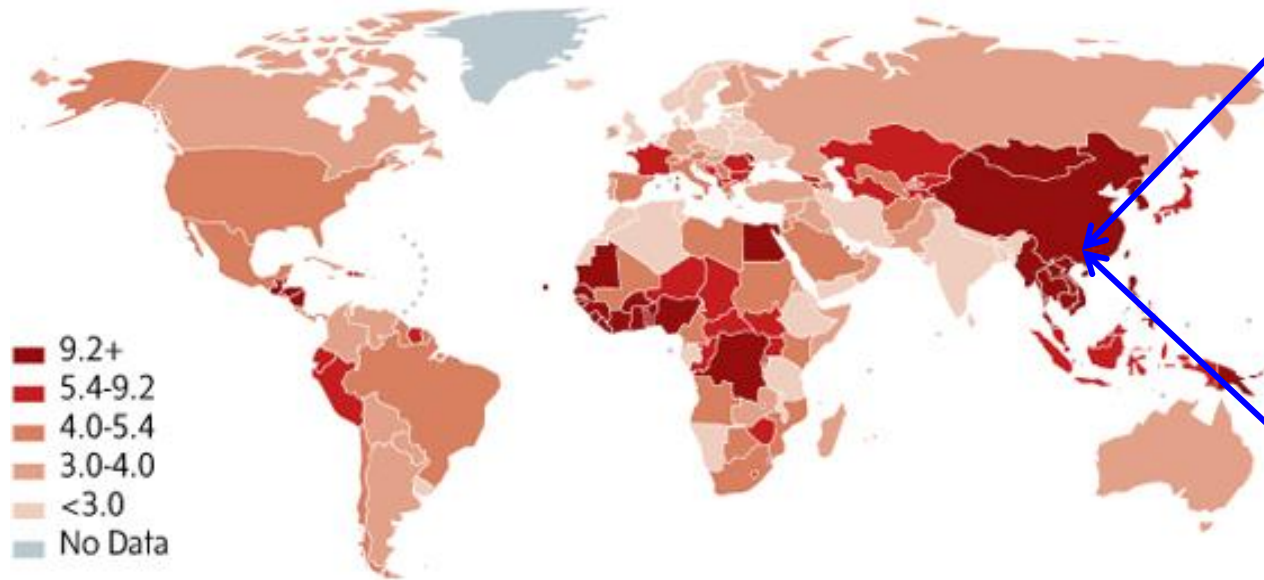
PhD Candidate

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Liver cancer – Huge epidemiological impact

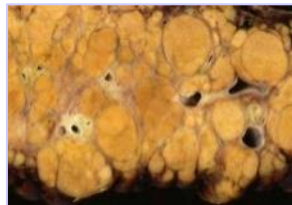
LIVER CANCER
Mortality rate per 100,000, both sexes



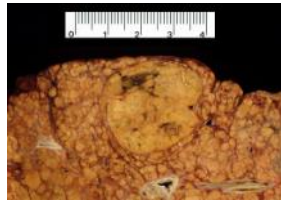
55% of all new liver cancer cases worldwide (500,000 - 600,000 cases/ year) occur in China

2nd commonest fatal cancer in China; 3rd in HK

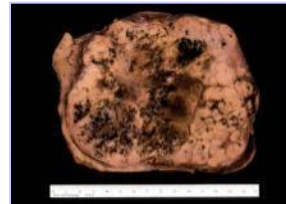
HBV/HCV infection/
alcoholism



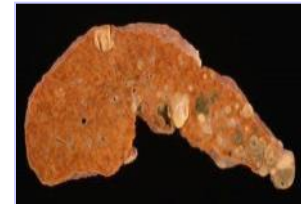
Cirrhotic liver



Dysplastic nodule



HCC



Metastatic HCC



Pre-malignant



Malignant



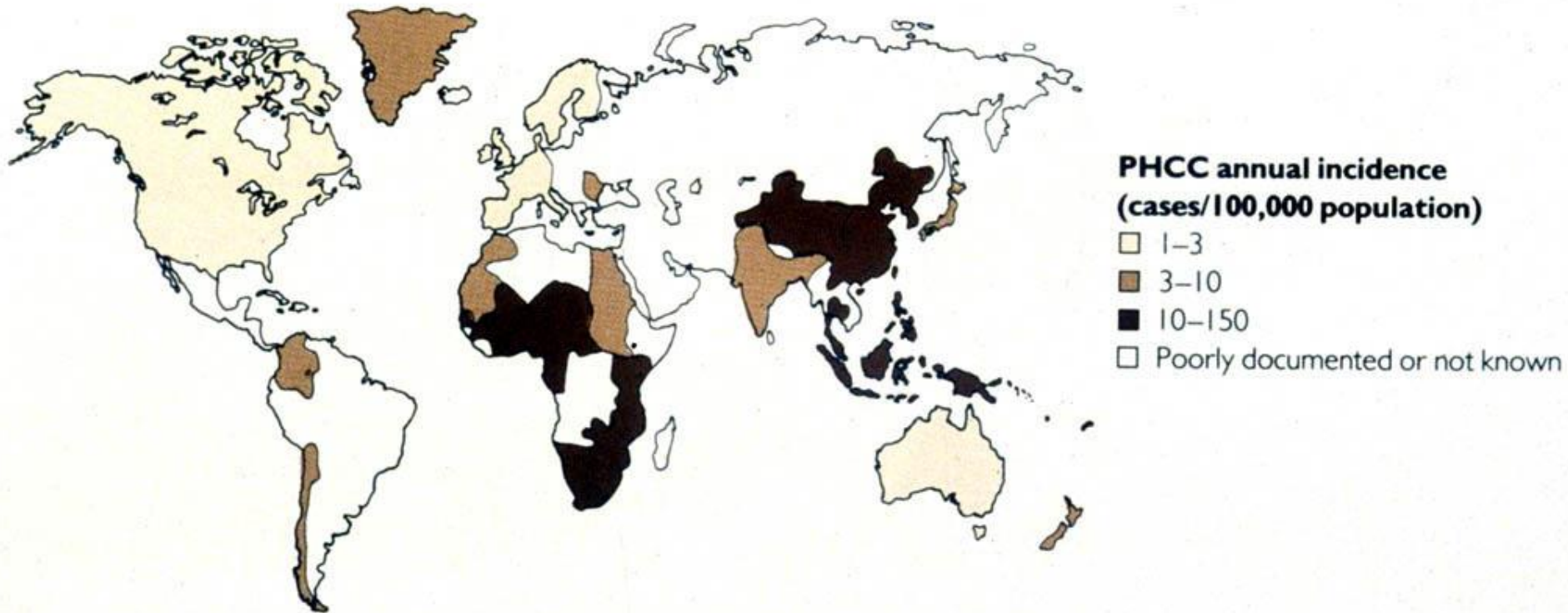
Liver Cancer & Hepatitis B Virus (HBV)



10% of the Hong Kong population are HBV carriers



Liver Cancer & Hepatitis B Virus (HBV)

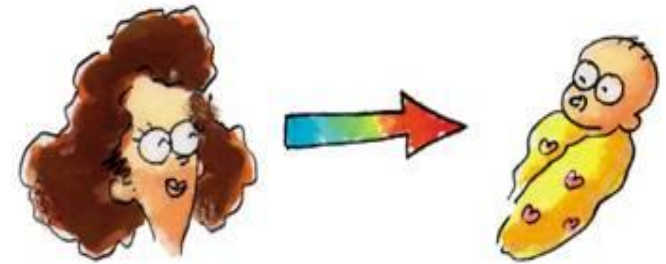


Geographic variation: Striking correspondence between areas where HCC is common and areas where HBV is prevalent



Hepatitis B virus

- Transmission through blood/body fluid
- Maternal transmission for **HBV**

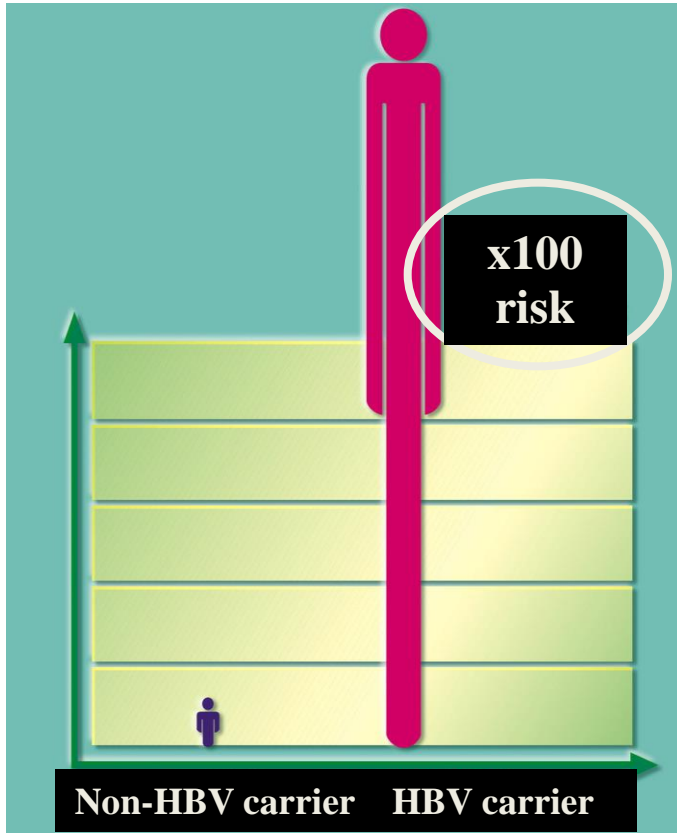


- Causes carrier state, acute and chronic hepatitis or end-stage liver
- Casual relationship with liver cancer

**Vaccine available for
HBV**



Liver cancer



>80% of liver cancer patients are HBV carriers



Liver cancer - challenges

Treatment far from perfect!

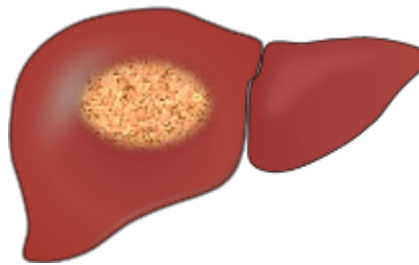
No patient stratification for treatment

“One-size-fits-all”

Molecular drugs

The only FDA-approved Sorafenib has modest effect

Health care burden



Social impact

Peak age of patients: 45-60 years, at prime age of life

Deadly cancer

High recurrence rate, poor survival, 80% inoperable

Resistant to chemodrugs

Resistant to conventional chemotherapy



Liver cancer – curative treatments

- **Surgical resection:** 5-year survival 55%, high recurrence rate
- **Liver transplantation:** best cure with 5-year survival 75%, only for early HCC; limited liver donor availability

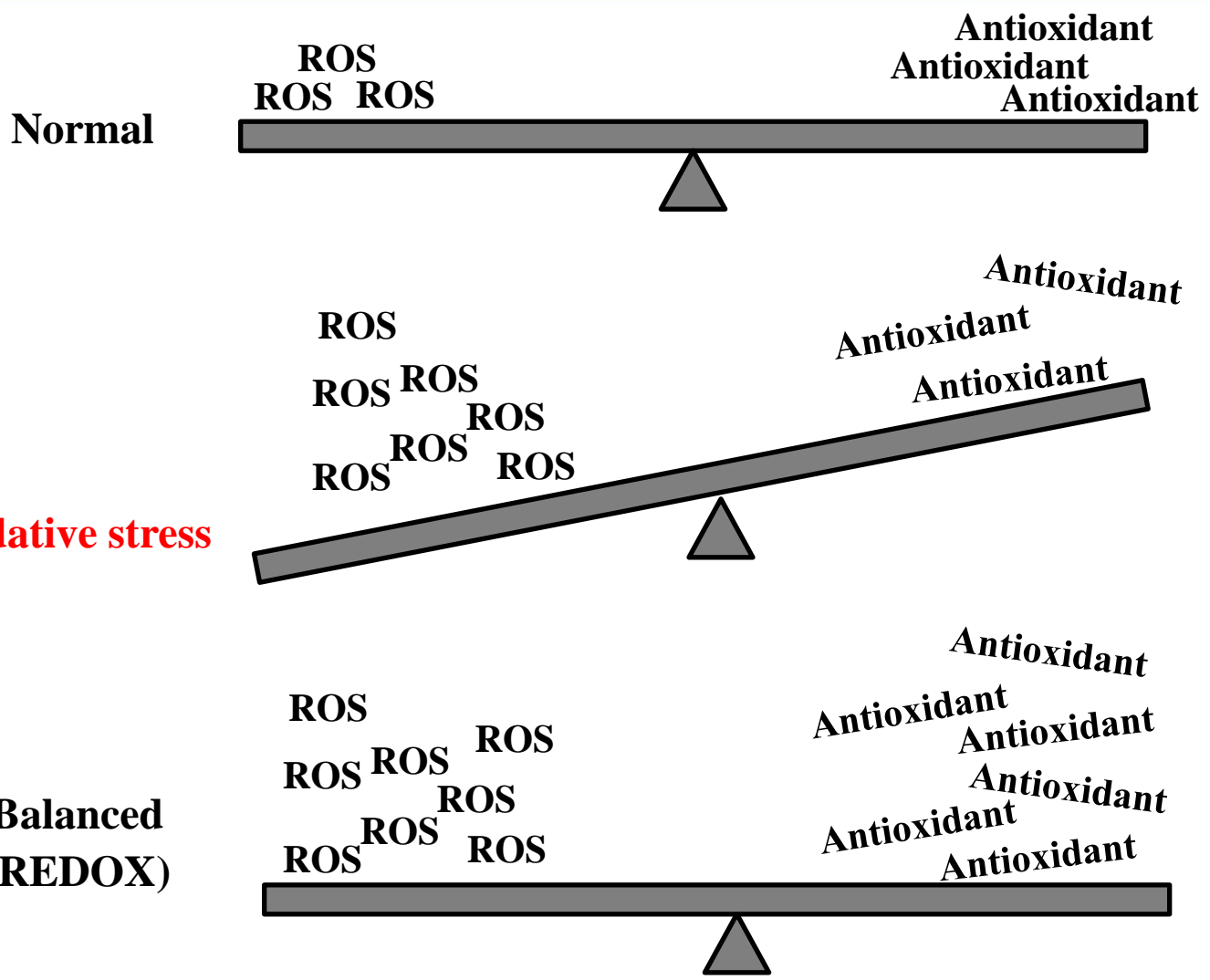


Reactive Oxygen Species & Antioxidants

- **Reactive Oxygen Species (ROS)**
 - Side-products of oxygen (O_2) metabolism
- **Antioxidants**
- Antioxidants are molecules that inhibit ROS
- Vitamin A
 - Milk, egg yolk, carrots
- Vitamin C
 - Fresh vegetables and fruits (orange, lemon, tomato)
- Vitamin E
 - Nuts, whole grains
- Antioxidant supplements contain high dose of antioxidants

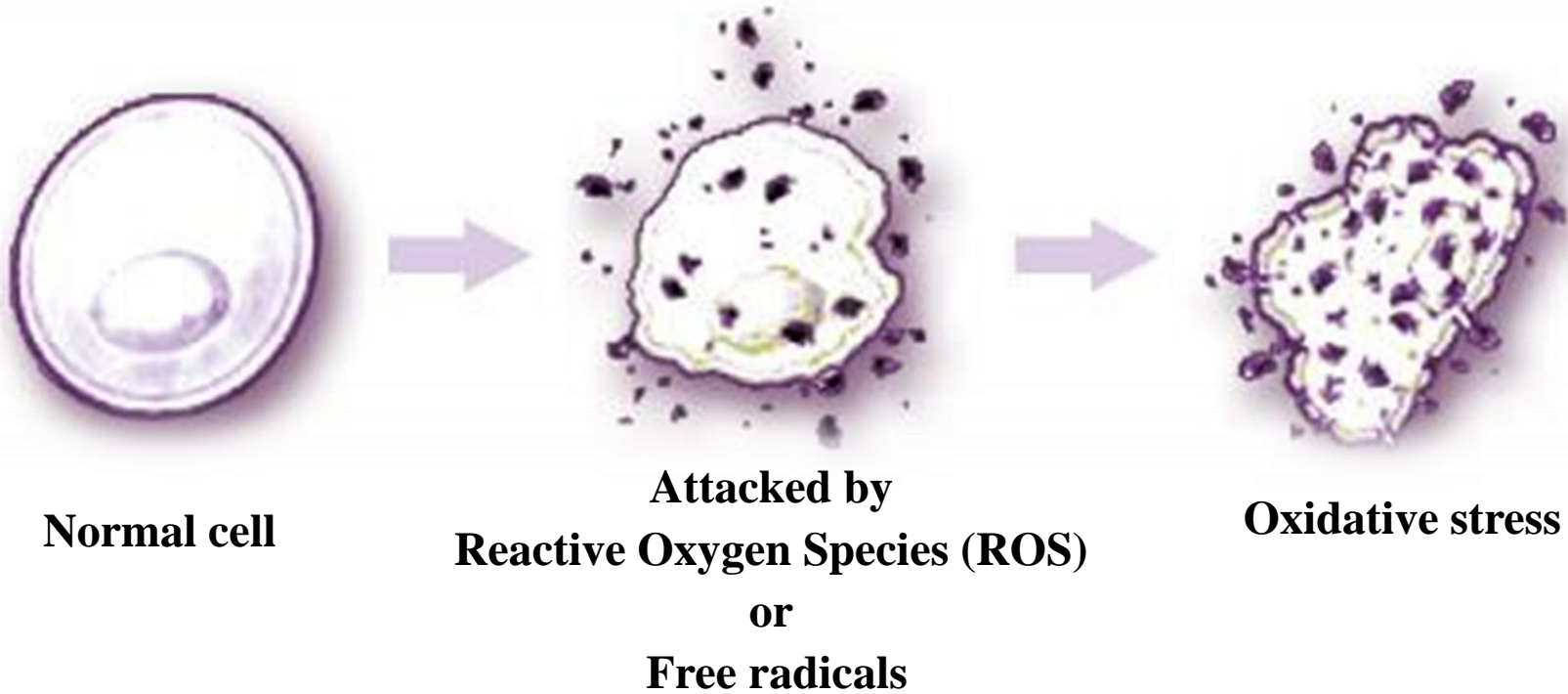


Oxidative stress





Oxidative stress



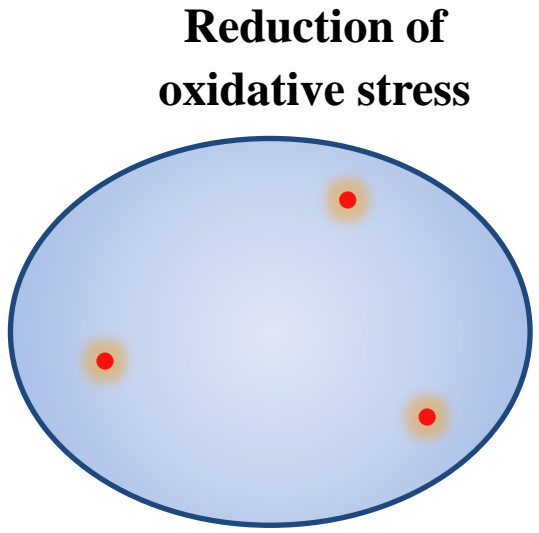
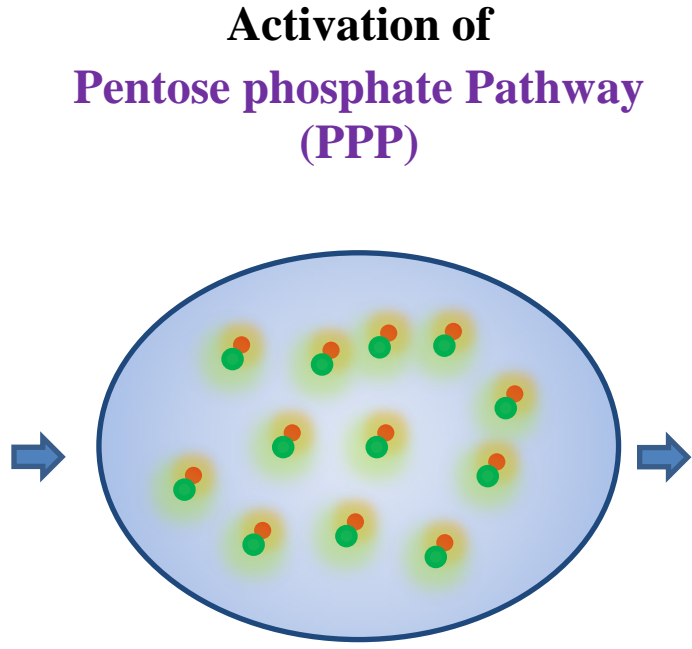
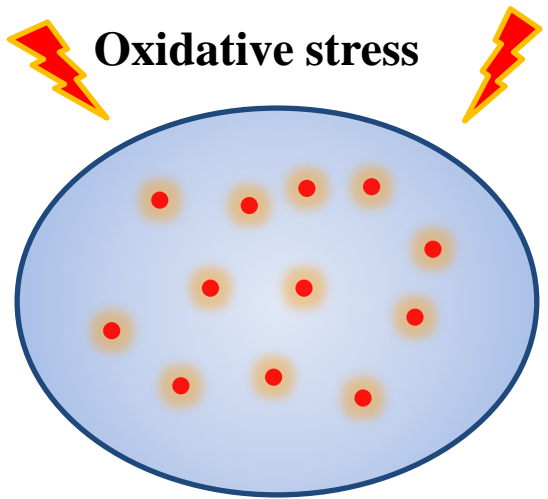
Oxidative stress is a disturbance in the balance between the production of ROS and antioxidant defenses.



Liver cancer cells need antioxidants

ROS 

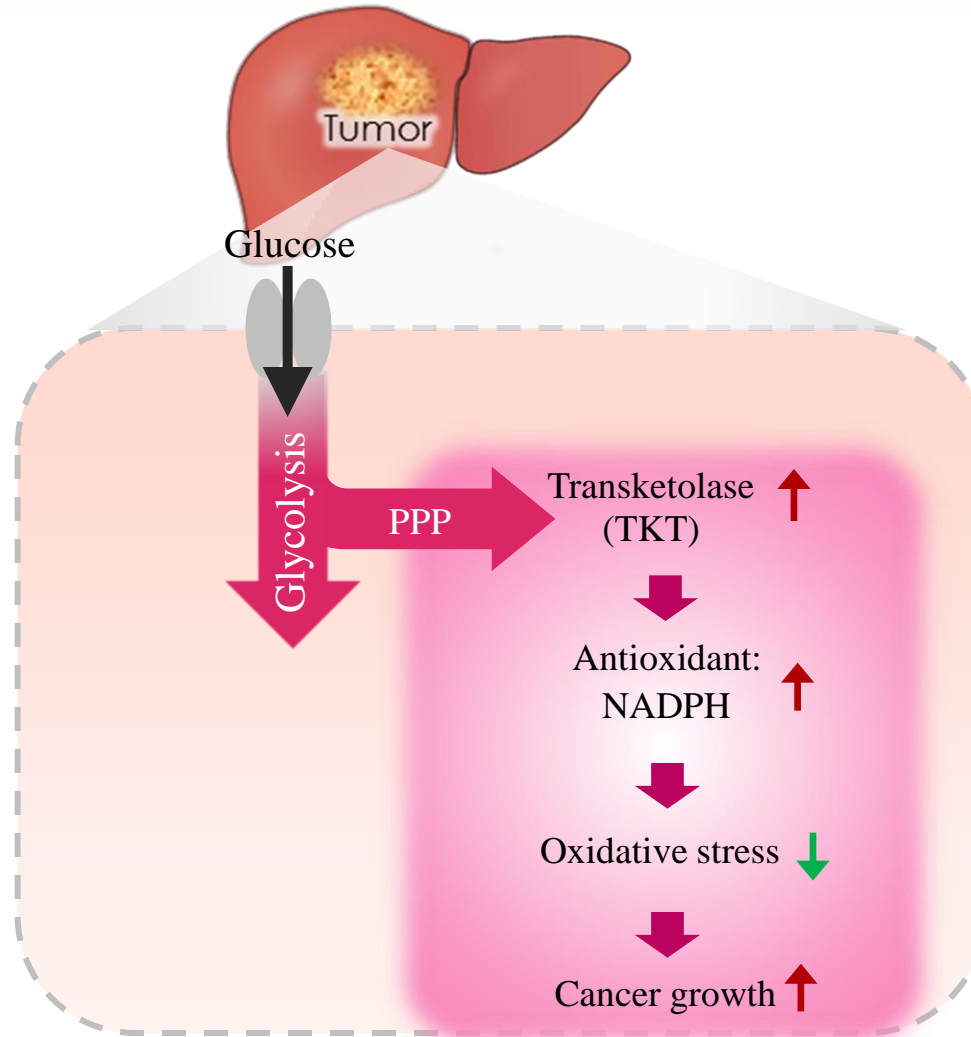
Antioxidant 



Liver cancer cells

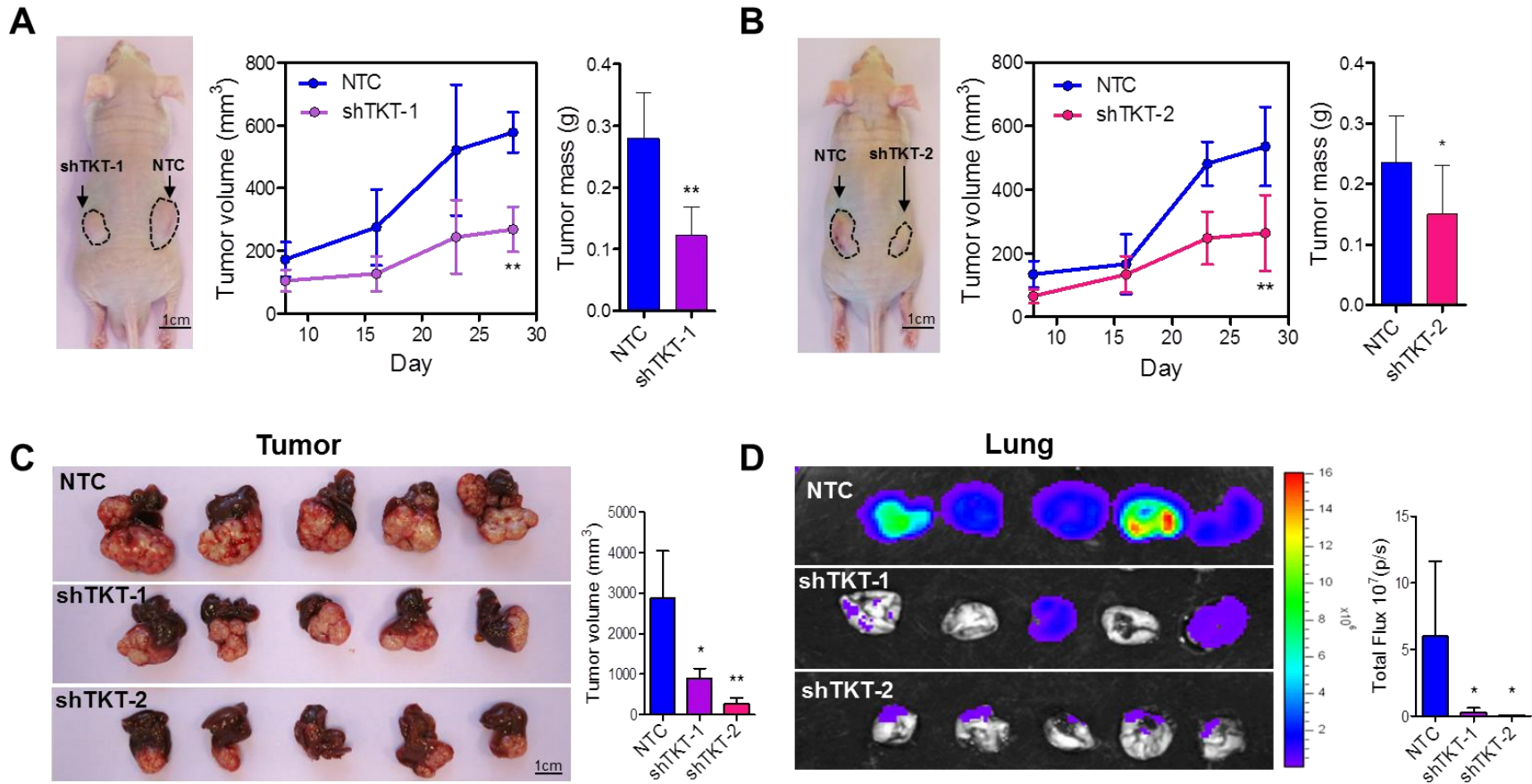


Liver cancer cells use TKT enzyme in the PPP to produce antioxidant



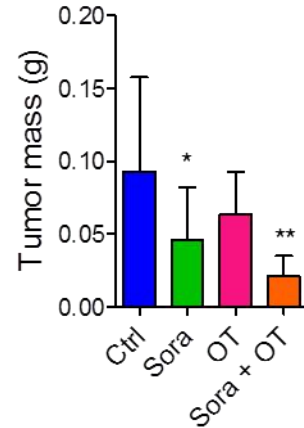
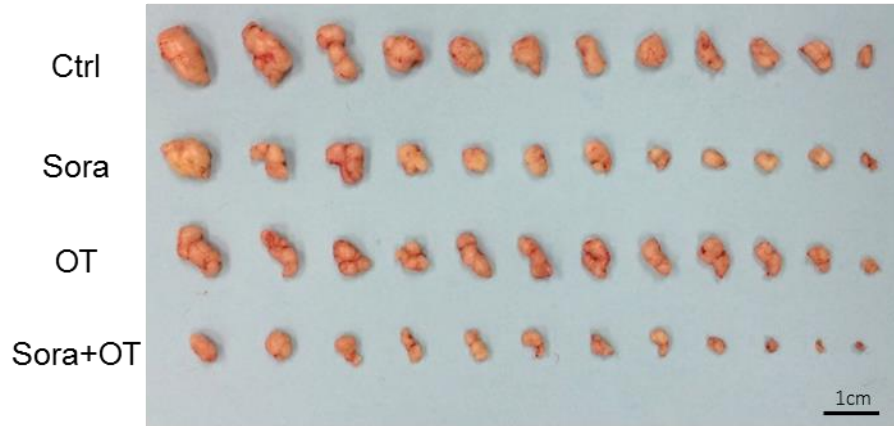
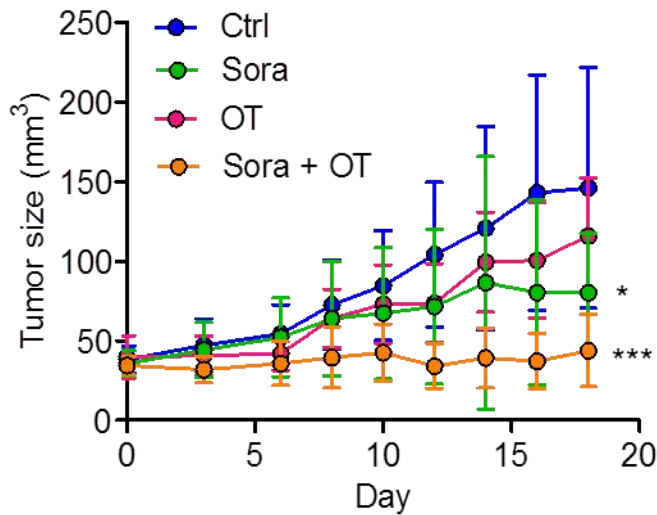


TKT promotes liver cancer growth in mice





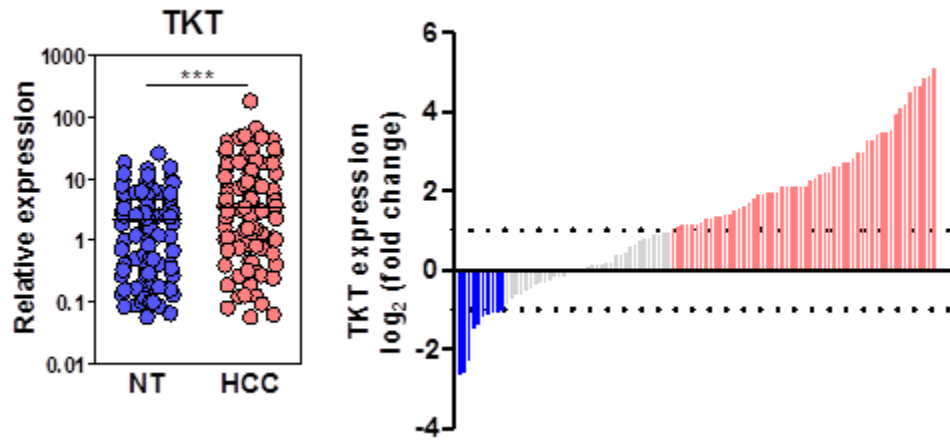
Blocking PPP with chemical, oxythiamine, suppresses liver cancer growth



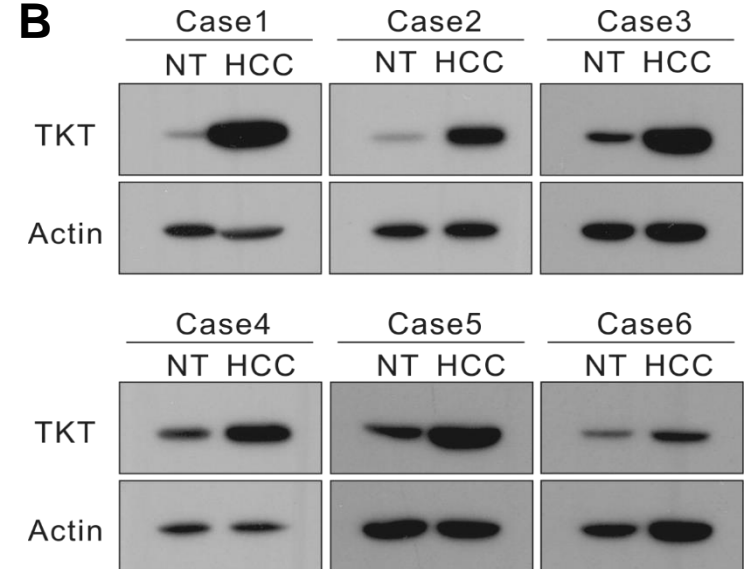


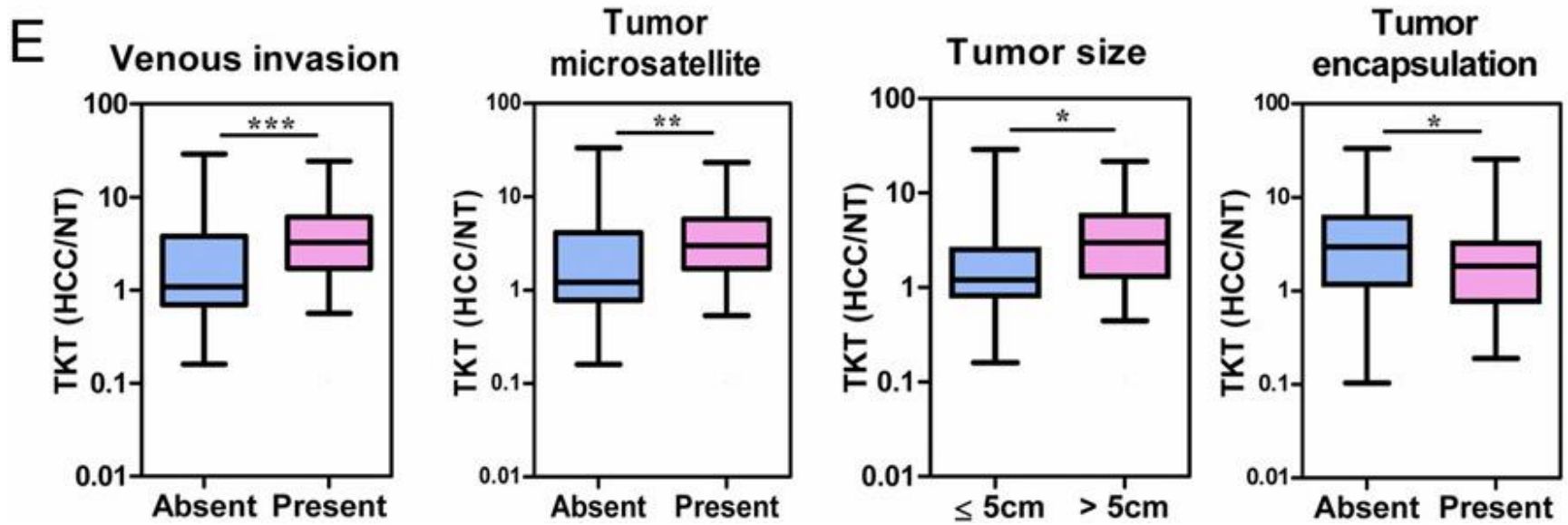
TKT is activated in liver cancer

A



B

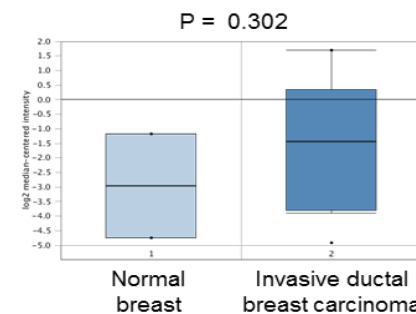
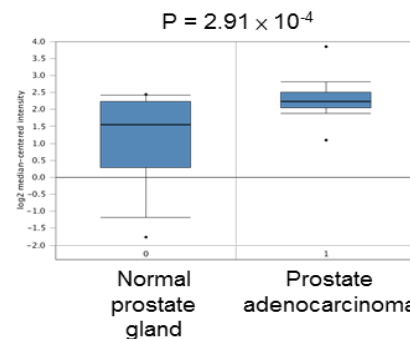
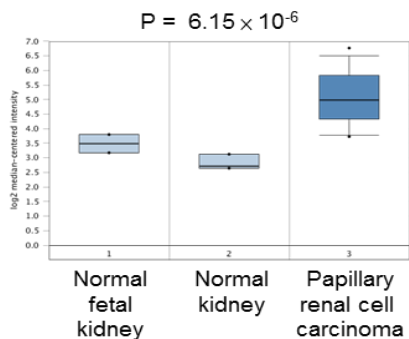
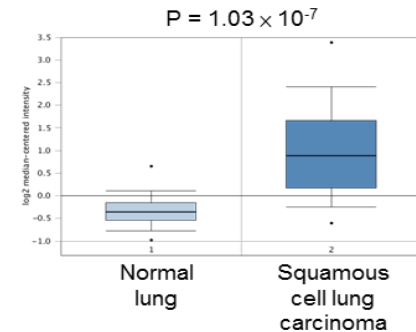
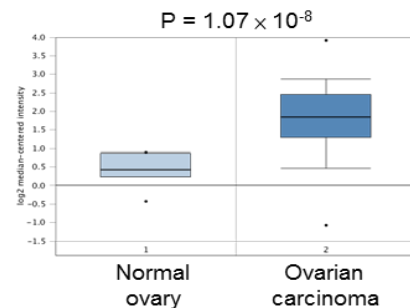
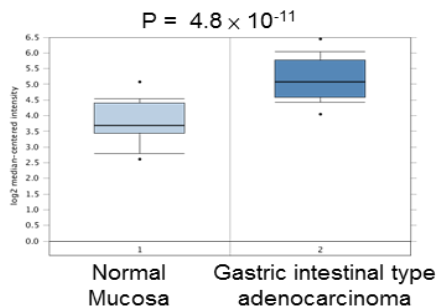
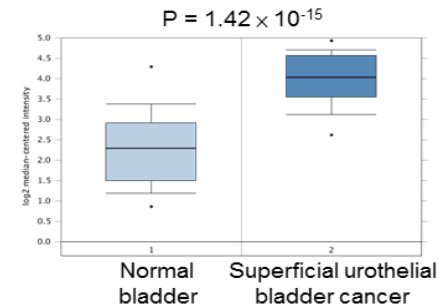
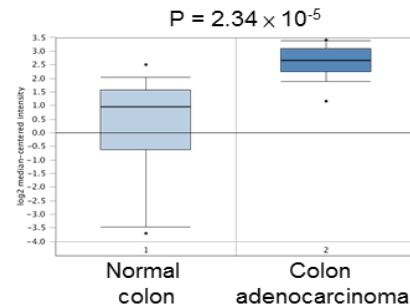
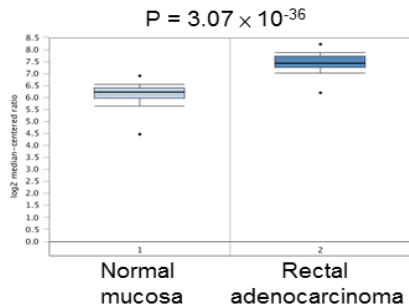




Higher TKT expression levels in patients' liver cancer are associated with a large cancer size and high spreading (metastatic) ability



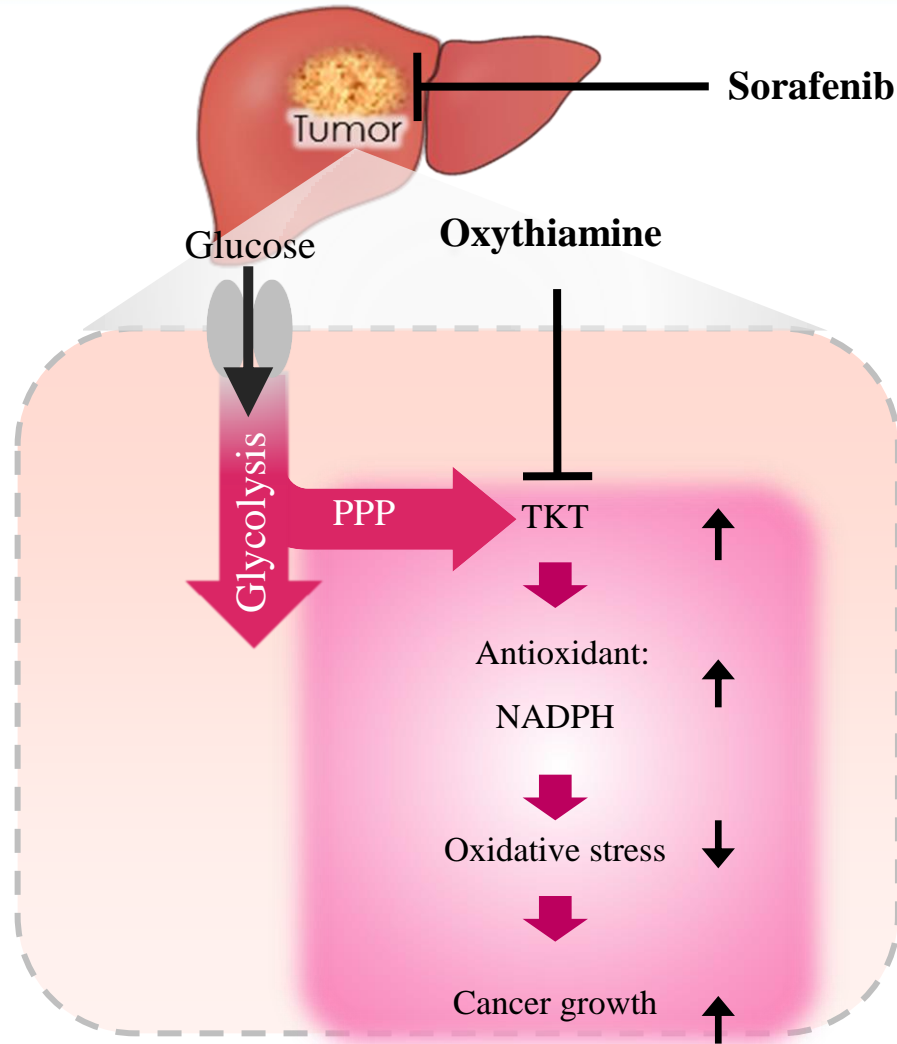
TKT is also activated in other cancers (e.g. Colorectal, Lung Cancer)



(OncoPrint)



Research Summary





Future studies

- HKU research team is conducting a further study
 - identify additional anti-oxidant producing pathways in liver cancer
 - evaluate the therapeutic efficacy of drugs against antioxidant-producing pathways in the suppression of liver cancer and the combined effect with chemotherapy
- Aim: develop molecular targets



Suggestions

- Liver cancer patients should have a balanced diet
- High intake of antioxidant supplements may not be beneficial to cancer patients



Q & A