高雄醫學大學附設中和紀念醫院
Kaohsiung Medical University Chung-Ho Memorial Hospital

院級研究型主治醫師如何協助本院醫師提升研究能量

袁行修

104年9月24日

醫研部組織成員

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行政院衛生署第二期(103-106年)癌症研究計畫
申請書

計畫名稱: 以改善患者存活及生活品質為中心思考的整合性癌症轉譯研究

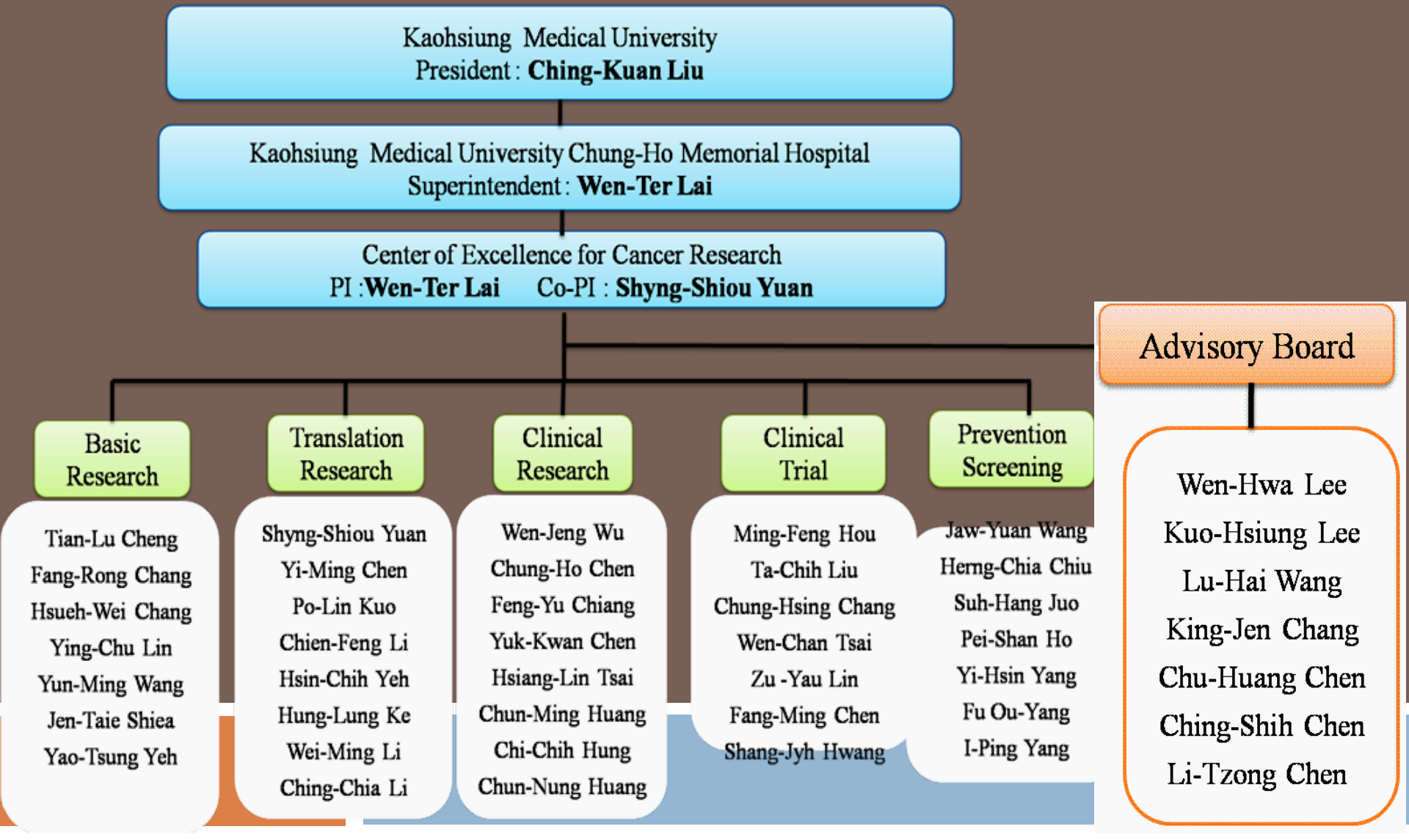
Integrated cancer translational research focused on the improvement of patient survival and life quality

申請機構: 財團法人私立高雄醫學大學附設中和紀念醫院
Kaohsiung Medical University Hospital, Kaohsiung Medical University

計畫主持人(PI): 賴文德 Wen-Ter Lai
協同主持人(CO-PI): 袁行修Shyng-Shiou Yuan
協同/分項計畫主持人(Program 1): 陳中和 Chung-Ho Chen
協同/分項計畫主持人(Program 2): 侯明鋒 Ming-Feng Hou
協同/分項計畫主持人(Program 3): 王照元 Jaw-Yuan Wang
協同/分項計畫主持人(Program 4): 吳文正 Wen-Jeng Wu

Organization Chart of the Cancer Research Project

Teaching | Research | Service

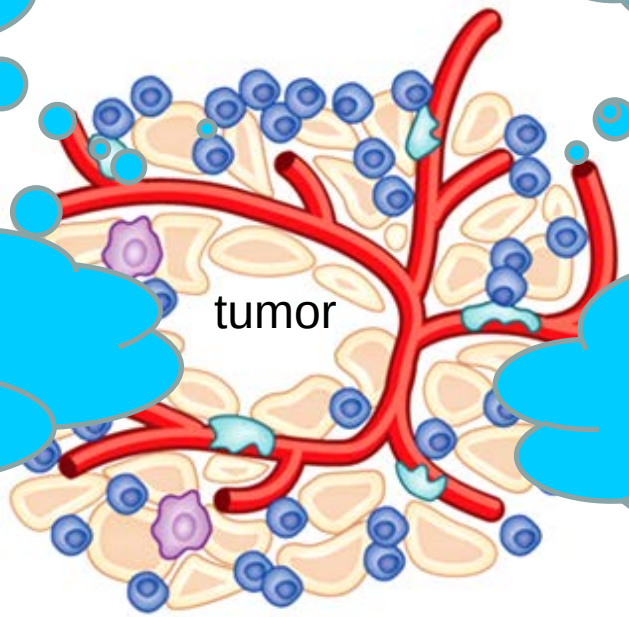


Research Directions

- Therapeutic anti-cancer drugs
- Mechanistic study of cancers

DNA repair proteins
(MRE11, RAD50, NBS1, RAD51...)

Adipocytokines
(resistin, visfatin, adiponectin, leptin, omentin...)
Bioactive lipids



Cancer stem cells
Adipose-derived stem cells
(breast)

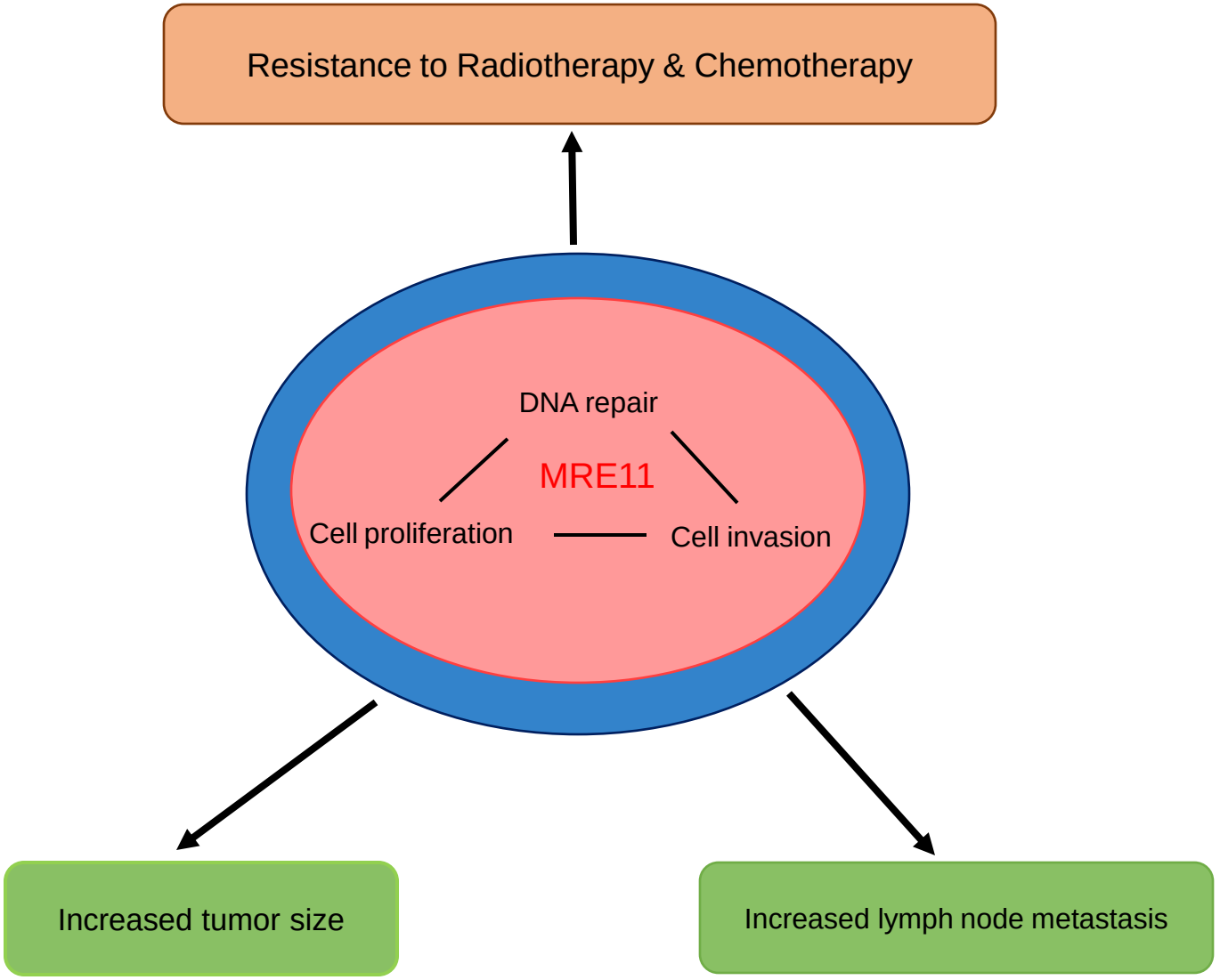
Anti-cancer compounds
- Natural products
- Synthetic compounds
(WYCs, CYT-Rxs...)

Tumor microenvironment

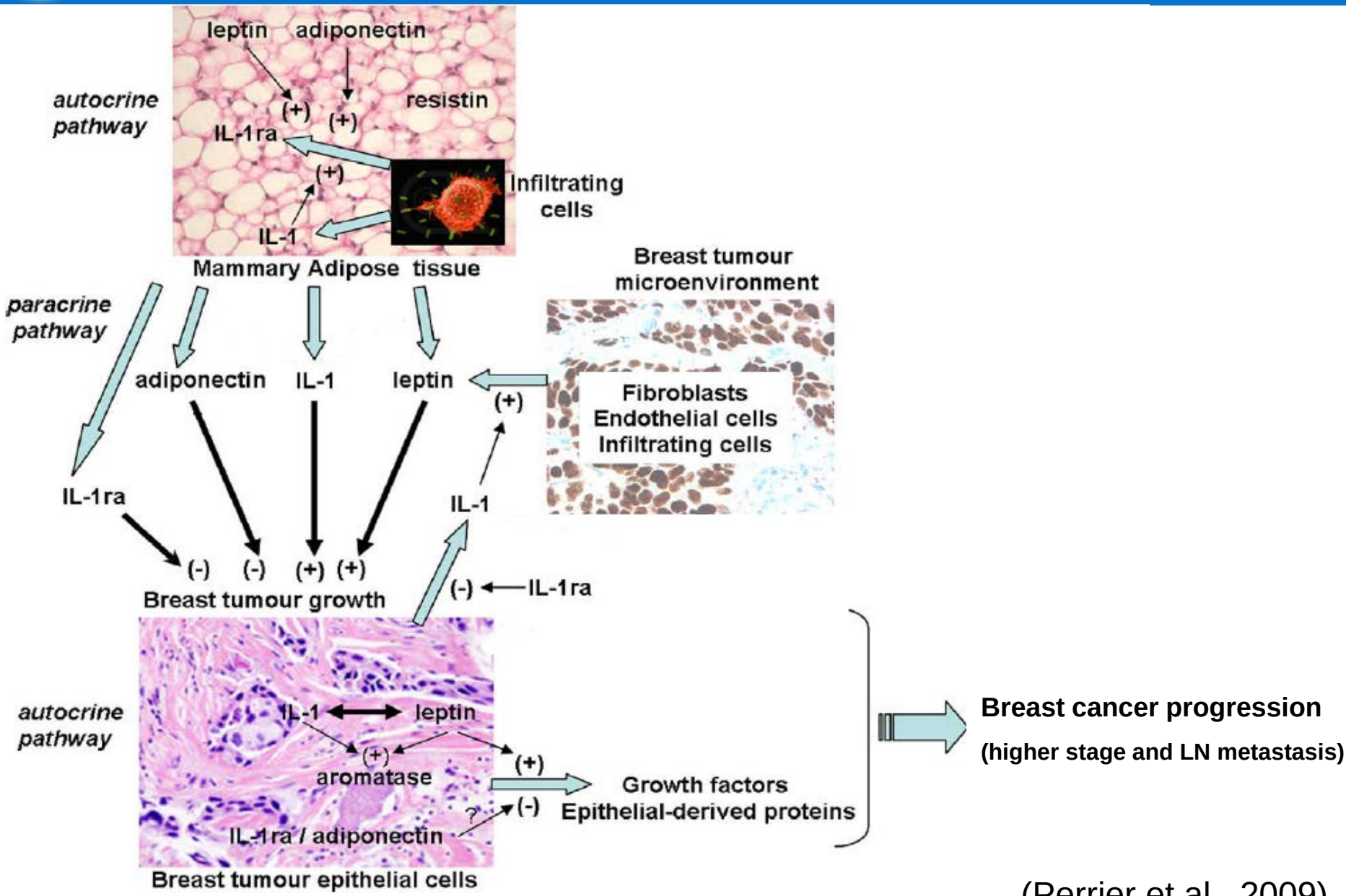
Nanomedicine for imaging and treatment

Joint projects with colleagues

- Resistin作為食道癌預後因子的研究
- Rad51作為食道癌預後因子的研究
- 基質金屬蛋白酵素(MMPs)與Nrf2的交互作用在原發型自發性氣胸探討及影響
- 肺癌幹細胞轉移的轉譯應用
- MRE11蛋白調控肺癌細胞生長之作用機轉
- Id 蛋白在肺癌調控上扮演重要角色


Resistance to Radiotherapy & Chemotherapy
DNA repair
MRE11
Cell proliferation
Cell invasion
Increased tumor size
Increased lymph node metastasis

Adipocytokines and Breast Cancer Progression



(Perrier et al., 2009)

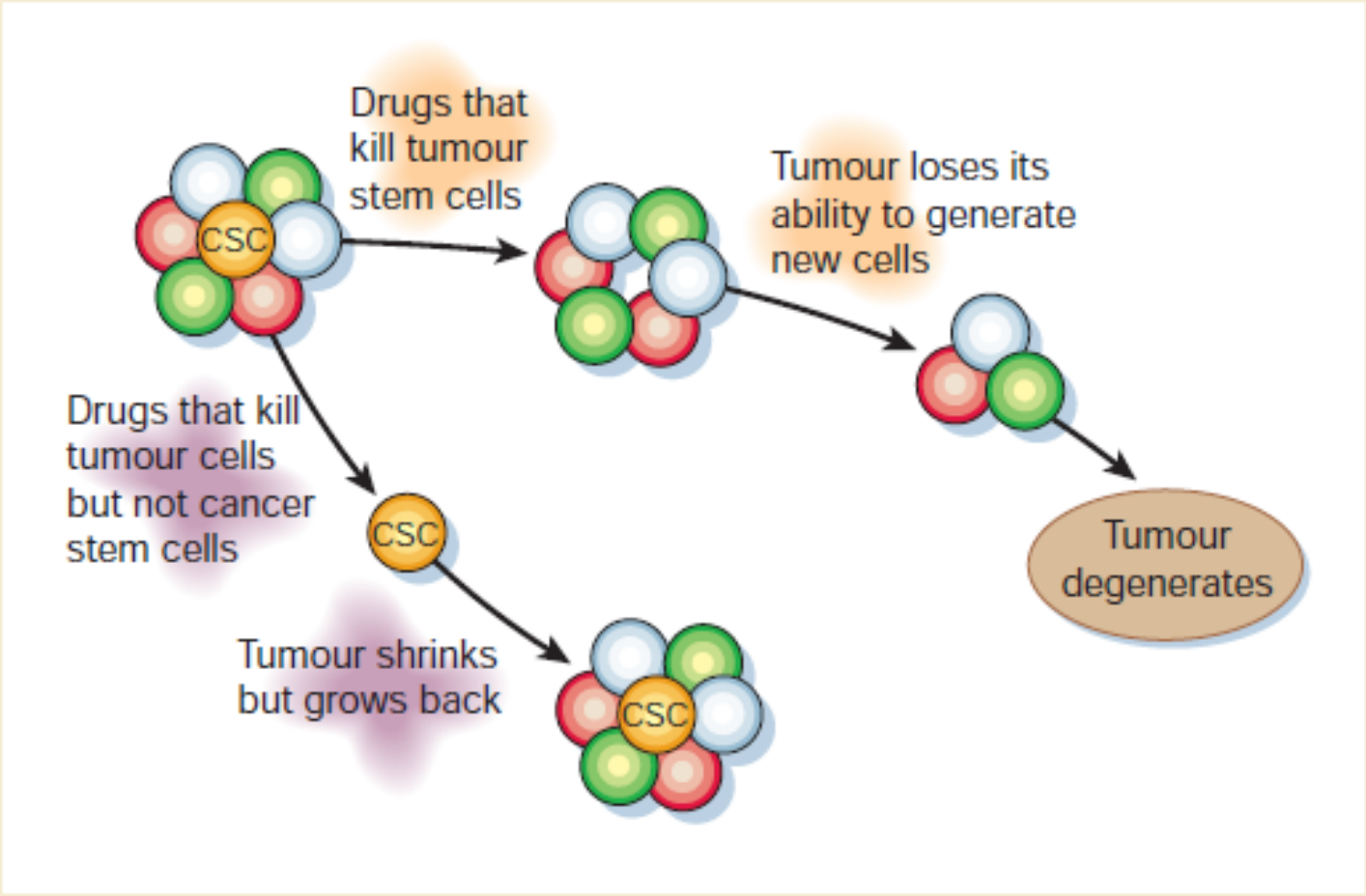
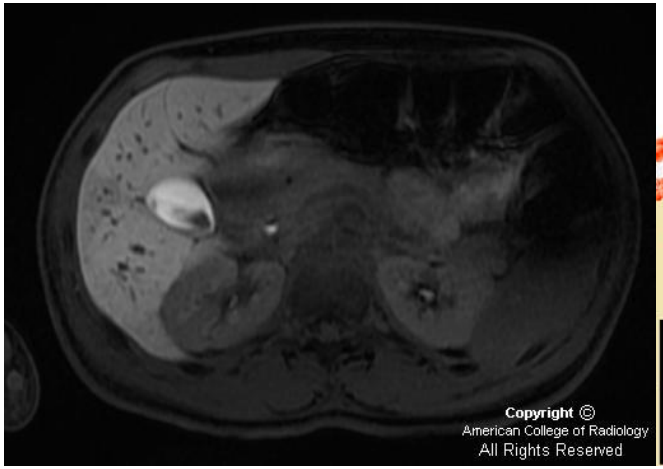
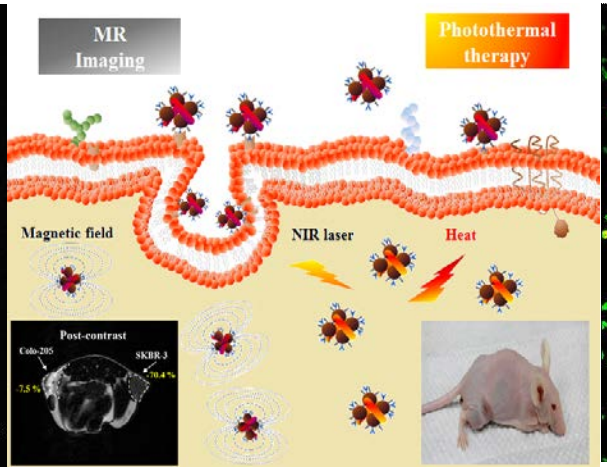


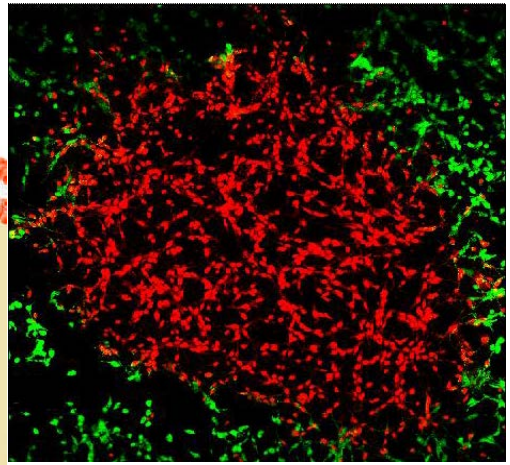
Figure 5 Conventional therapies may shrink tumours by killing mainly cells with limited proliferative potential. If the putative cancer stem cells are less sensitive to these therapies, then they will remain viable after therapy and re-establish the tumour. By contrast, if therapies can be targeted against cancer stem cells, then they might more effectively kill the cancer stem cells, rendering the tumours unable to maintain themselves or grow. Thus, even if cancer stem cell-directed therapies do not shrink tumours initially, they may eventually lead to cures.

(Reya et al., 2001)

Dual Functional AuNRs@MnMEIOs Nanoclusters for MR Imaging and Photothermal Therapy

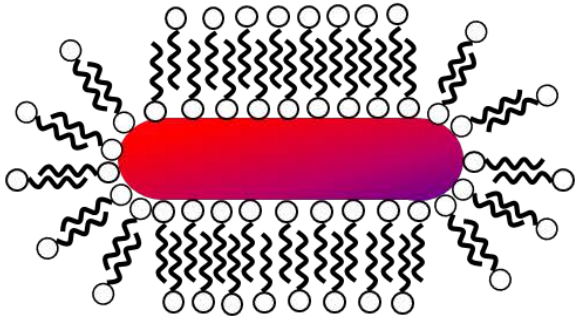




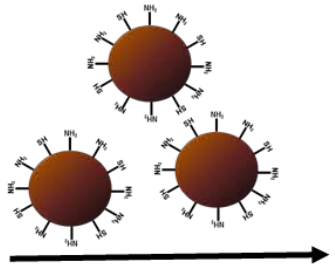


Biomaterials 2014, (Accepted)

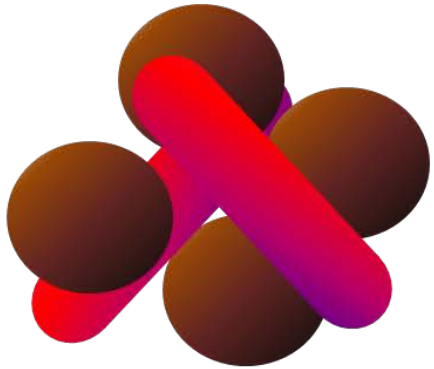
AuNRs@MnMEIOs nanoclusters



CTAB-AuNRs

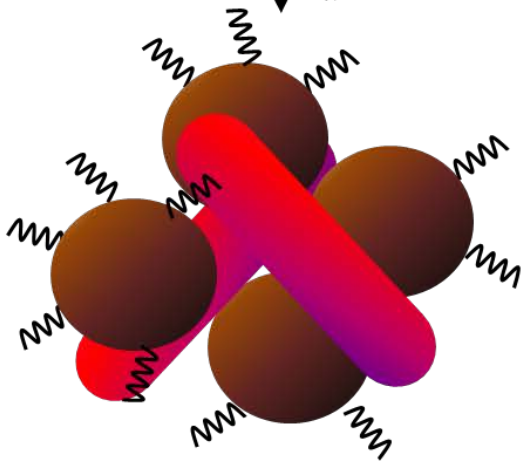


Functionalized MnMEIO



AuNRs@MnMEIOs

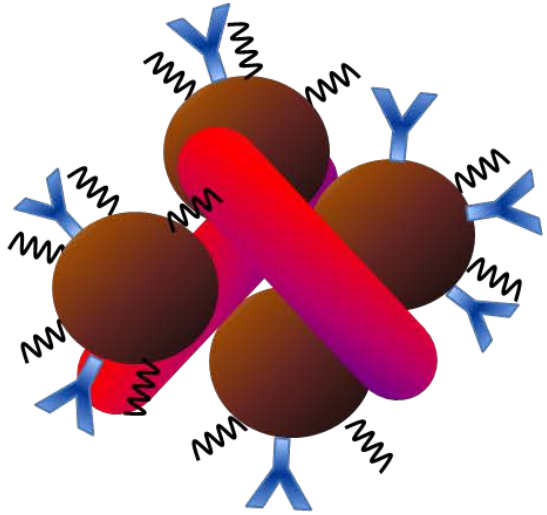
PEG-Ac



AuNRs@MnMEIOs-PEG

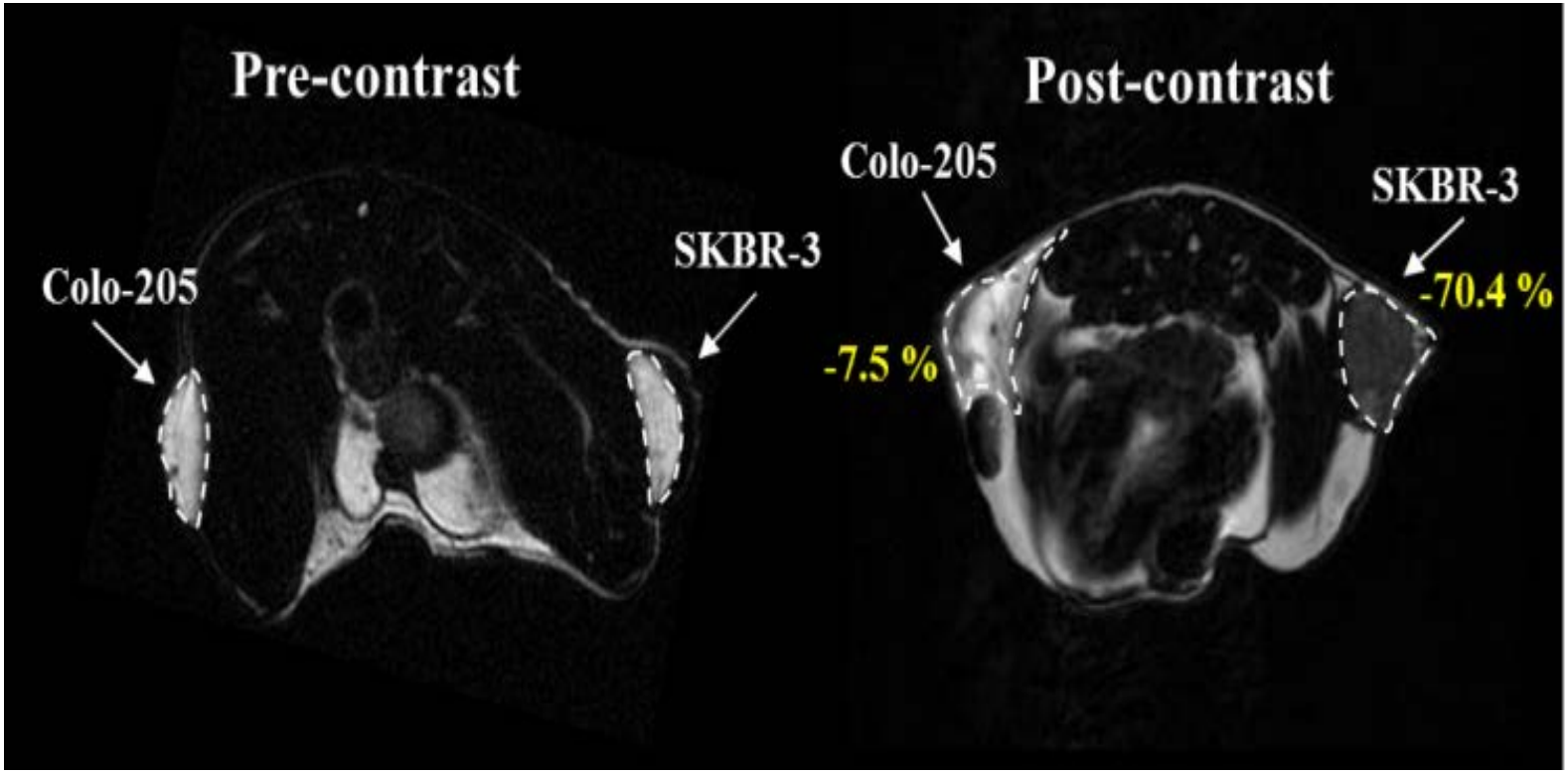
Herceptin

EDC/NHS



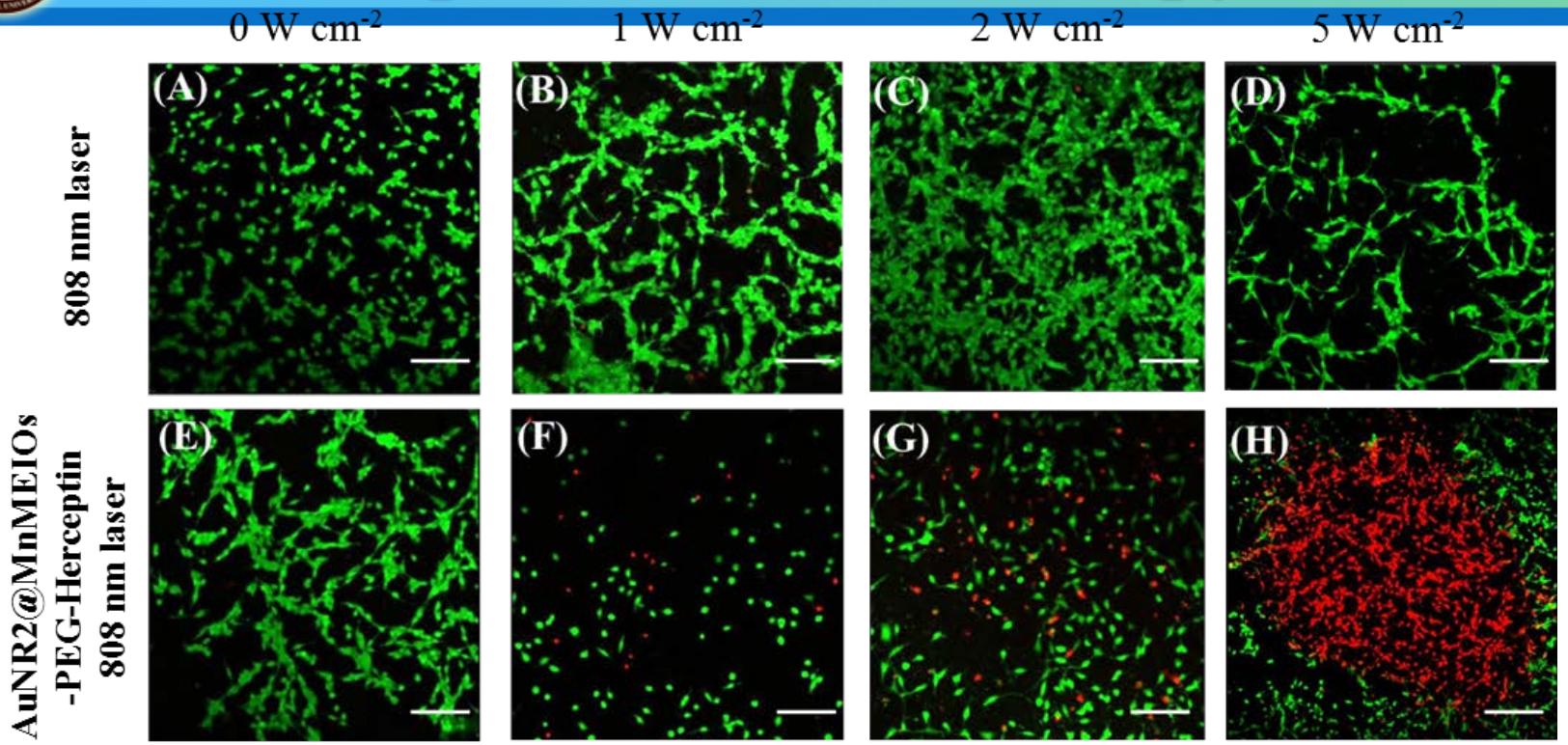
AuNRs@MnMEIOs-PEG-Herceptin

In-vivo MR imaging



In vivo T_2*-weighted* MR images of AuNRs@MnMEIOs-PEG-Herceptin accumulating in tumors bearing mice. Different contrast enhancements between SKBR-3 and Colo-205 is most likely attributed to ligand-receptor-mediated internalization of AuNRs@MnMEIOs-PEG-Herceptin by targeted cells.

In vitro photothermal therapy



Cells incubated with AuNRs@MnMEIOs-PEG-Herceptin and then irradiated by an 808 nm laser for 10 min at different power densities. The first row shows laser alone while the second row AuNRs@MnMEIOs-PEG-Herceptin and 808 nm laser treatment. Each column shows cells treated at specific laser intensity: 0 W cm^{-2} ((A), (F)), 1 W cm^{-2} ((B), (G)), 2 W cm^{-2} ((C), (H)), and 5 W cm^{-2} ((d), (i)) Viable cells appear green from calcein AM staining while red areas of PI fluorescence are cells destroyed by photothermal irradiation. It is demonstrated that AuNRs@MnMEIOs-PEG-Herceptin could kill cells completely through the photothermal effect induced while the power density is higher than 5 W cm^{-2}. While neither the AuNRs@MnMEIOs-PEG-Herceptin itself nor the laser irradiation alone can kill SKBR-3 cells.

In vivo photothermal therapy

	Day 0	Day 20	Final
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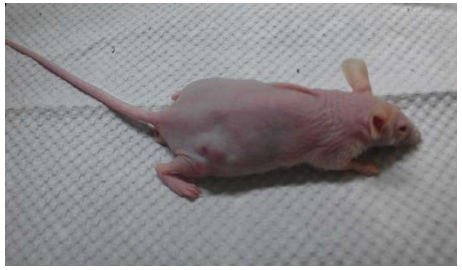
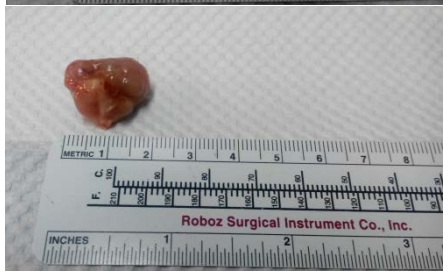
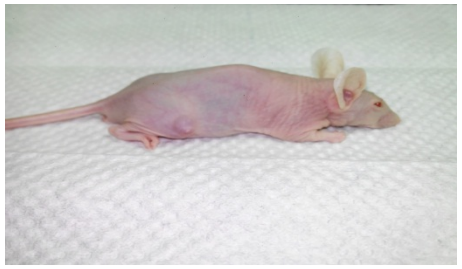
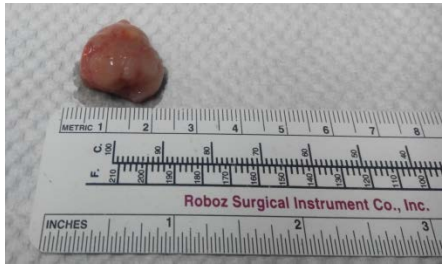
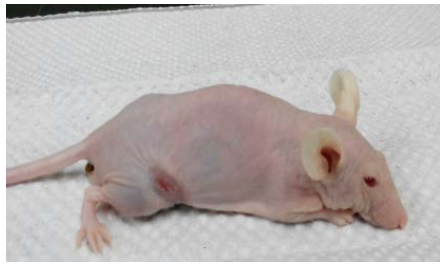
Only laser			
Only NP			
Laser + NP			

Selected Publication List

1. Kao YH, Lin YC, Tsai MS, Sun CK, **Yuan SS**, Chang CY, Jawan B, Lee PH. Involvement of the nuclear high mobility group B1 peptides released from injured hepatocytes in murine hepatic fibrogenesis. Biochim Biophys Acta. 2014 Sep;1842(9):1720-32. doi: 10.1016/j.bbadis.2014.06.017. (**11/74,** Biophysics, **IF=5.089**)
2. Chuang YC, Lin CJ, Lo SF, Wang JL, Tzou SC, **Yuan SS*** （**Correspondence**）,, Wang YM*. Dual functional AuNRs@MnMEIOs nanoclusters for magnetic resonance imaging and photothermal therapy. Biomaterials. 2014 May;35(16):4678-87. (**2/77**, Engineering, Biomedical, **IF=8.312**)
3. Chen YH, Tsai JC, Cheng TH, **Yuan SS**, Wang YM. Sensitivity evaluation of NBD-SCN towards cysteine/homocysteine and its bioimaging applications. Biosens Bioelectron. 2014 Jun 15;56:117-23. (**1/27**, Electrochemistry, **IF=6.451**)
4. Chen YJ, Wu SC, Chen CY, Tzou SC, Cheng TL, Huang YF, **Yuan SS**** （**Correspondence**）,Wang YM**. Peptide-based MRI contrast agent and near-infrared fluorescent probe for intratumoral legumain detection. Biomaterials, 35(1):304-15, 2014. (**2/77**, Engineering, Biomedical, **IF=8.312**)
5. Chen YJ, Cheng YJ, Hung AC, Wu YC, Hou MF, Tyan YC, **Yuan SS*** （**Correspondence**）, The synthetic flavonoid WYC02-9 inhibits cervical cancer migration/invasion and angiogenesis via MAPK14 signaling. Gynecologic Oncology, 131(3):734-43, 2013. (**7/78**, Obstetrics & Gynecology, **IF= 3.678**)
6. Lo S, **Yuan SS**, Hsu C, Cheng YJ, Chang YF, Hsueh HW, Lee PH, Hsieh YC. Lc3 Over-expression Improves Survival and Attenuates Lung Injury Through Increasing Autophagosomal Clearance in Septic Mice. Ann Surg, 257(2):352-63, 2013. (**1/202**, SURGERY, **IF=7.188**)

Selected Publication List (Continuted)

7. **S-S Yuan***（**Correspondence**）, M-F Hou, Y-C Hsieh, C-Y Huang, Y-C Lee, Y-J Chen, S Lo. Role of MRE11 in Cell Proliferation, Tumor Invasion, and DNA Repair in Breast Cancer, J Natl Cancer Inst,104(19):1485-502, 2012 (**8/202**,ONCOLOGY, **IF=15.161**)
8. Y-C Lee, Y-J Chen, C-C Wu, S Lo, M-F Hou, **S-S Yuan***（**Correspondence**）. Resistin expression in breast cancer tissue as a marker of prognosis and hormone therapy stratification, Gynecol Oncol, 125(3):742-750, 2012 (**7/78**, Obstetrics & Gynecology, **IF=3.687**)
9. Y-C Lee, Y-H Yang, J-H Su, H-L Chang, M-F Hou, **S-S Yuan***（**Correspondence**）. High visfatin expression in breast cancer tissue is associated with poor survival, Cancer Epidemiol Biomarkers Prev, 20(9): 1892-1901, 2011. (**12/160**, PUBLIC, ENVIRONMENTAL & OCCUPATIONAL HEALTH, **IF=4.324**)
10. H-M Chen, F-R Chang, Y-C Hsieh, Y-J Cheng, K-C Hsieh, L-M Tsai, A-S Lin, Y-C Wu, **S-S Yuan***（**Correspondence**）. A novel synthetic protoapigenone analogue, WYC02-9, induces DNA damage and apoptosis in DU145 prostate cancer cells through generation of reactive oxygen species, Free Radic Biol Med, 50(9): 1151-1162, 2011. (**15/123**, ENDOCRINOLOGY & METABOLISM, **IF=5.710**)
11. C-H Hsieh, P-Y Pai, H-W Hsueh, **S-S Yuan**, Y-C Hsieh. Complete induction of autophagy is essential for cardioprotection in sepsis, Ann Surg, 253(6):1190-1200, 2011. (**1/202**, SURGERY, **IF=7.188**)
12. H Zhao, F Ou-Yang, I-F Chen, M-F Hou, **S-S Yuan**, H-L Chang, Y-C Lee, R Plattner, S-E Waltz, S-M Ho, J Sims, S-C Wang. Enhanced resistance to tamoxifen by the c-ABL proto-oncogene in breast cancer. Neoplasia, 12(3): 214-223, 2010. (**28/202**, ONCOLOGY, **IF=5.398**)
13. H-M Chen , Y-C Wu , Y-C Chia , F-R Chang , H-K Hsu, Y-C Hsieh , C-C Chen , **S-S Yuan***（**Correspondence**）. Gallic acid, a major component of Toona sinensis leaf extracts, contains a ROS-mediated anticancer activity in human prostate cancer cells, Cancer Lett, 286(2) : 161-171, 2009. (**33/202**, ONCOLOGY, **IF=5.016**)

高雄醫學大學附設中和紀念醫院
Kaohsiung Medical University Chung-Ho Memorial Hospital

Thank You for Your Attention