

Le jeûne de courte durée en concomitance de la chimiothérapie

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Sion

5.9.2014

Soins en Oncologie Suisse

5ème journée romande de formation continue

**Le jeûne de courte durée (STS)
en concomitance de
la chimiothérapie (ou la radiothérapie)**

DSR (*differential stress resistance*)

DSS (*differential stress sensitization*)

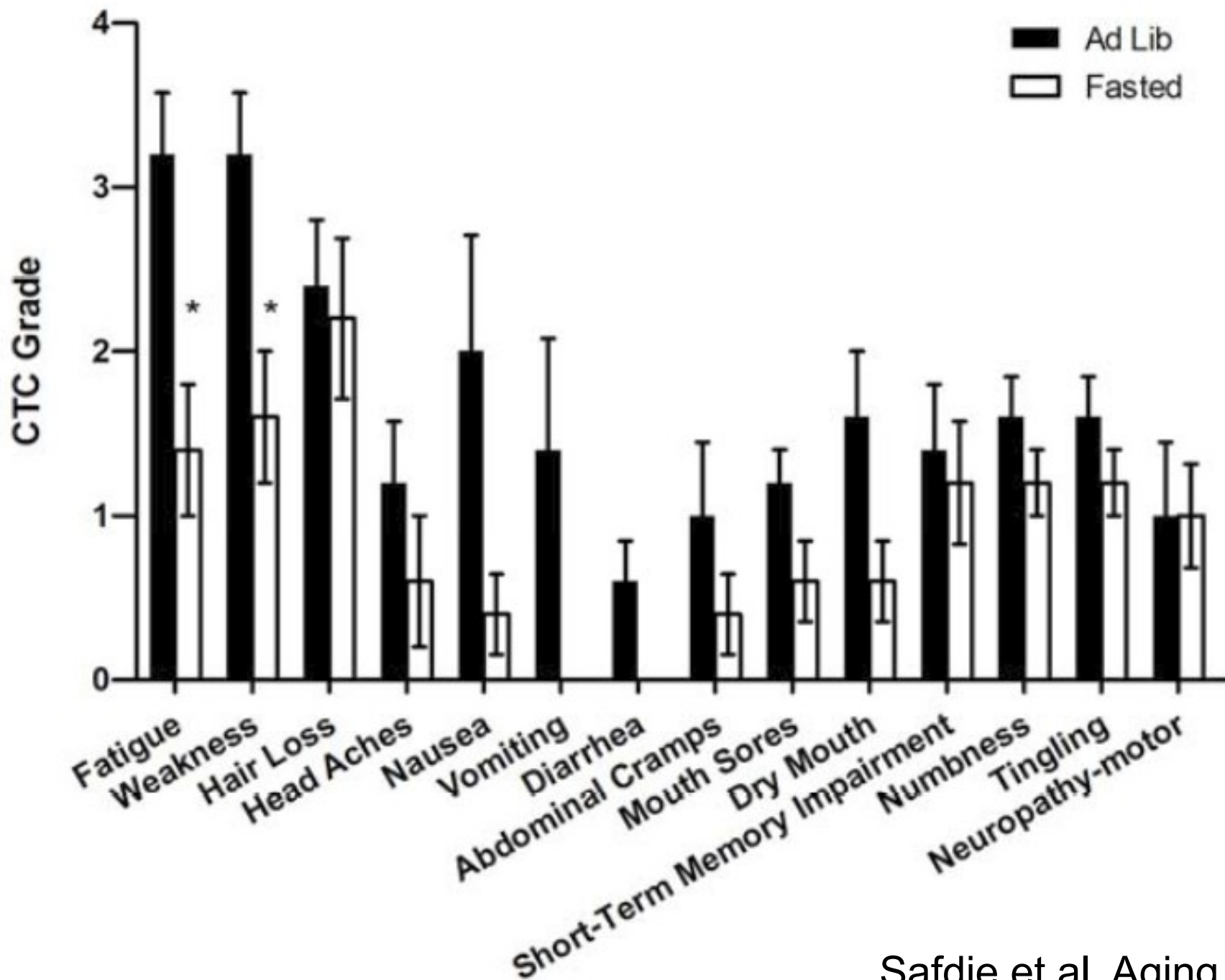
Études cliniques en cours

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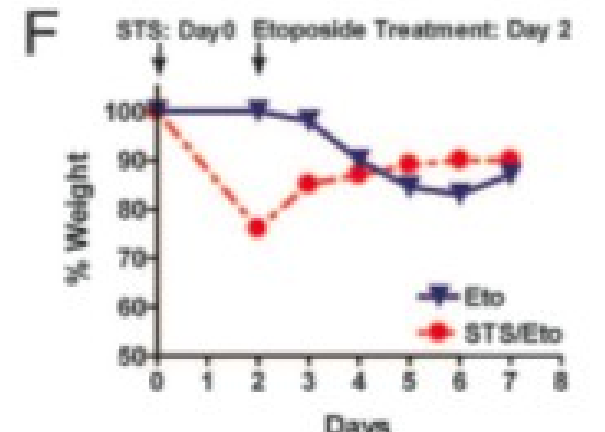
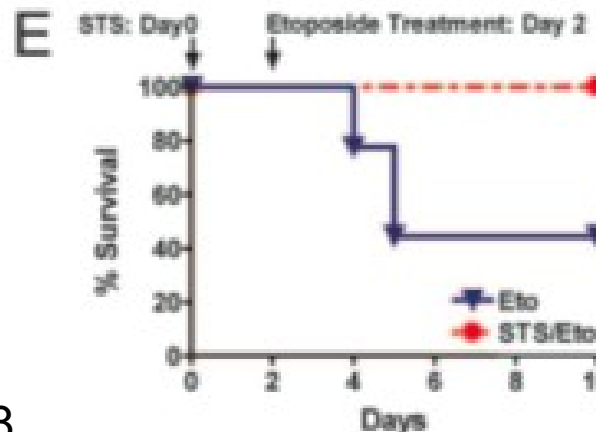
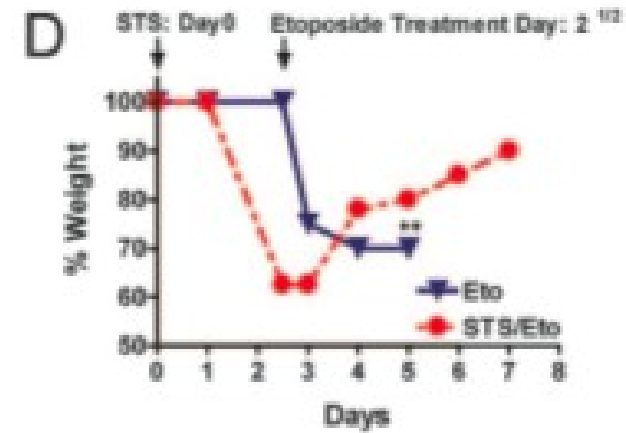
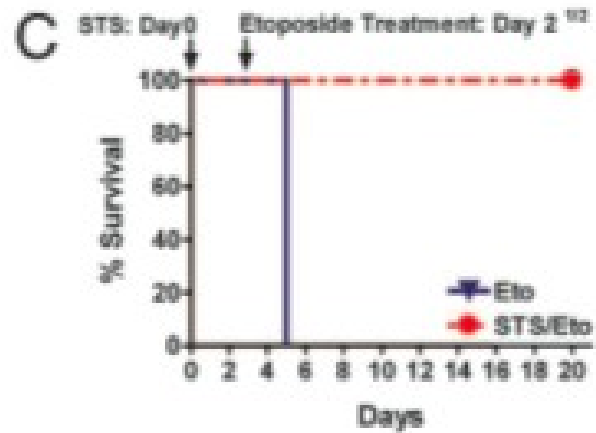
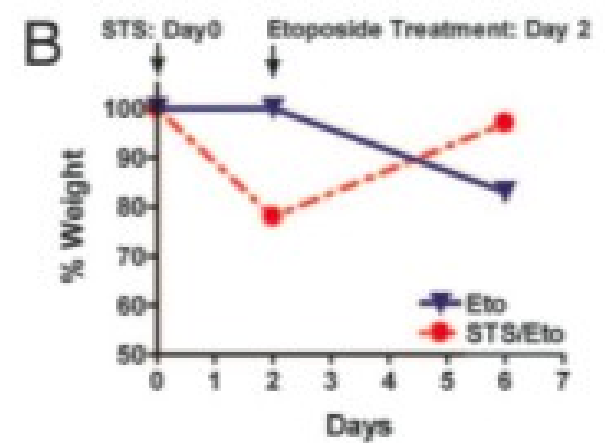
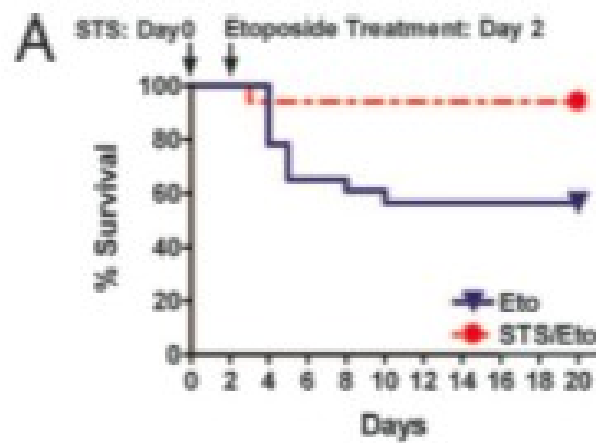
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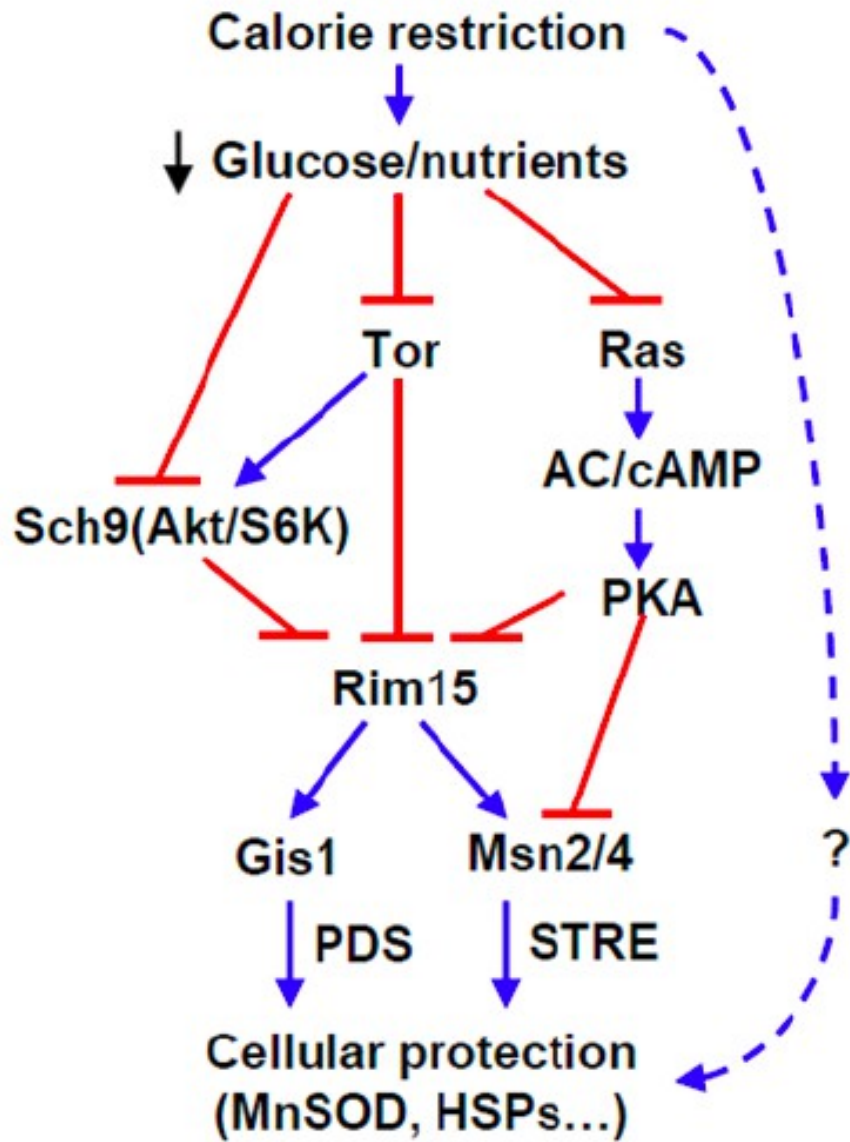
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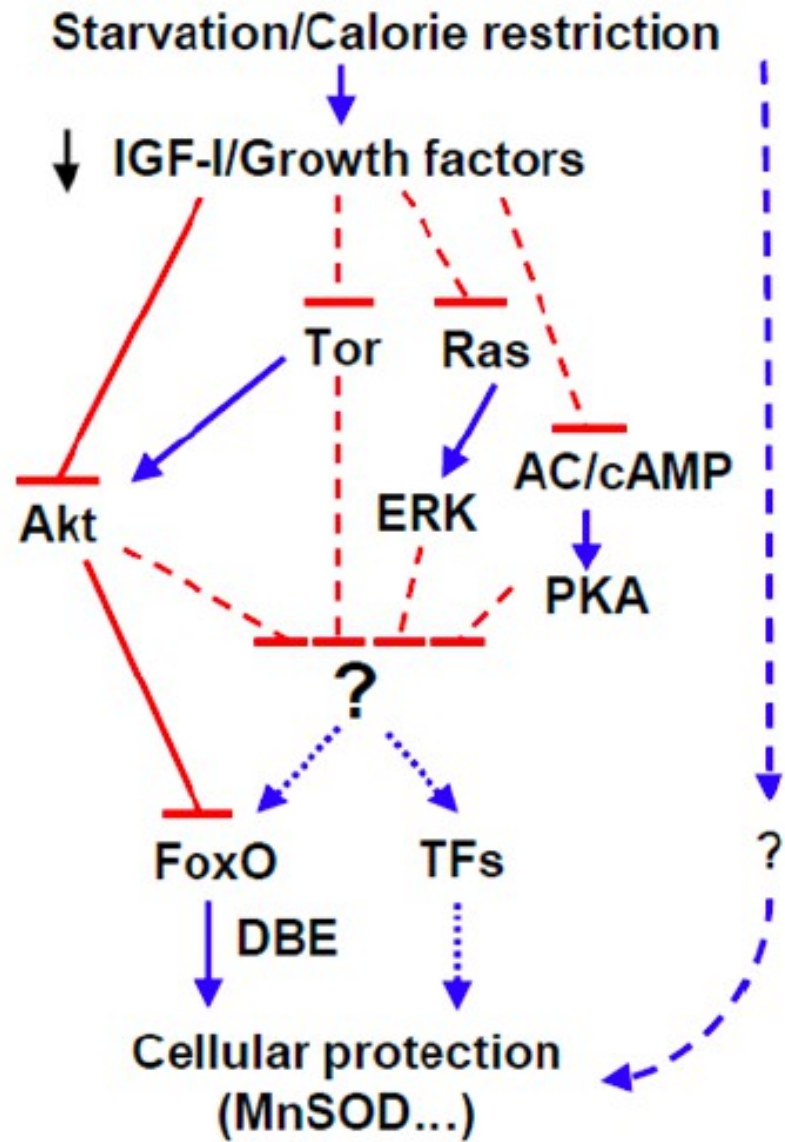
3 souches souris:
 48h jeûne avant
 Etoposide 80mg/kg



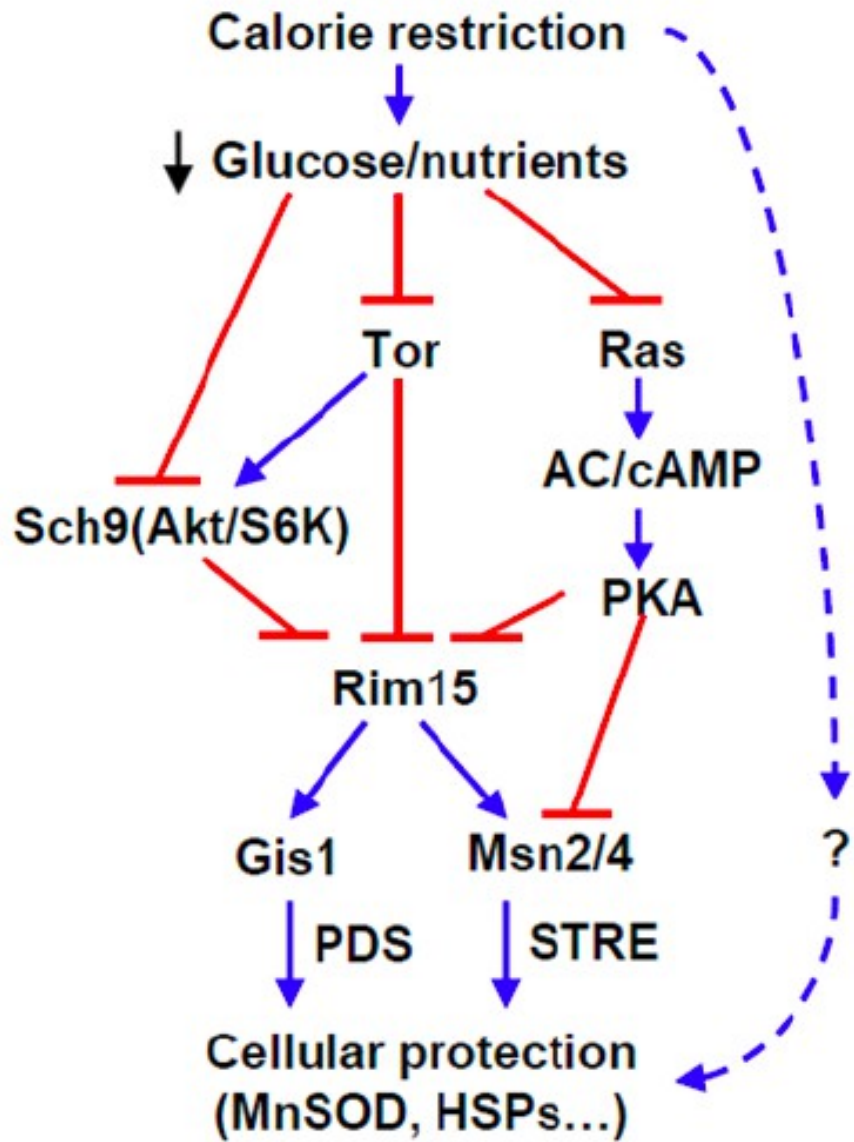
Yeast



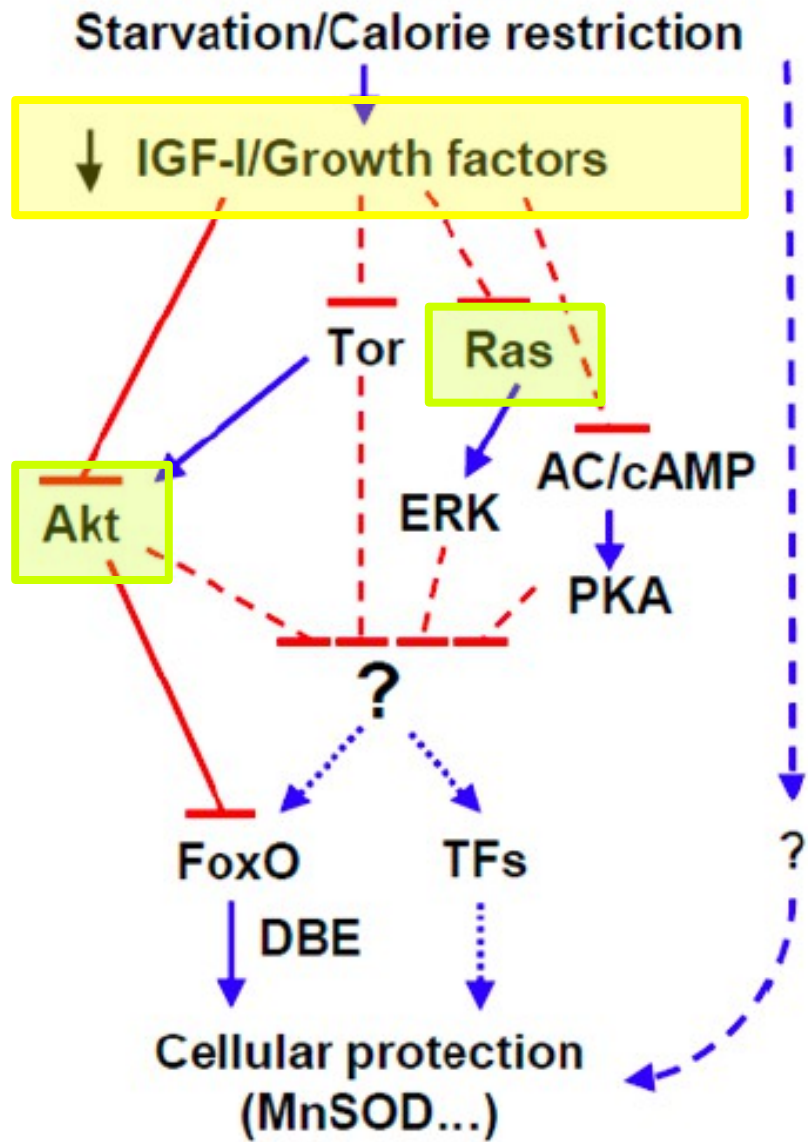
Mice/Rats



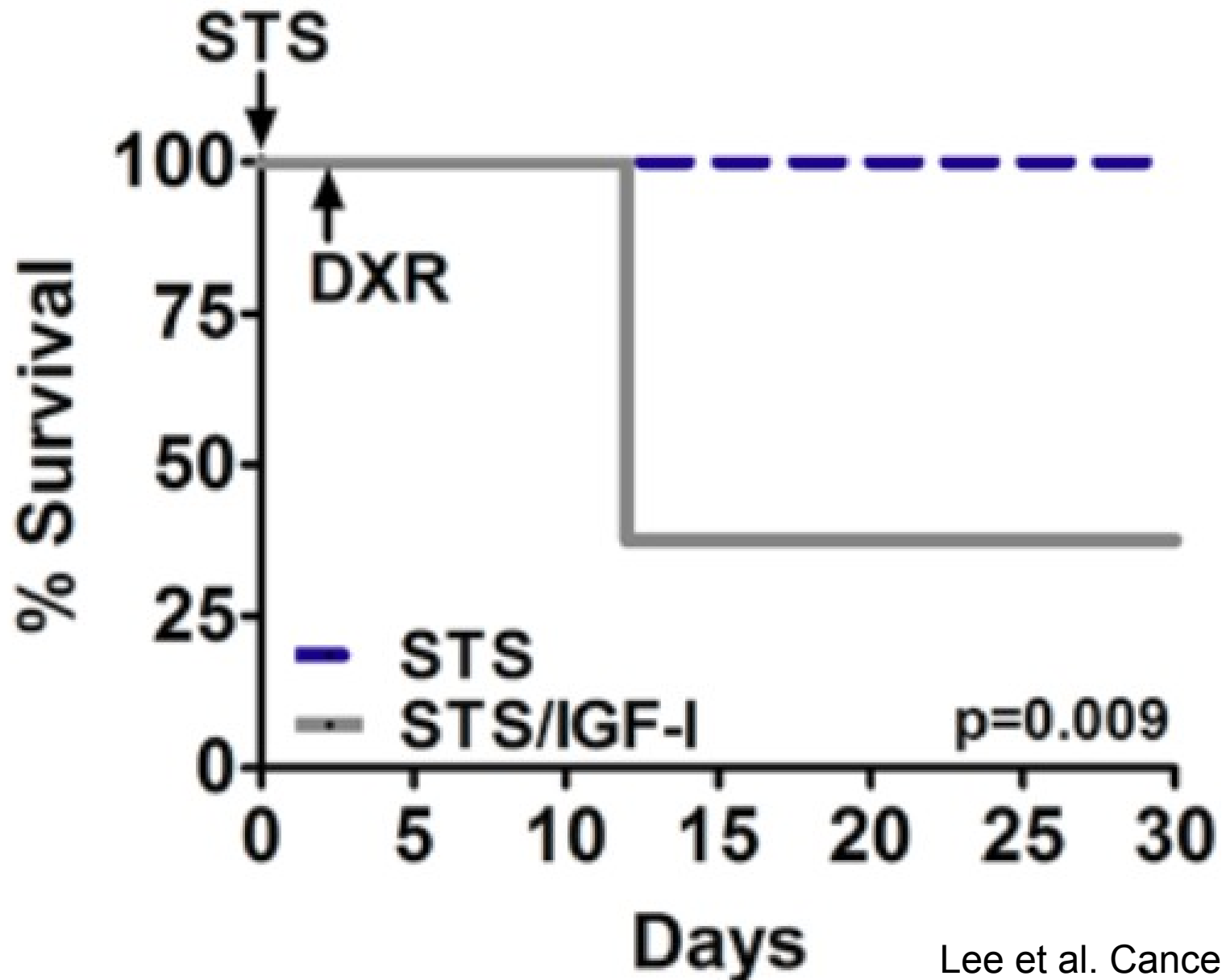
Yeast



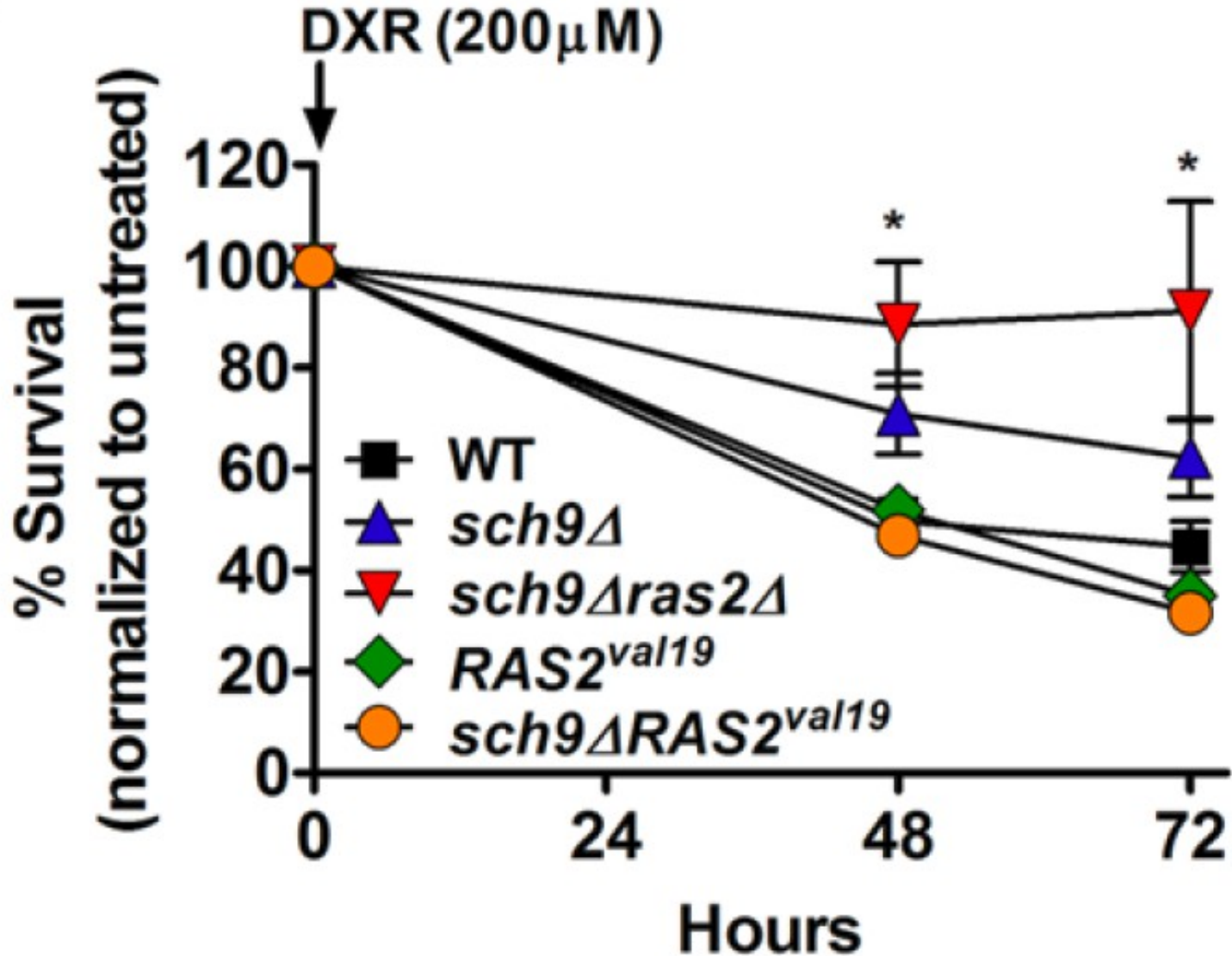
Mice/Rats



DSR: IGF-I role



DSR: Ras and Akt pathways role



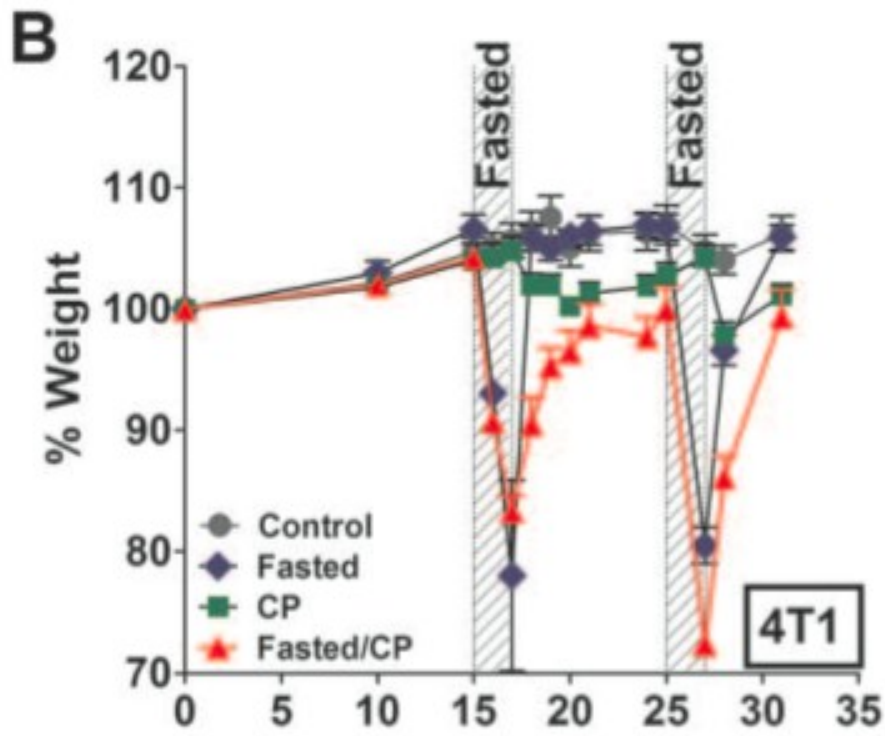
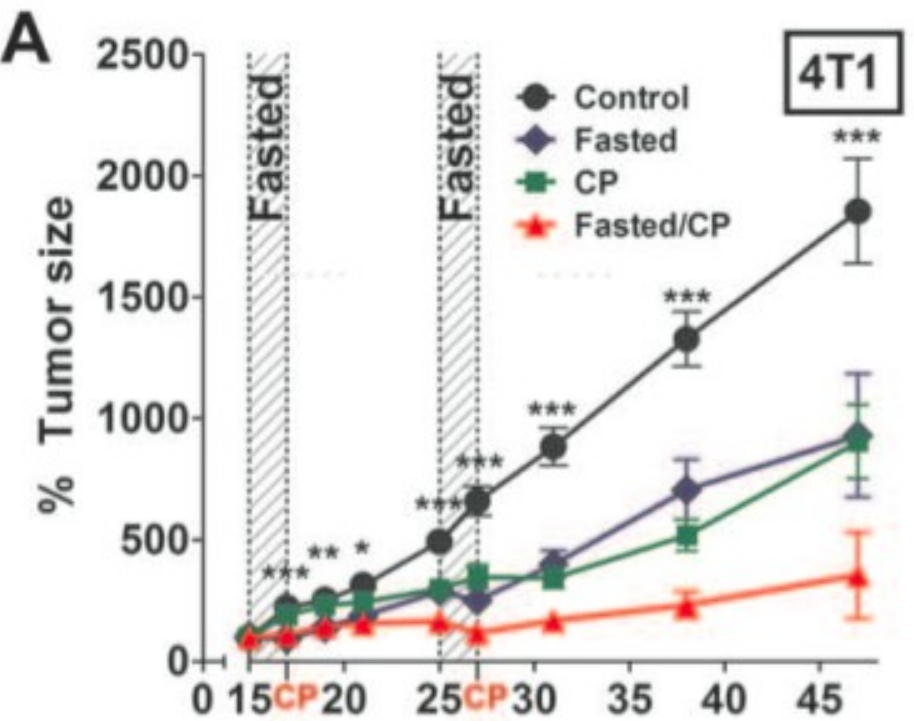
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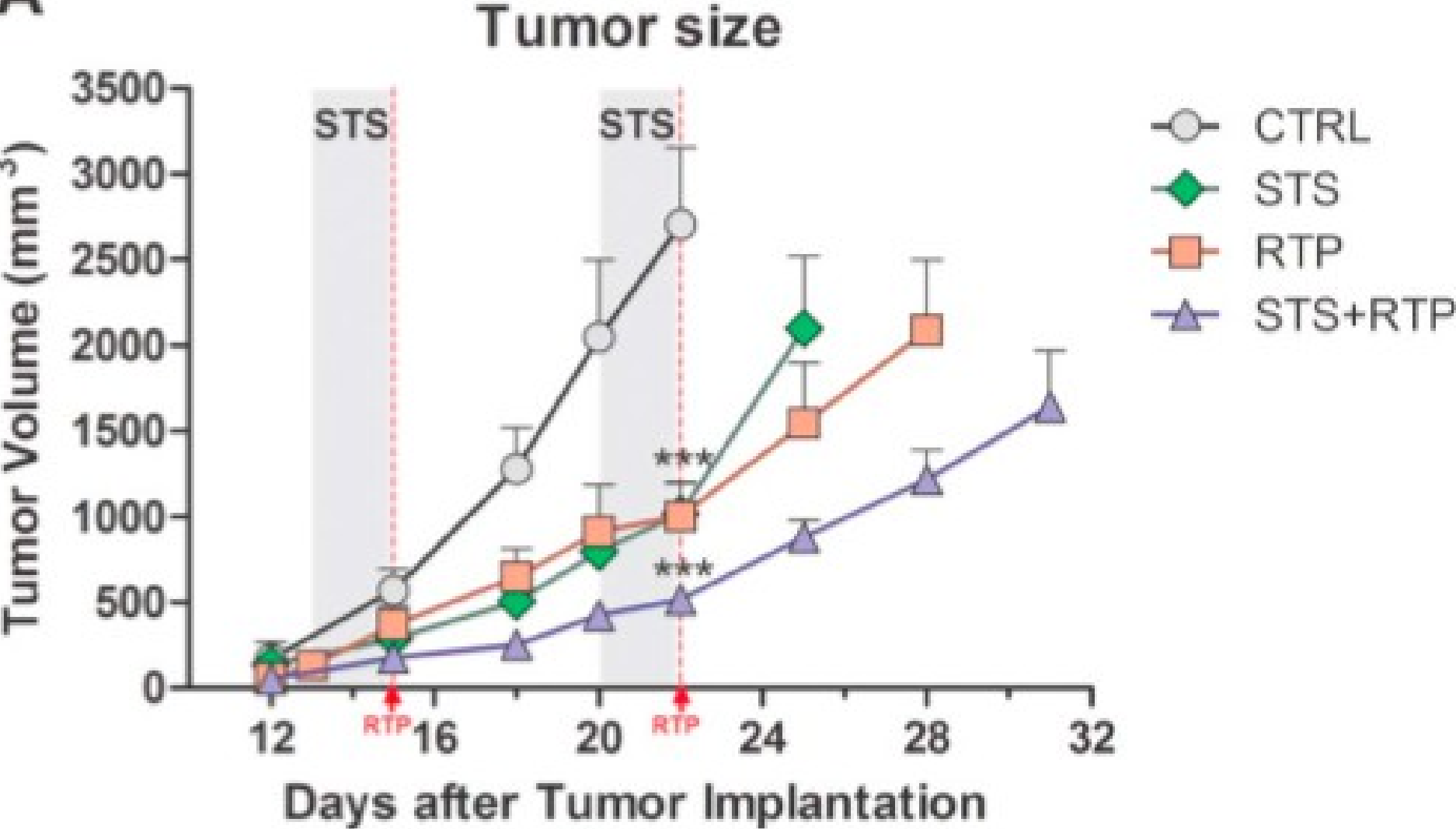
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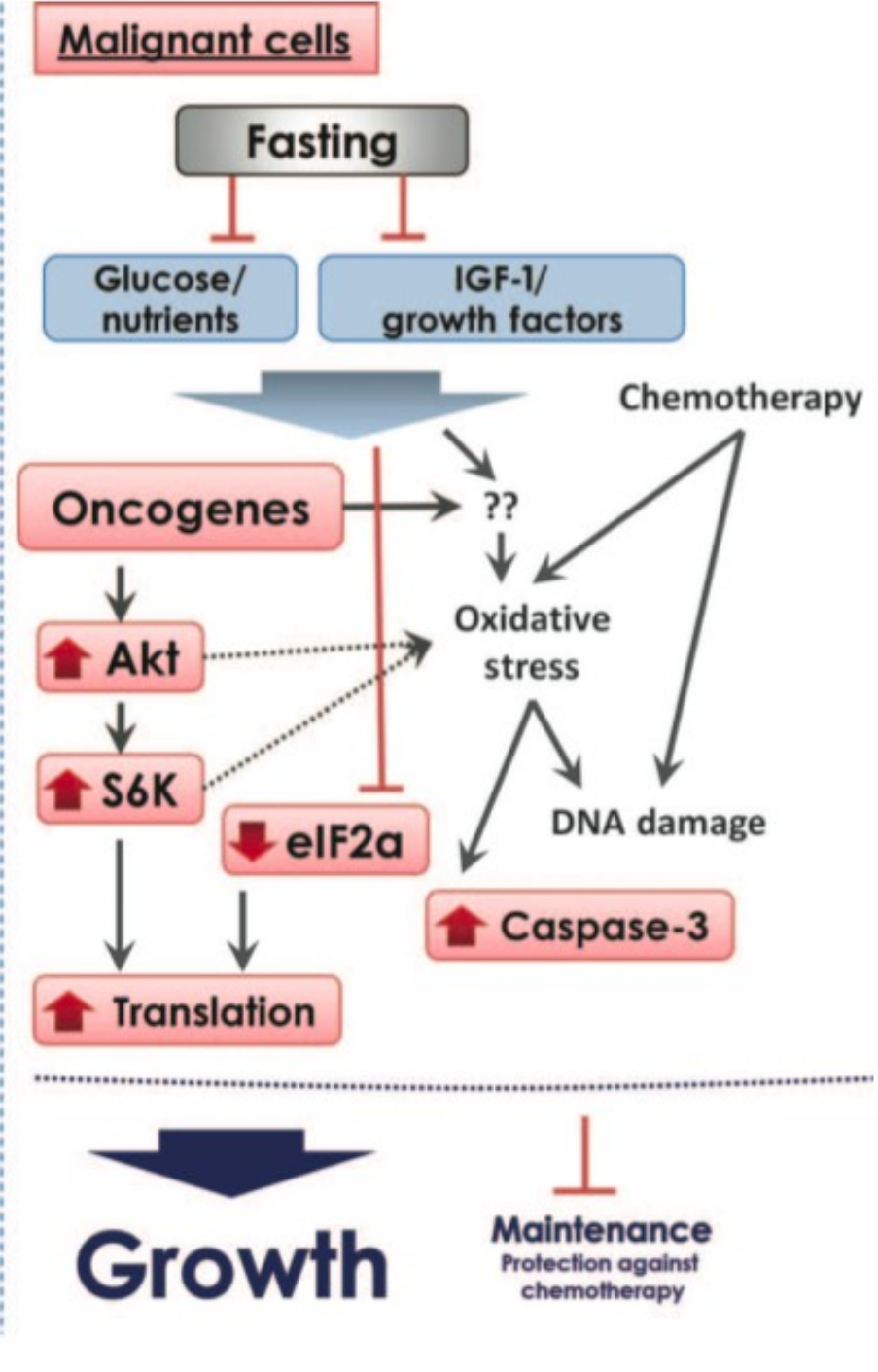
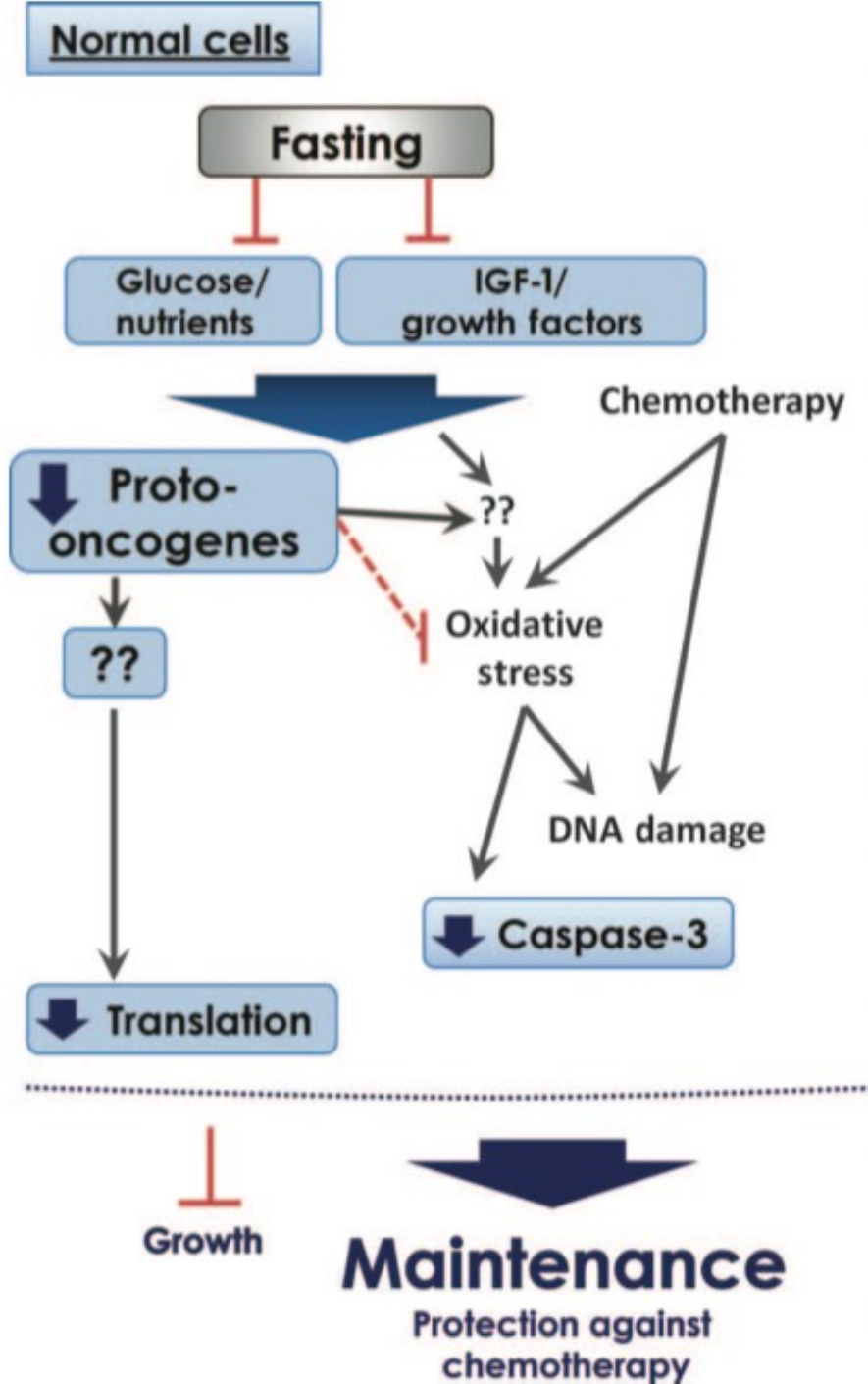
DSS: breast cancer xenograft - chemotherapy



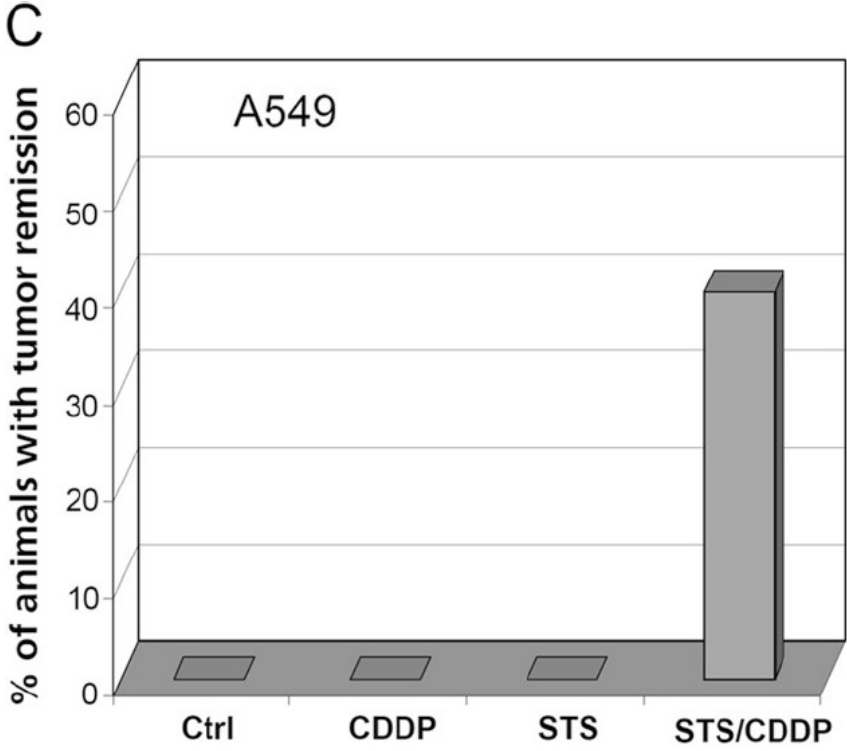
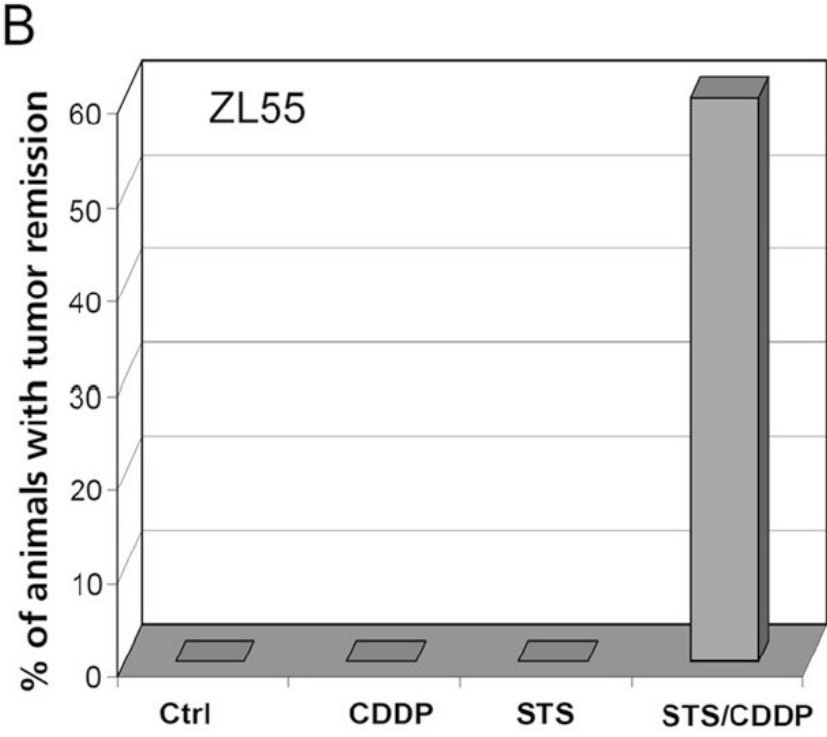
DSS: glioblastoma xenograft - radiotherapy

A

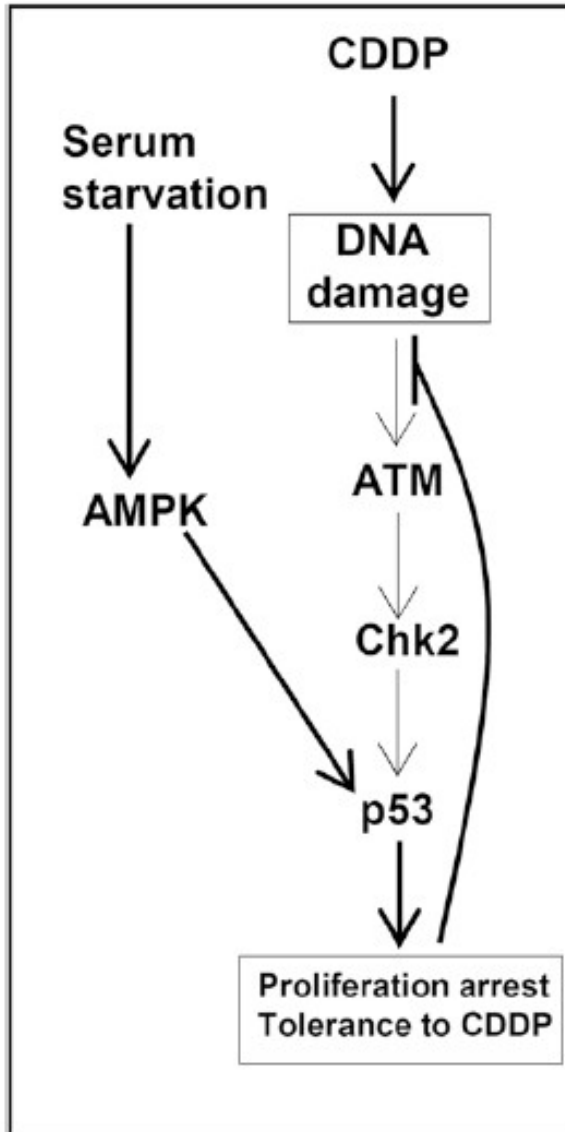




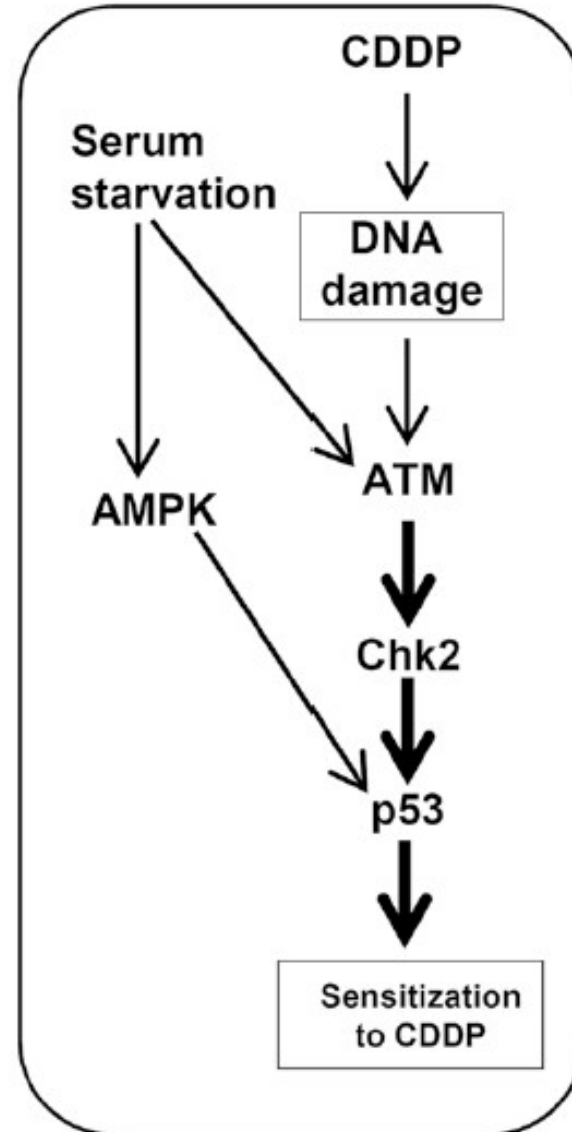
DSS: mesothelioma and pulmonary cancer xenografts CR



Normal cells



Cancer cells



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Études cliniques en cours

Ongoing short-term starvation studies

Norris NCT00936364 2009-2016 randomized: safety

Mayo NCT01175837 2010-2015 non-randomized: safety

Leiden NCT01304251 2011-2012 randomized: efficacy

Berlin NCT01954836 2013-2014 randomized: efficacy

Conclusions STS

- 1) Absence d'évidences pour le recommander
- 2) Rationnel scientifique intéressant
- 3) Nécessité recherche clinique

2008 Raffaghello, PNAS

Starvation-dependent differential stress resistance protects normal but not cancer cells against high-dose chemotherapy

2009 Safdie, Aging

Fasting and cancer treatment in humans: a case series report

2010 Longo, Trends Pharmacol Sci

Calorie restriction and cancer prevention: Metabolic and molecular mechanisms

2010 Lee, Cancer Res

Reduced levels of IGF-I mediate differential protection of normal and cancer cells in response to fasting and improve chemotherapeutic index

2010 Raffaghello, Cell Cycle

Fasting and differential chemotherapy protection in patients

2011 Lee, Oncogene

Fasting vs dietary restriction in cellular protection and cancer treatment: from model organisms to patients

2012 Lee, Sci Transl Med

Fasting cycles retard growth of tumors and sensitize a range of cancer cell types to chemotherapy

2012 Lee, Drug Resistance Update

Starvation, detoxification, and multidrug resistance in cancer therapy

2012 Safdie, PLoS One

Fasting Enhances the Response of Glioma to Chemo- and Radiotherapy

2013 Shi, BMC Cancer

Starvation-induced activation of ATM/Chk2/p53 signaling sensitizes cancer cells to cisplatin

2013 Champ, The Oncologist

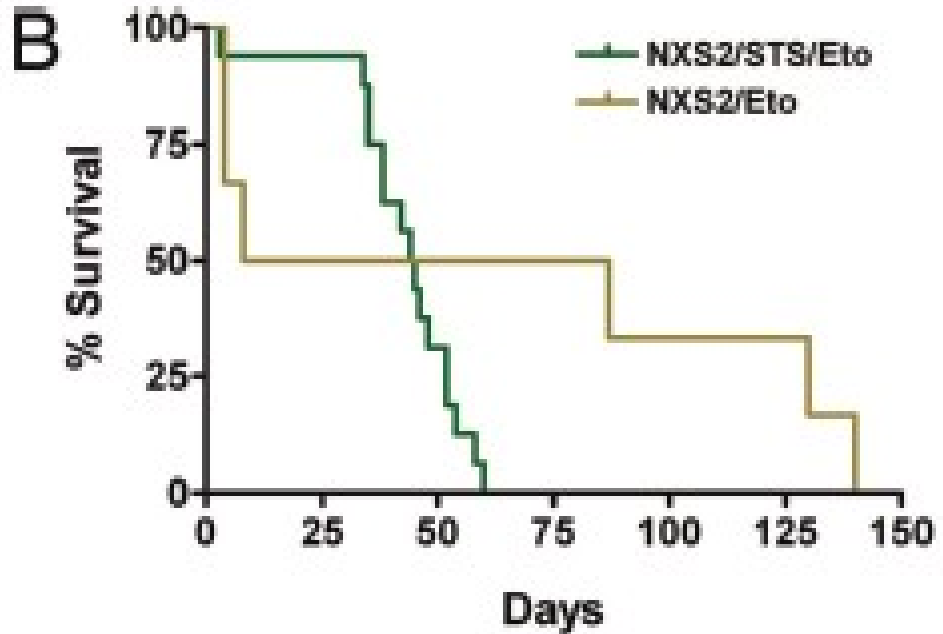
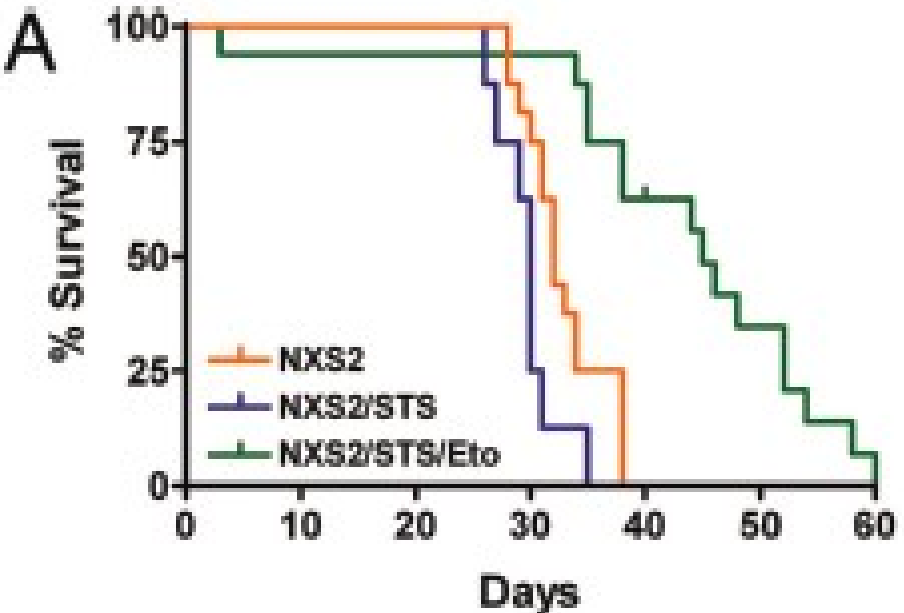
Nutrient restriction and radiation therapy for cancer treatment: when less is more

Conclusions STS

- 1) Technique qui peut protéger cellules saines et sensibiliser cellules tumorales à la chimiothérapie
- 2) Rôles axes IGF1/Akt/Ras et AMPK/ATM
- 3) Nécessité recherche clinique

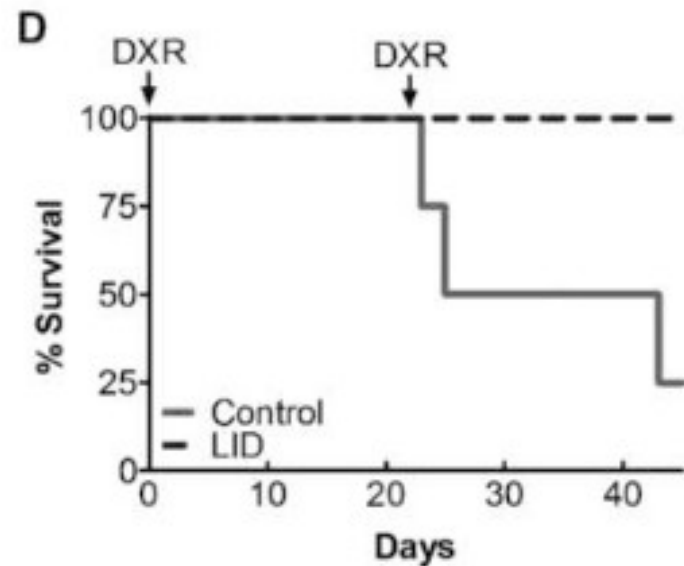
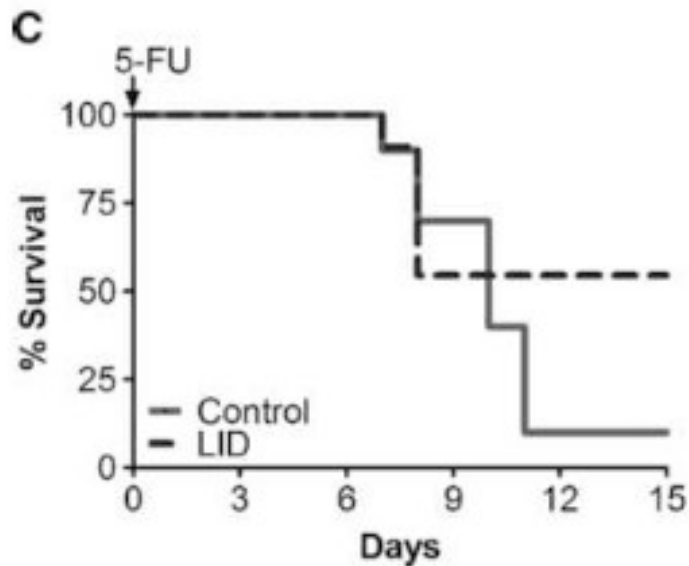
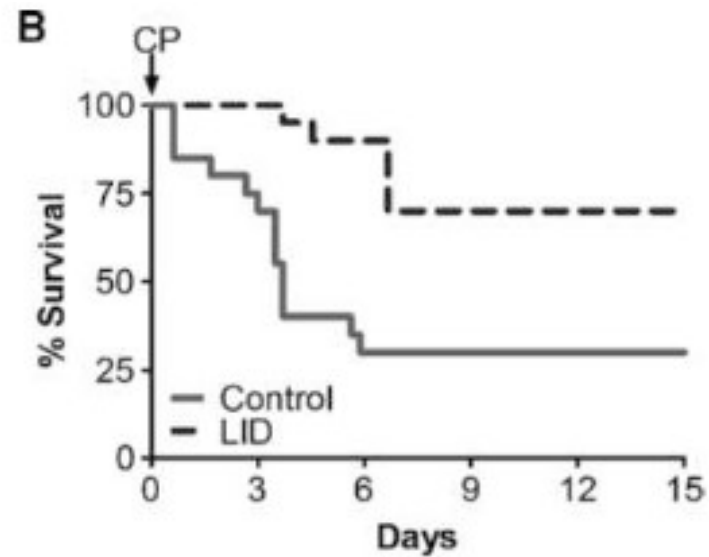
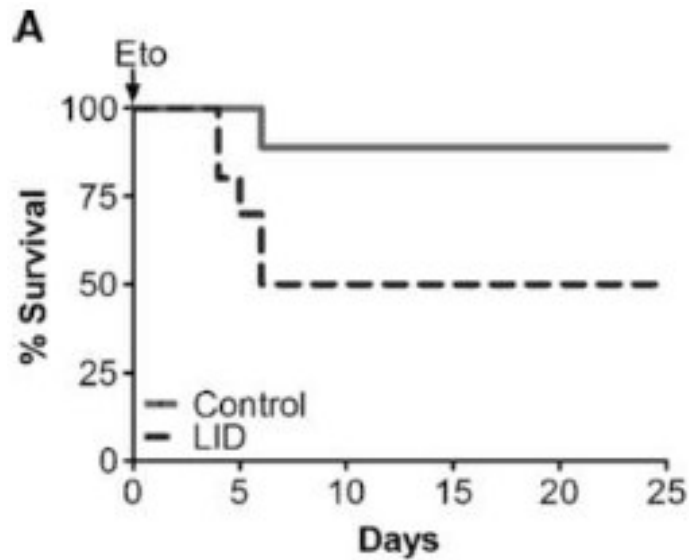
Is cancer protected by STS against chemotherapy?

Inoculated mice with neuroblastoma

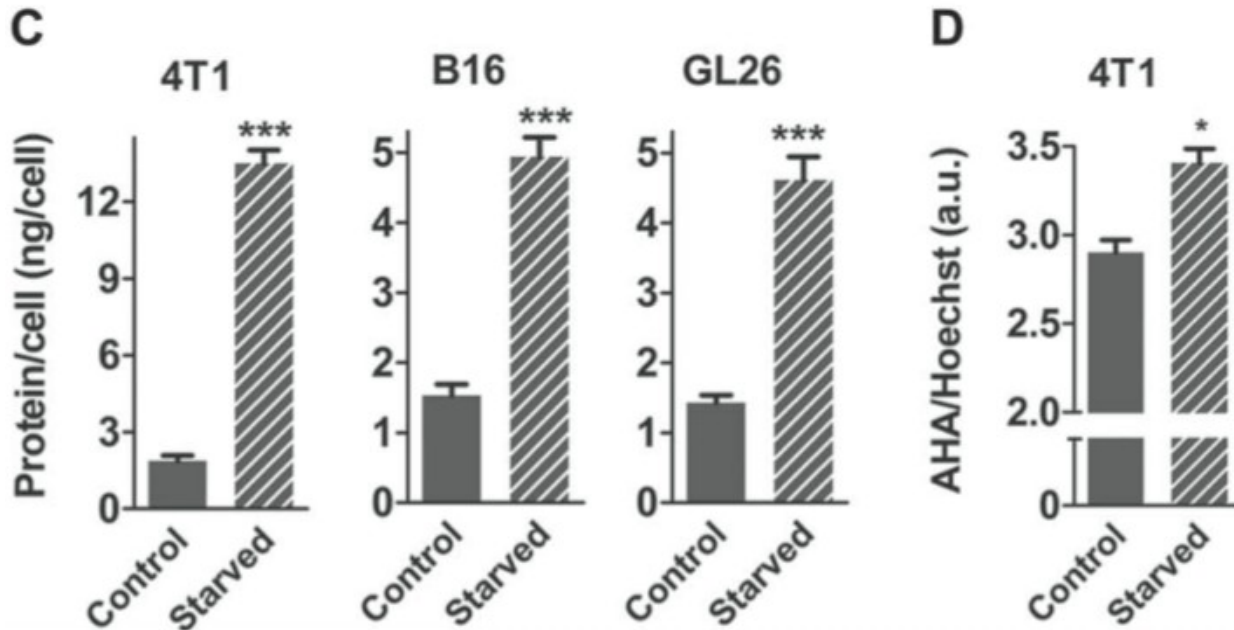
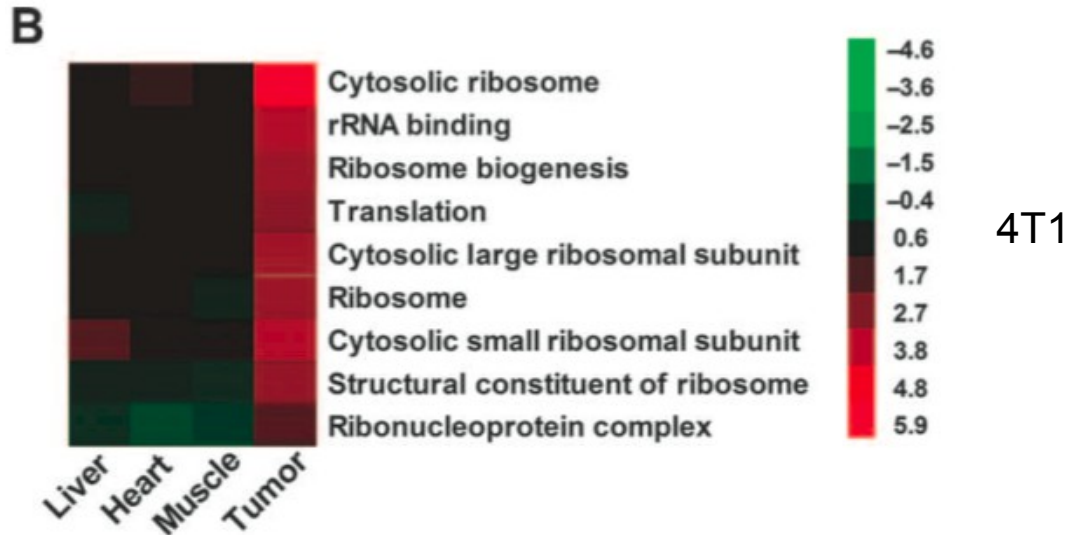


Are normal cells sensitized by STS to chemotherapy?

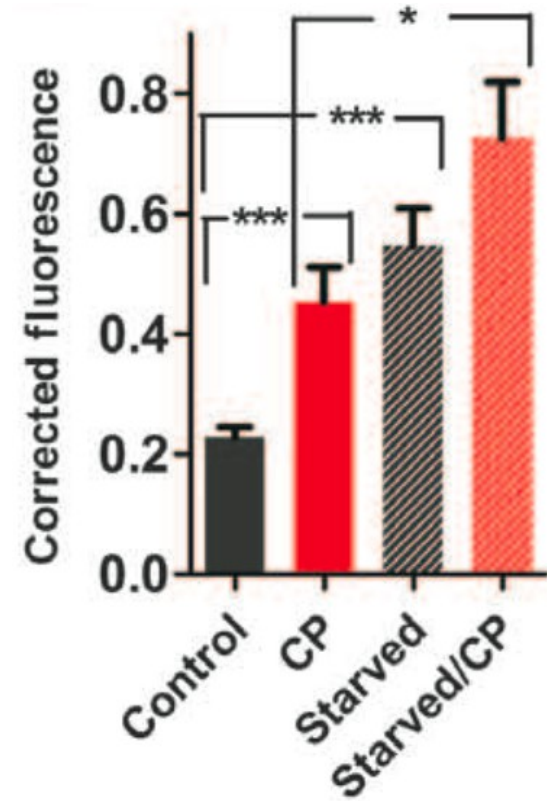
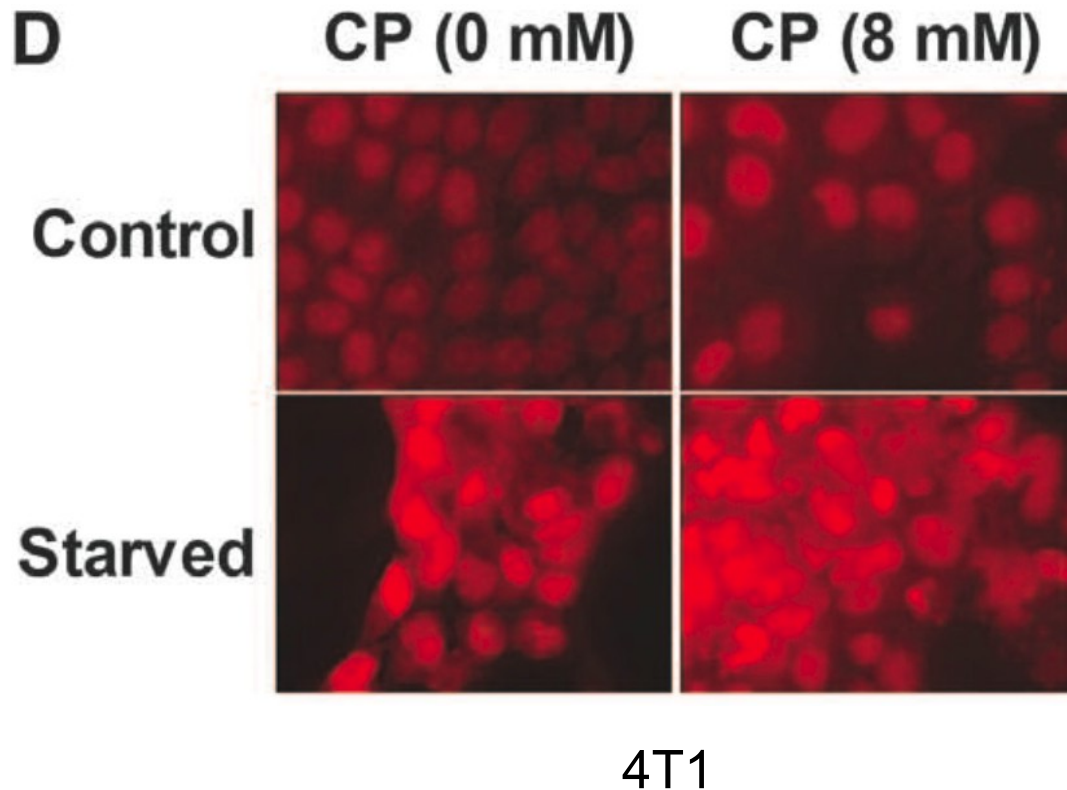
Chemotherapy in LID mice



DSS: translation role



DSS: reactive oxygen species role



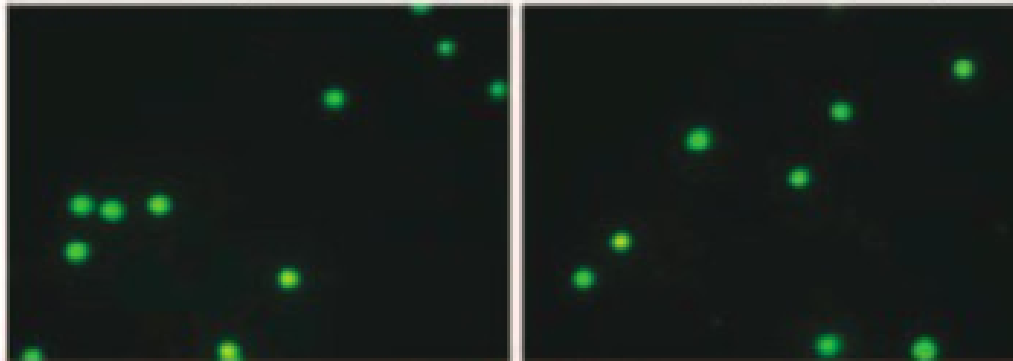
DSS: DNA damage role

B

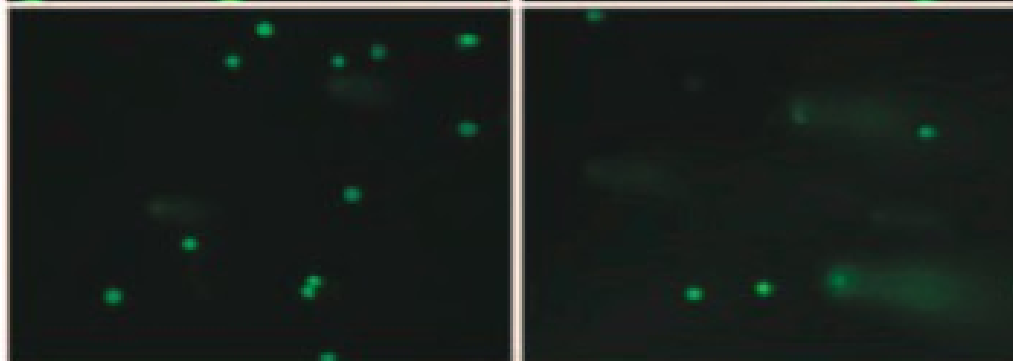
DXR (0 mM)

DXR (1 μ M)

Control



Starved



B16

