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Tandem Cytotoxic Drug Delivery & p53-Status-Independent Apoptosis Promotion

Lead University of the Sciences Inventor: Zhiyu Li, Ph.D.

Unmet Need Targeted and long-lasting formulations of chemotherapeutics with low doses and few side effects

Opportunity

Simple formulations to delivery two or more therapeutics to cancers with similar pharmacokinetic profiles. Easier to manufacture than nano / micro particles. Good to use in combination with immune checkpoint inhibitors.

Unique Attributes

- Apoptotic agent that acts independently of cancer cell's p53 genotype.
- Has attractive pharmacokinetic profile (such as serum half-life, tissue penetration, and accumulation in cancer cells) (Figure 1).
- Easy to produce and formulate. No covalent protein conjugation needed.
- Interacts with 4 distinct cellular targets, reducing the possibility of development of resistance
- Drug carrier, medical device as well as a therapeutic.

Clinical Applications

- **To sensitize the responses of cancers to chemotherapeutics.**

  rHSA-p53 synergizes with methotrexate , 5-flurouracil (Figure 2), paclitaxel, cisplatin, and doxorubicin in SJSA-1, MDA-MB-231, and MCF7

- **To co-deliver fatty acid-modified chemotherapeutics for optimal efficacy and minimum toxicity.**

  rHSA-p53 complexed with fatty acid-modified 5-flurouracil (FA-5FU, Figure 3) and fatty acid-modified paclitaxel (FA-Paclitaxel, Figure 4) shows much higher cytotoxicity.

- **To synergize with HER2-targeting albumin fusion protein (rHSA-(ZHER2)2) against HER2-positive cells.**

  rHSA-(ZHER2)2 is an albumin fusion protein inhibiting the proliferation of HER2-positive SKBR3 cells. It shows different mechanism from Herceptin and synergizes with rHSA-p53 (Figure 5).

Stage of Development Preclinical Studies

Intellectual Property US Patent No. 8,598,311; Pending Application No. 62/083,010

Collaboration Opportunity Actively seeking licensee for commercialization or collaboration to complete preclinical studies.

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References

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2. Brian Rogers, Daoyuan Dong, Zhijun Li, and Zhiyu Li. (2015) Recombinant Human Serum Albumin Fusion Proteins and Novel Applications in Drug Delivery and Therapy. Current Curr Pharm Des, 21(14):1899-907
3. Joshi, M., Yao, N., Myers, K.A., and Li, Z., (2013) Human Serum Albumin and p53-Activating Peptide Fusion Protein is Able to Promote Apoptosis and Deliver Fatty Acid-Modified Molecules, PLOs One, 8(11), e80926.

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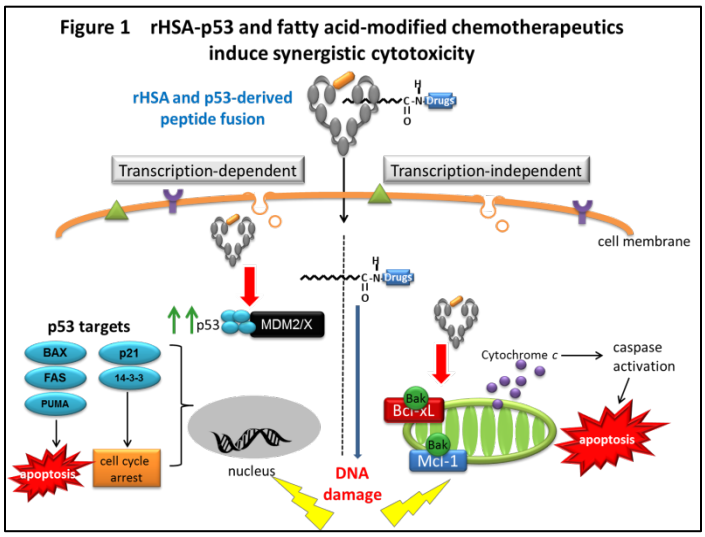

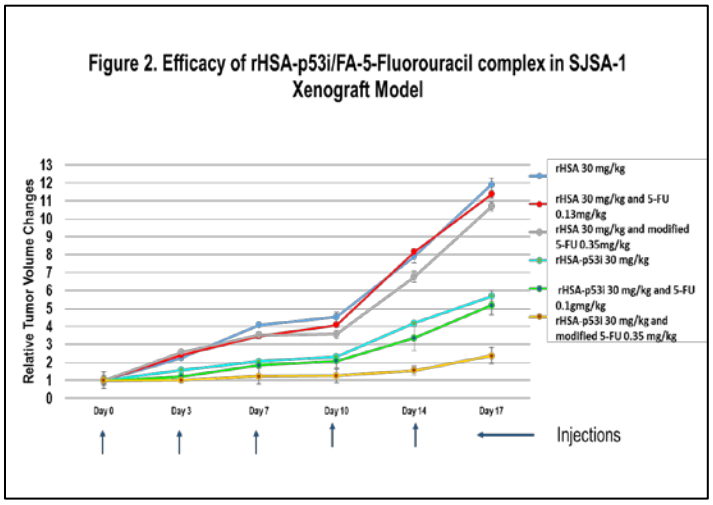

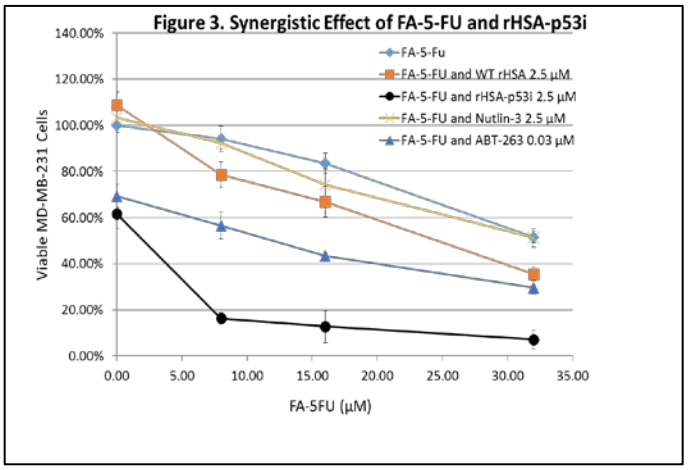

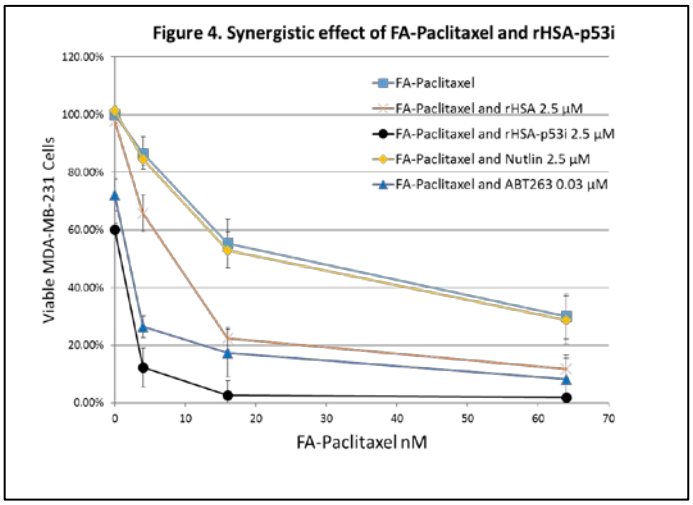

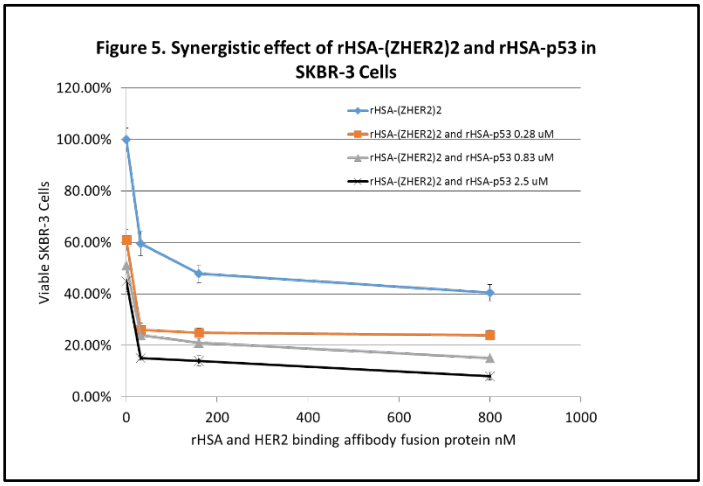
Figure 5. Synergistic effect of rHSA-(ZHER2)2 and rHSA-p53 in SKBR-3 Cells
120.00%
100.00%
80.00%
60.00%
40.00%
20.00%
0.00%
Viable SKBR-3 Cells
0
200
400
600
800
1000
rHSA and HER2 binding affibody fusion protein nM
rHSA-(ZHER2)2
rHSA-(ZHER2)2 and rHSA-p53 0.28 uM
rHSA-(ZHER2)2 and rHSA-p53 0.83 uM
rHSA-(ZHER2)2 and rHSA-p53 2.5 uM