Medical Nutrition on Cancer Research and Therapy

University of Southern California

Nimni and Cordoba Tissue Engineering and Drug Discovery Lab

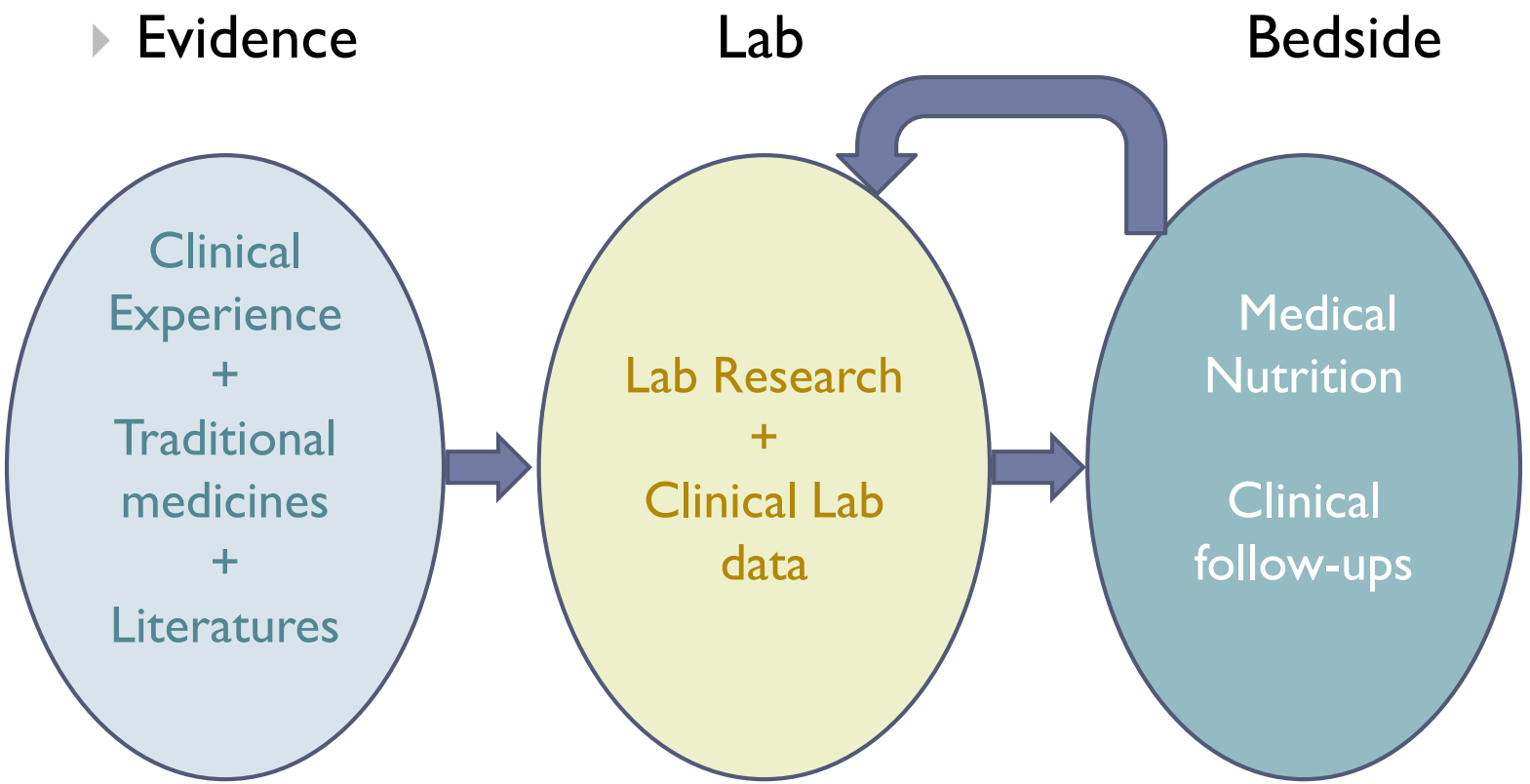
Our Hypothesis

- **FACTs**
  - Cancer is a metabolism diseases
  - Cancer microenvironment suppresses immune functions

- **Hypothesis**
  - Reprogramming cancer cell metabolism will enable cancer cells to re-differentiate with reduced growth rate and to be recognizable by immune cells

Our Strength

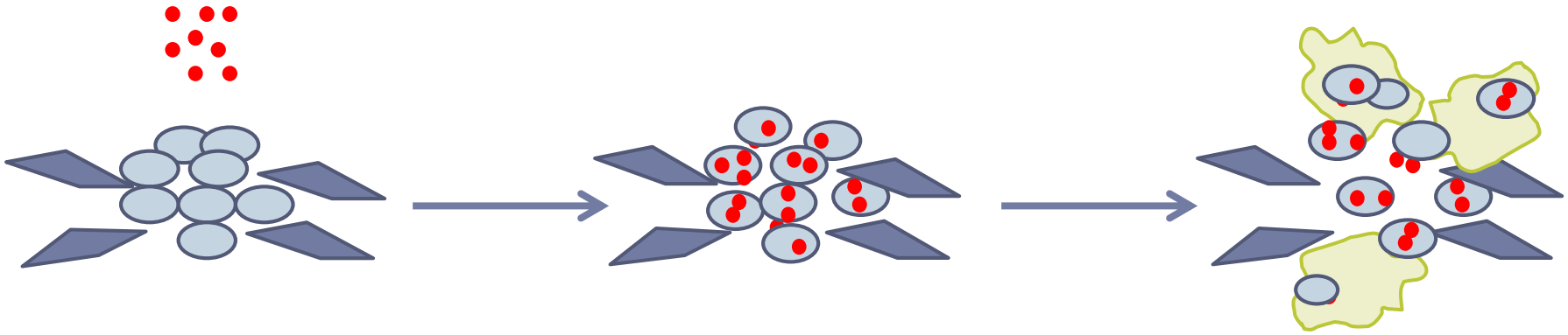
- Evidence-based and integrative
  - Combine clinical outcomes and lab research



Our Approach

- Models:
  - 3D culture system to reflect tumor heterogeneity and metabolite accumulation
  - Co-culture (with stromal, macrophage, NK cells) to reflect tumor and environmental cells interactions
- Reagents: chemical and nanoparticles forms of
  - Trace metals
  - Phytochemicals
  - Small molecules

Patented Technology



Highly proliferative tumor cells take ZCM complexes into cell passively with other cellular fuels

ZCM induces cellular metabolism reprogramming
- Alter cell morphology and membrane potential
- Alter Microenvironment

Re-activate microenvironment-suppressed innate immune functions
- NK cells
- macrophages M2

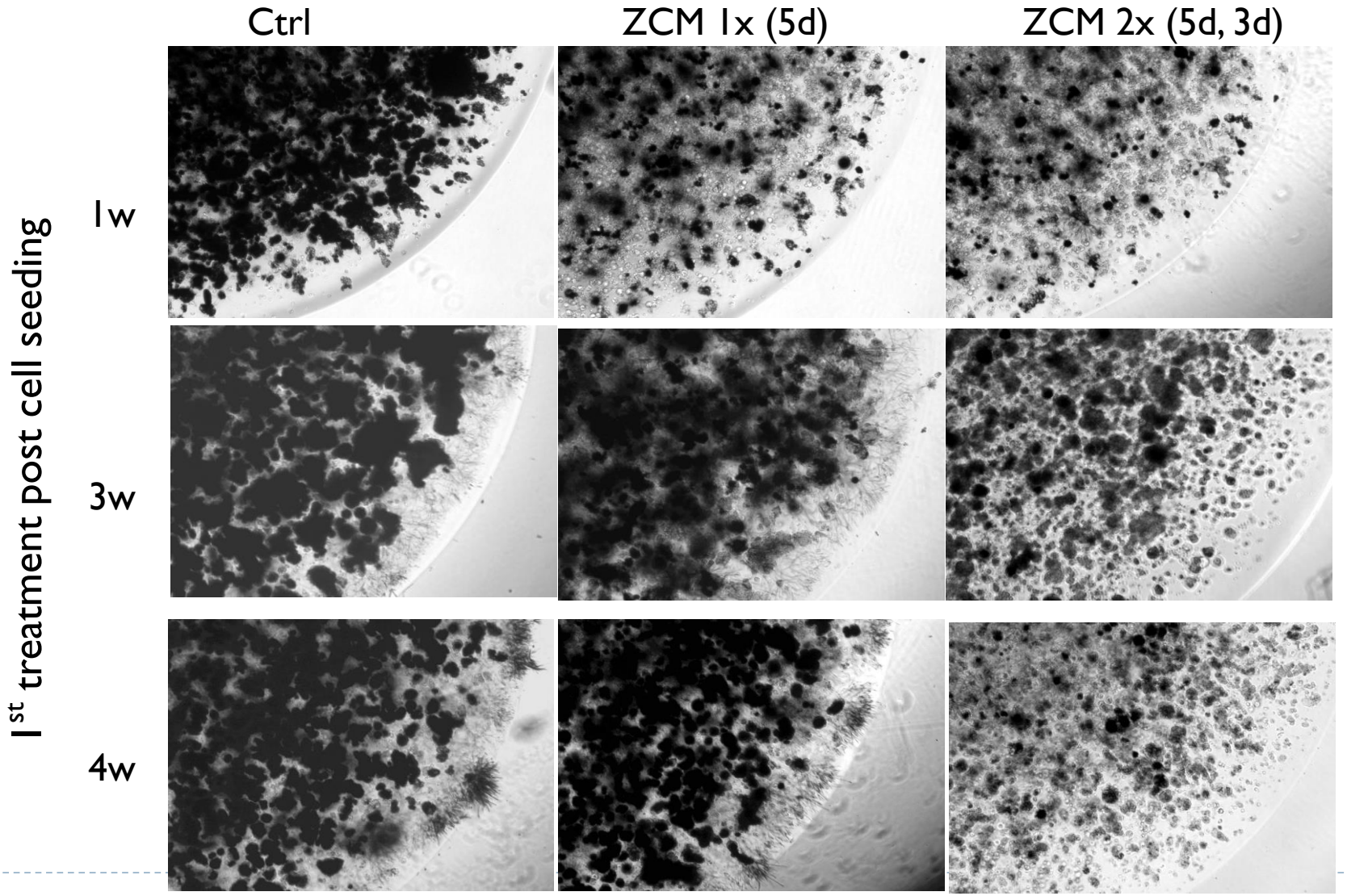
Technology highlights

Uptake

Metabolism reprogramming

Immune Function

ZCM Interrupts tomoroids



ZCM changes tumor cell mitochondrial membrane potential

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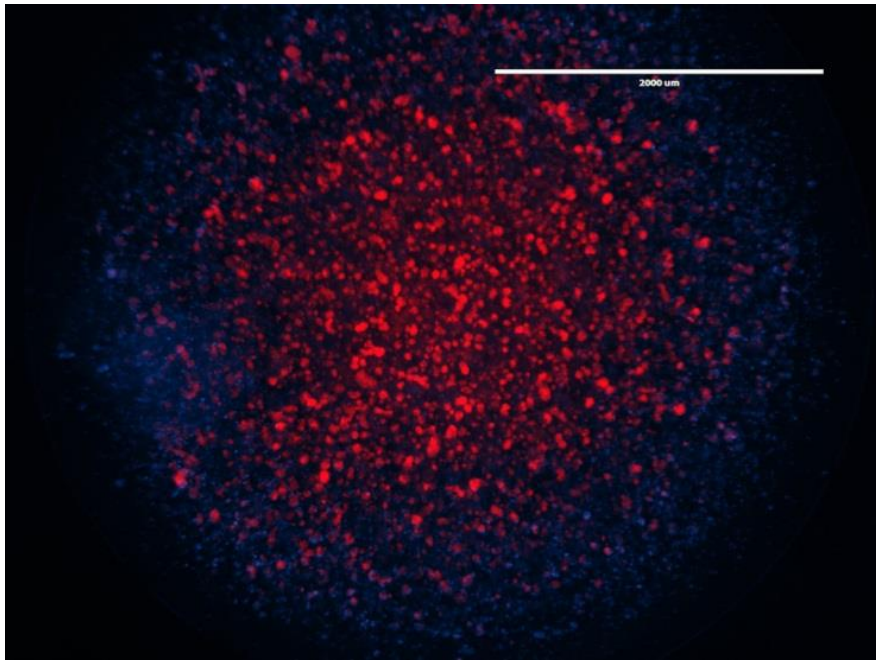
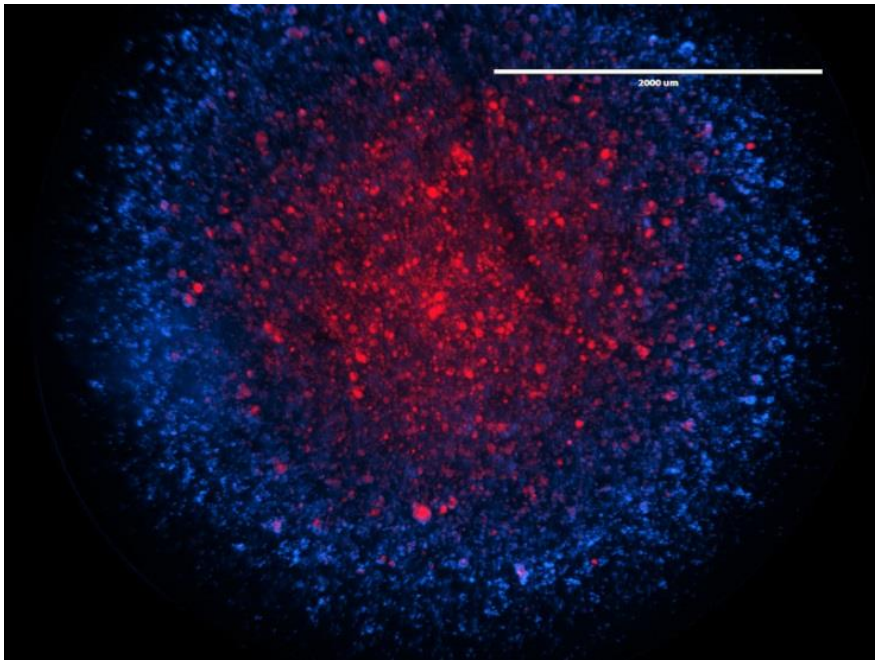


Hyperpolarized

ZCM treated



Less polarized

Rhodamine 123 (Red)
with Hoest 33342 (Blue)

ZCM Inhibits efflux pumps

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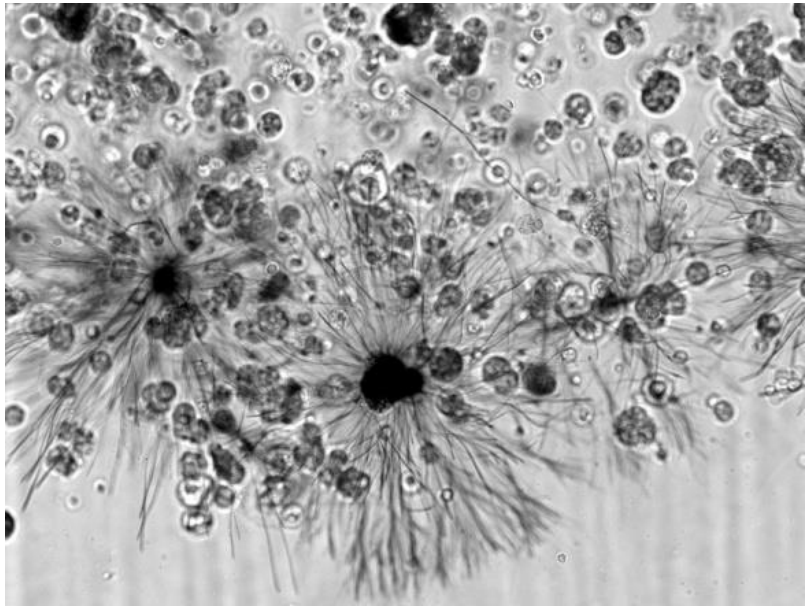
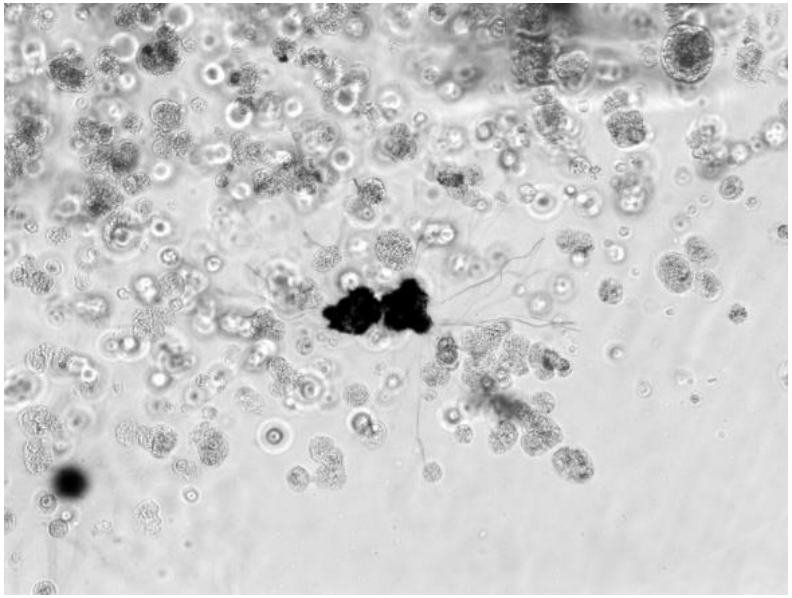


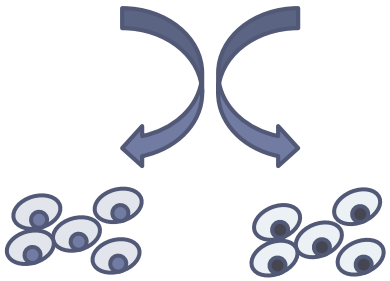
ZCM



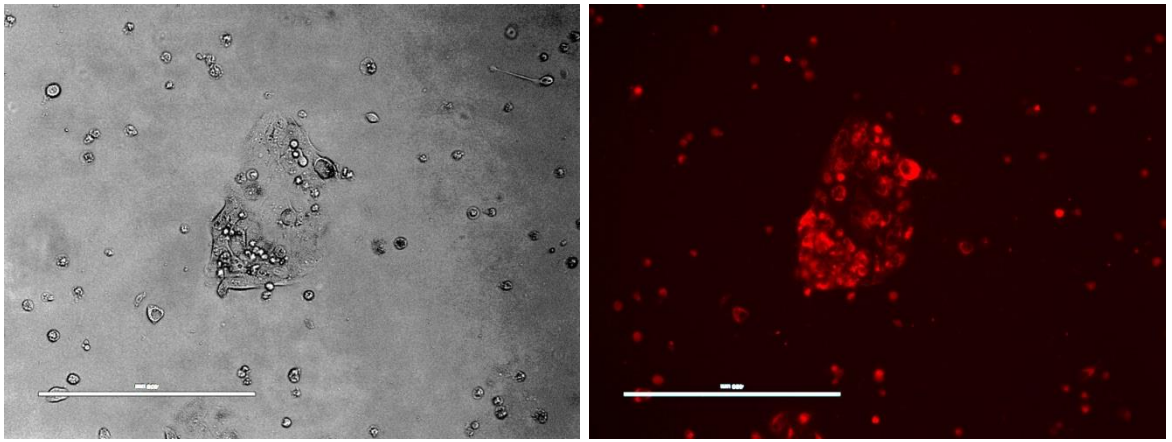
MTT staining, 18h

ZCM treated cells activate macrophage phagocytosis

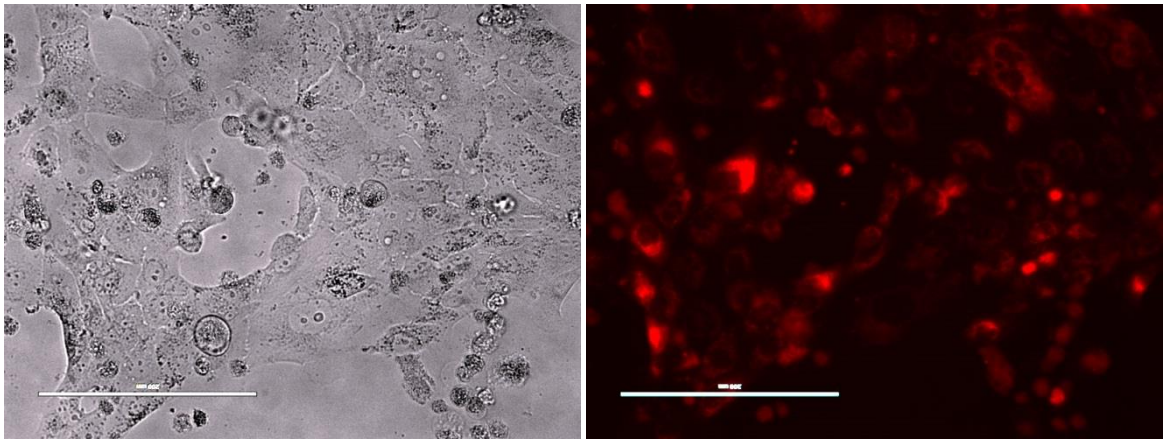
monocytes



-ZCM



+ZCM



Prove Efficacy in animal models

- ZCM reduces established tumor sizes in nude mice xenograft models

- Animal body weight didn't change in the course of treatment compared with animals treated with conventional chemo drugs

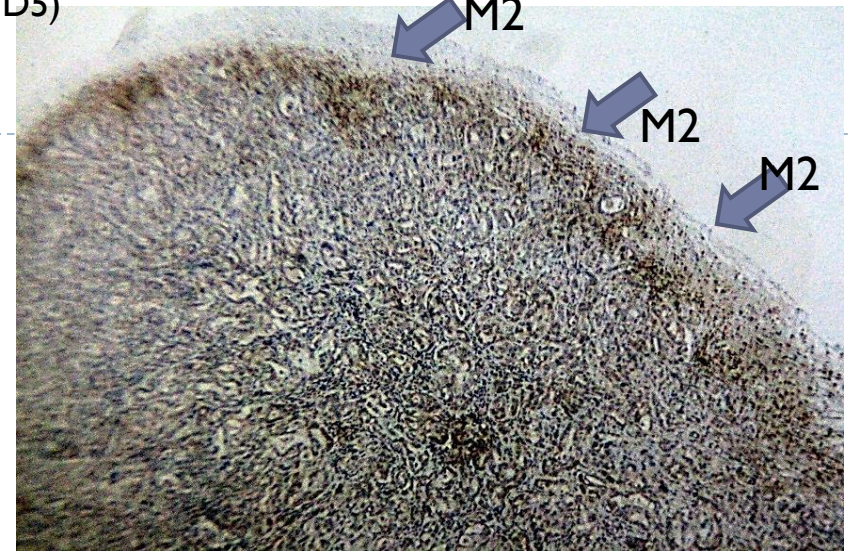
- Histology showed that microphage M2 cells invaded tumors from both outside through neighboring tissues and from intra-tumoral blood vessels through circulation

- Microphage M2 cleared the tumor cells by phagocytosis without inflammation reaction

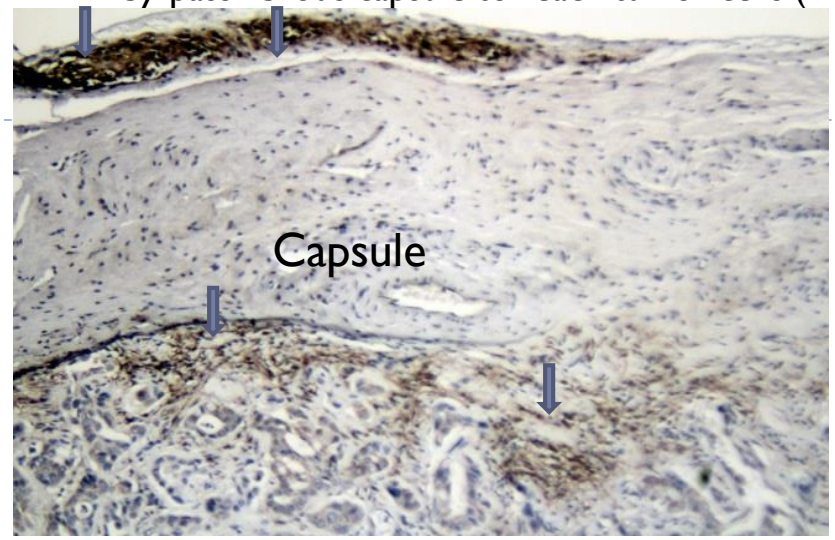
- Chemo drug Gemcitabine treated fresh normal tissue attracts significant inflammation reaction and involve both M1 and M2 reactions.

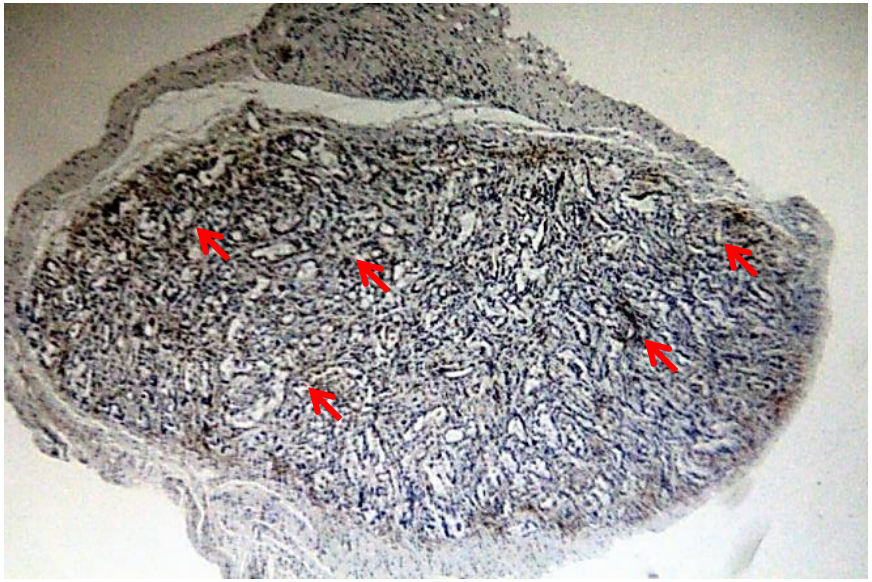
- We speculate NK cells cytolysis tumor cells

M2 cells clear Zn-SA treated tumor from periphery area (TD5)

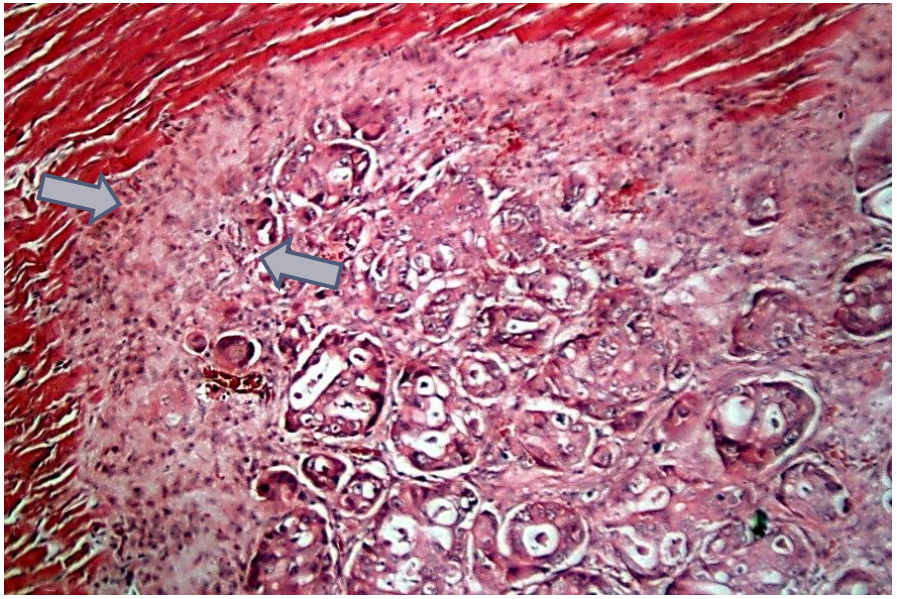


M2 accumulate at tumor periphery
M2 by-pass fibrous capsule to reach tumor cells (TD14)



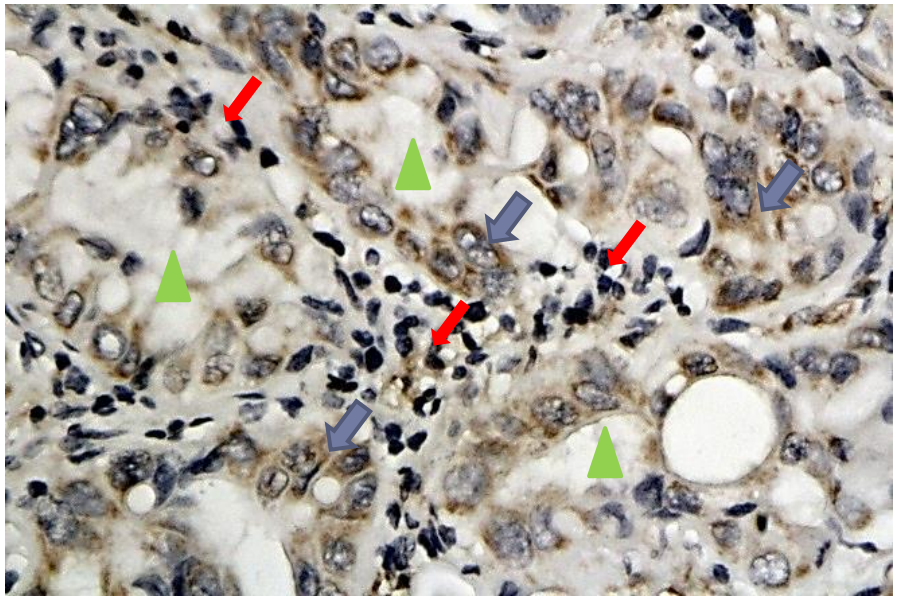


M2 cells clear tumor intra-tumorally through circulation

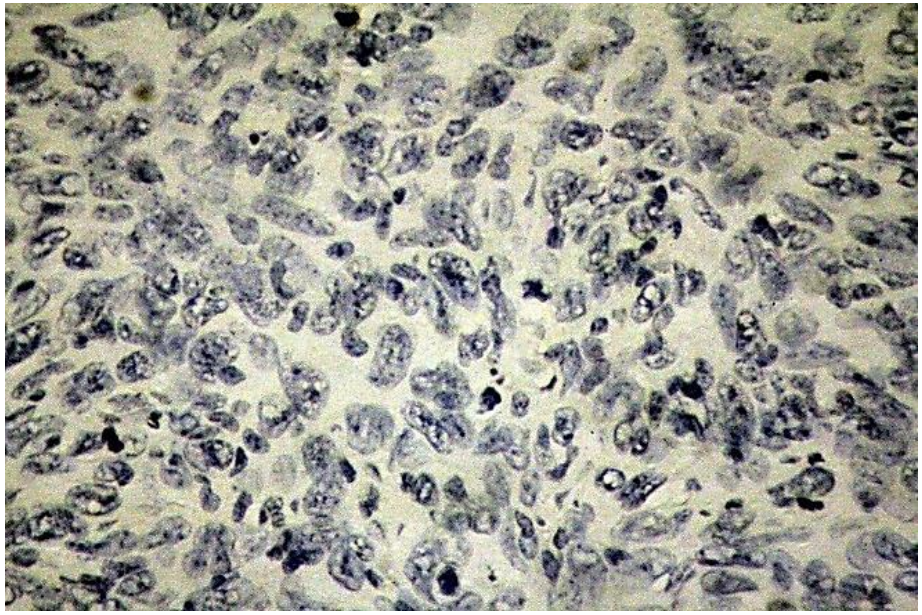


Forming a cancer-free-zone by M2 phagocytosis

Close look of ZCM -M2 treated tumor in animal models



ZCM treated tumor



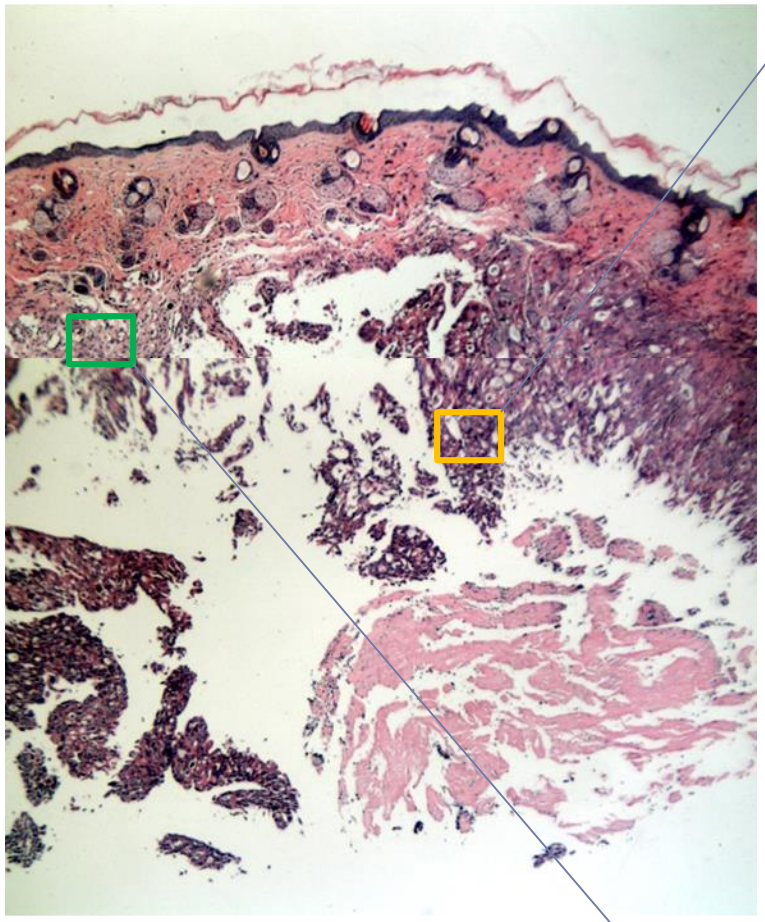
Non –treated tumor

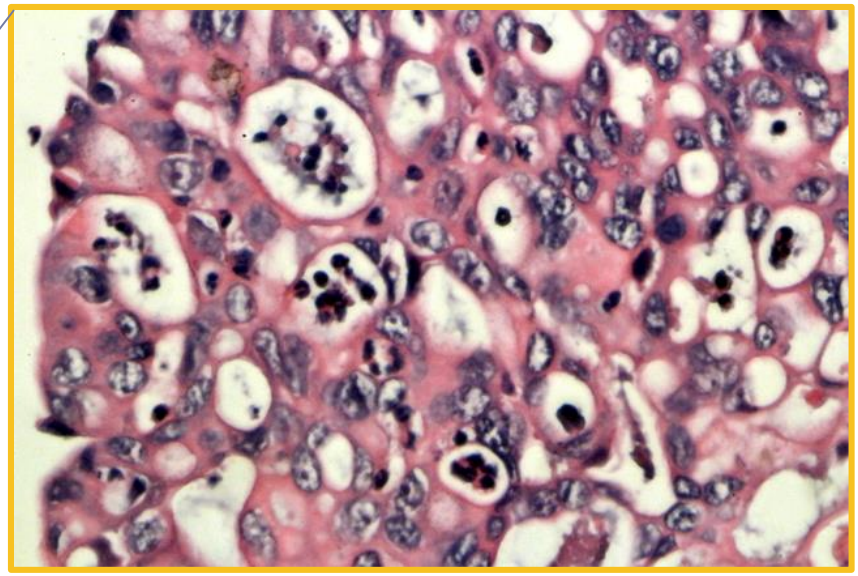
Microphage M2

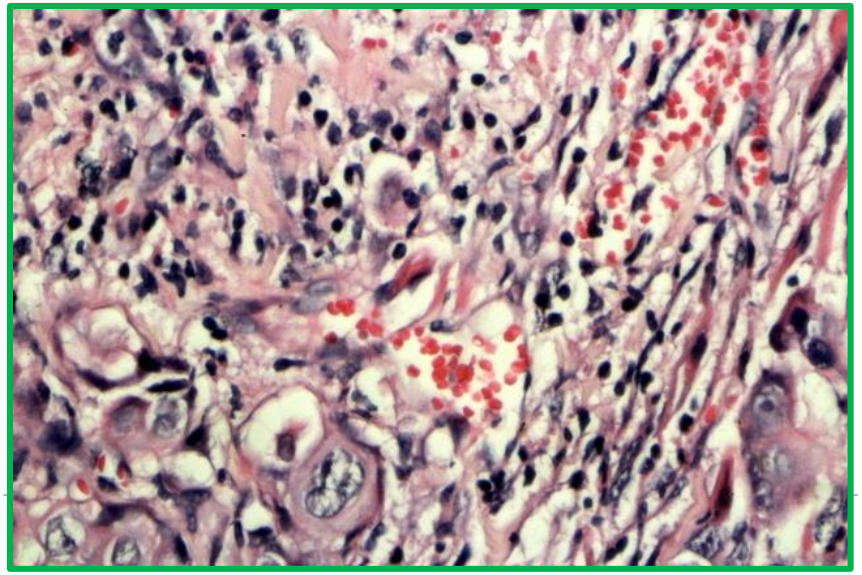
ZCM treated tumor cells

M2 cleared area

Treat established pancreatic (CFPAC) tumor (>500mm^3) for 60 days

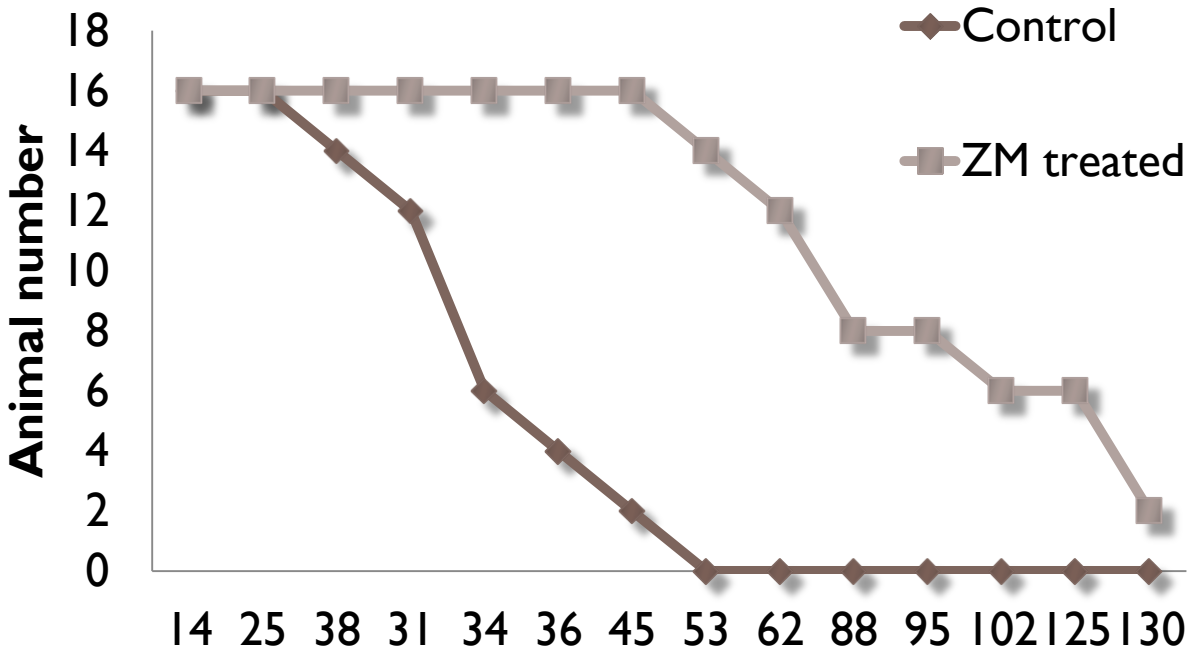






ZCM eradicates tumor

Overall animal survival on ZCM treatment

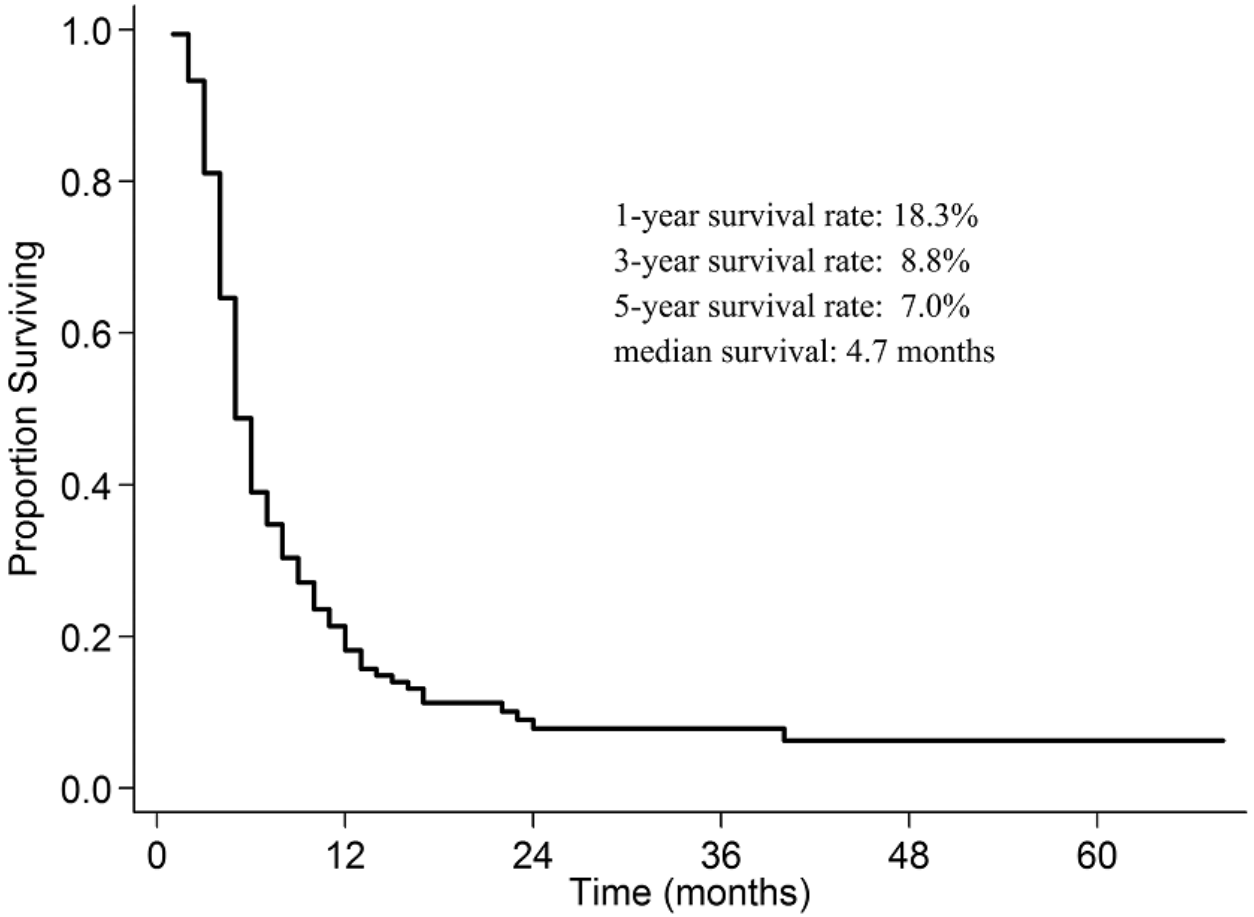


- Athymic nude mouse model, SubQ injection 2x 10^6 CFPAC per site, Bilateral
- Animal started to receive garage ZCM treatment on day 14 when tumor was established
- Animal health and overall survival rate were monitored

Clinical observations

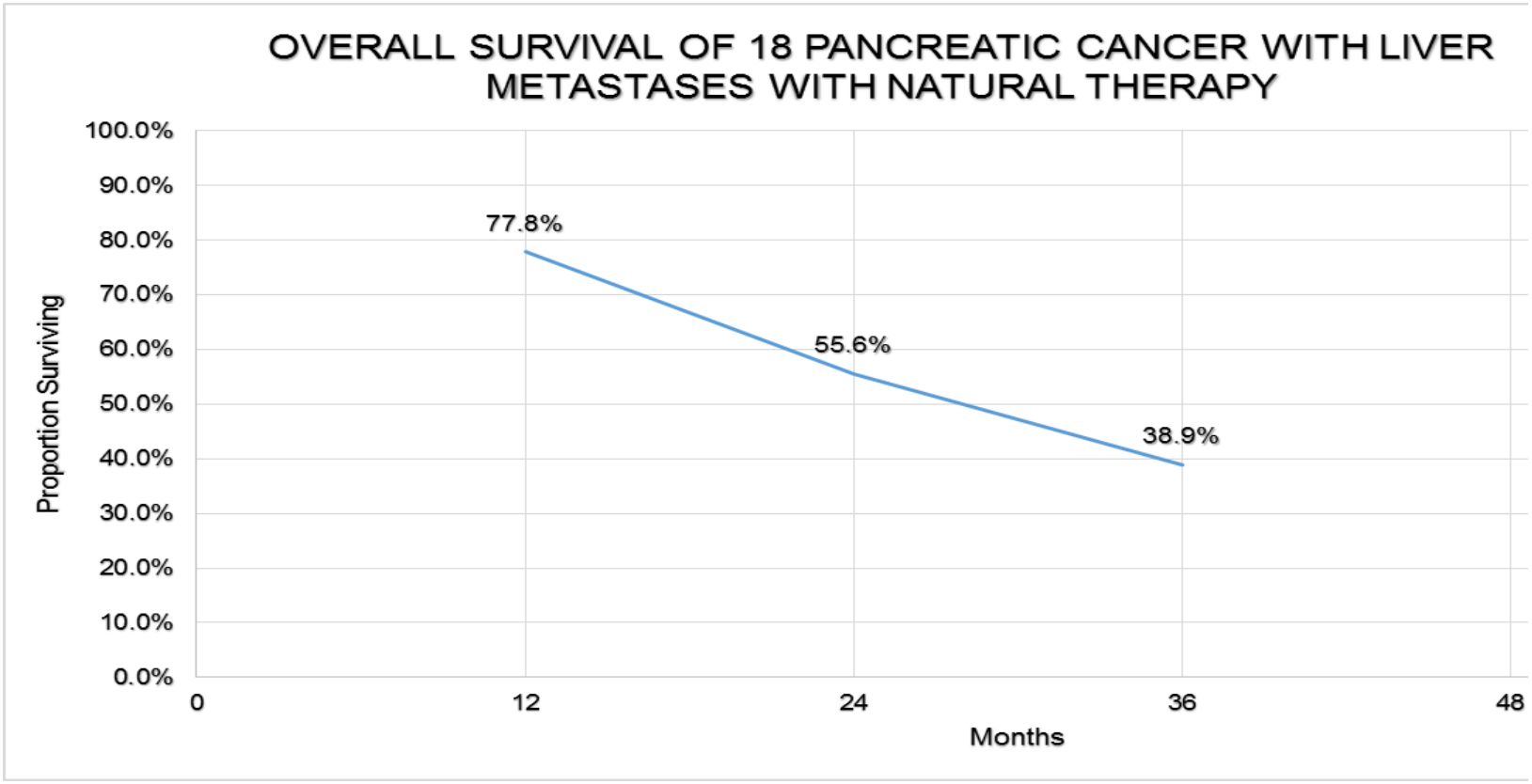
- Many terminal stage cancer patients in Vietnam and Belarus received medical nutrition as adjuvant therapy
- Cancer related pain, cachexia, cough, fever and anxiety were well controlled
- Patient survival rate significantly prolonged
- For example, 18 pancreatic cancer patients, receiving medical nutrition 3 year survival rate is 38.9% compared to 8.8% with multimodality treatments

Pancreatic cancer with liver metastases (PCLM)



Ouyang et al., Pancreas, 2011, 40(1): 120-125

Combinational treatment of PCLM with supplements containing ZCM



Clinical study in progression

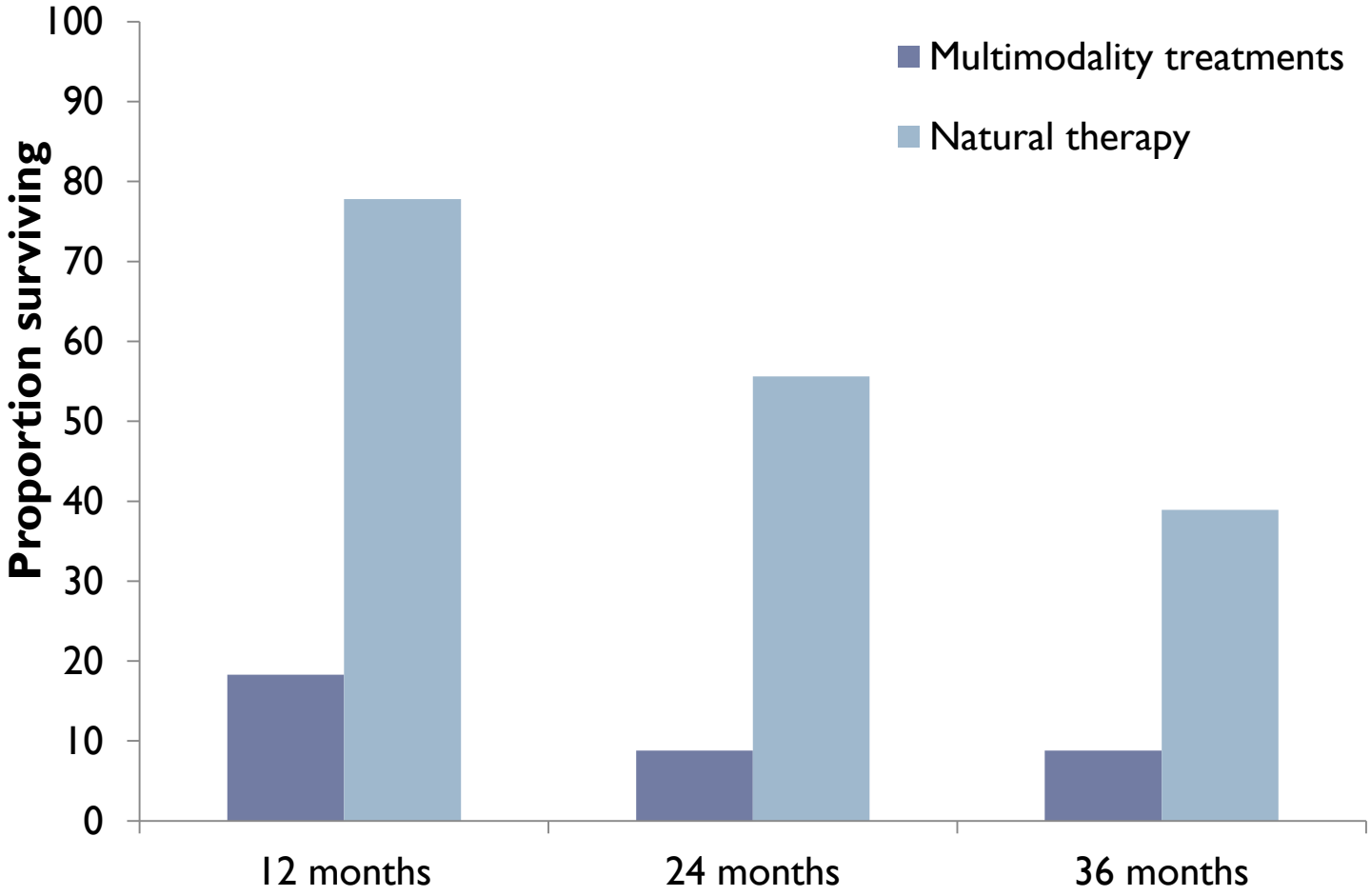
By Ba Hoang, Bo Han, Marcel Nimni
Cancer Center, Hanoi
University of Southern California

Note:

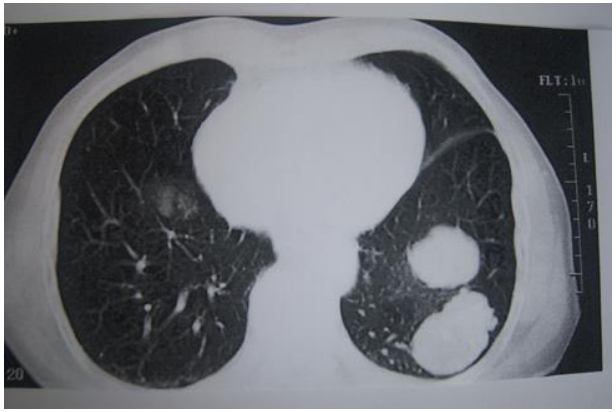
1 Years survival rate : 14/18 ≈ 77.8%
2 Years survival rate : 10/18 ≈ 55.6%
3 Years survival rate : 7/18 ≈ 38.9%

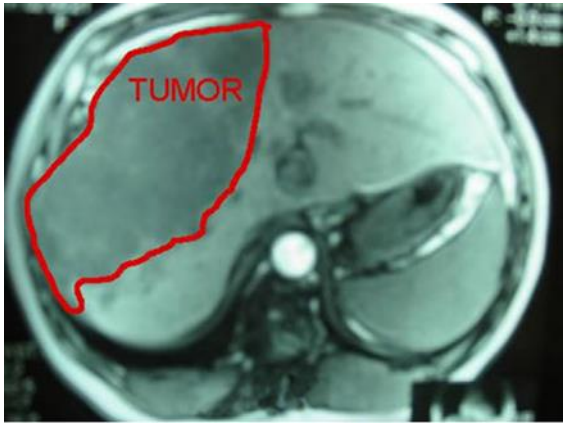
Median survival 14.6 months (36 months followed-up)

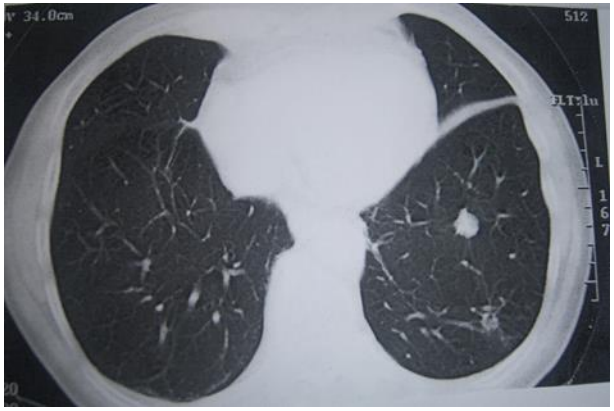
Comparative plot of multimodality treatments vs natural therapy

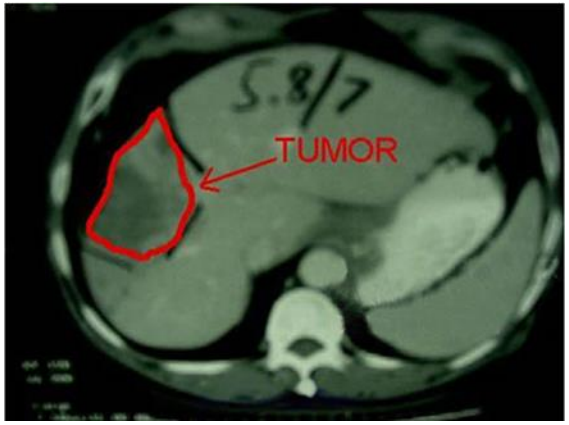


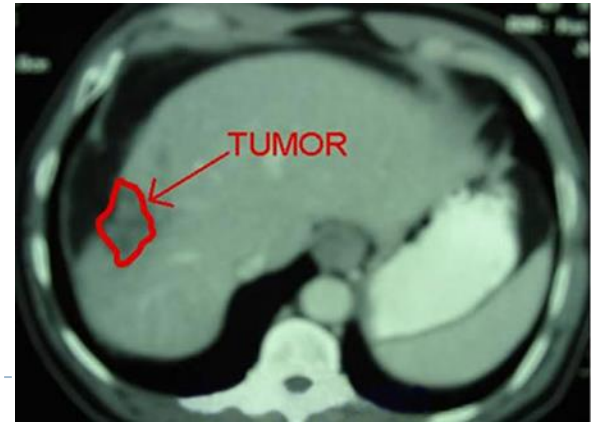
Other cases









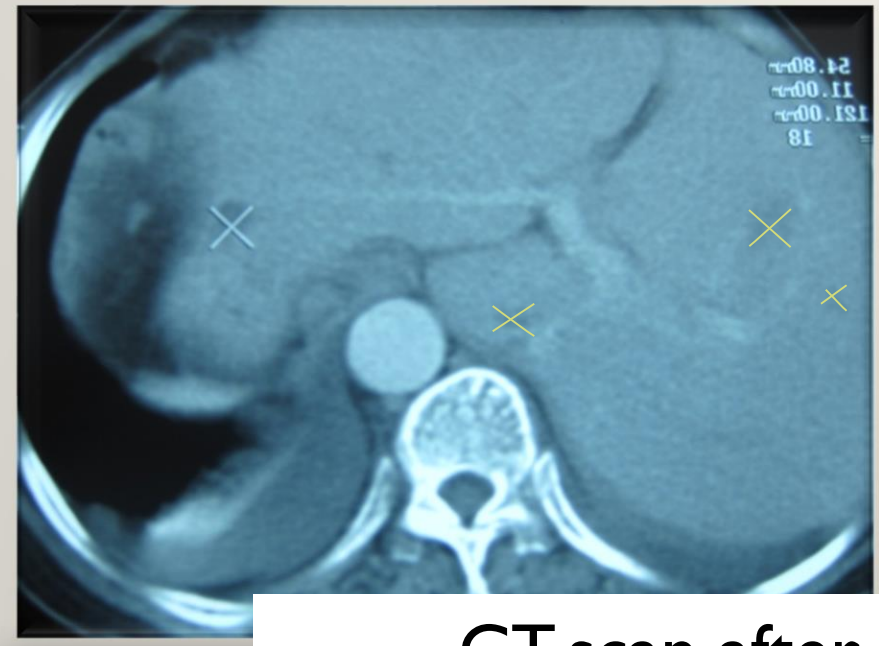


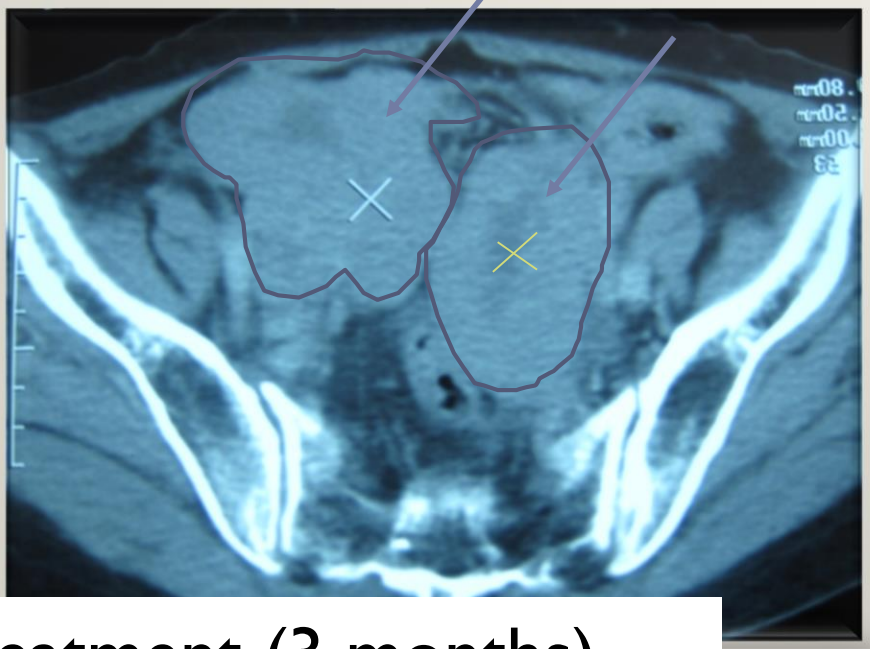
Topical treatment

Before ZCM treament

3 months with treatment of ZCM

CT-scan before treatment





CT-scan after treatment (3 months)