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Compositions for Treatment of HER2 Positive Cancers

Many early stage cancers have a high rate of survival if promptly diagnosed and treated. Survival rates for stage 1-3 breast cancer can be as high as 95% at the 5 year mark. Unfortunately, late stage cancers have a much lower survival rate; stage 4 breast cancer only has about a 20% survival rate at the 5 year mark. Metastatic cancers pose a particularly challenging problem because they can be difficult to contain once spread occurs. Many cancers, such as breast, ovarian, gastric, prostate, lung, and others are associated with HER2 overexpression, markedly so in the advanced stages. One method of treating HER2 positive cancers includes the use of drug-antibody conjugates (ADC) targeting the HER2 receptors. However, ADCs suffer from certain drawbacks, including a limited ability to penetrate cells and tissues, low payload, possible immune responses and high cost.

Researchers at Arizona State University have developed nanoparticle-based compositions for treating HER2 positive cancers. This is accomplished through a Peptide-DNA chimera nanocomplex that is both an efficient drug delivery system and an inhibitor of metastatic activity. The nanocomplex comprises a HER2 binding peptide (such as an affibody), a linker, and a polynucleotide segment. It is capable of non-covalently binding tens to hundreds of molecules of drug. Because the payload is so high and non-covalently bound, the drug can disassociate from the nanocomplex, providing greater dosages than current systems. Finally, the nanocomplex can be digested into non-toxic amino acids and nucleotides in vivo.

One nanocomplex-drug composition was tested in a BT474 tumor xenograft mouse model and showed effective accumulation in the HER2-overexpressing tumor region with low accumulation in all normal tissues and rapid metabolism (about 8 hours). Further, significant tumor growth inhibition was noticed with low systemic toxicity.

This portfolio provides new compositions that may develop into a novel class of anti-cancer treatments targeting HER2 positive cancers and potentially preventing the metastatic activity of those cancers.

Potential Applications

- Treatment for cancers associated with HER2 overexpression (breast, ovarian, gastric, prostate, lung, etc.)

  - HER2 overexpression can be higher in some late stage cancers, which currently lack an efficient method of treatment

Benefits and Advantages

- Can effectively treat cancers associated with overexpression of HER2
- Targets metastatic cancer cells, and may also inhibit metastasis
- Advantages over antibody-drug conjugation method currently used in treatment:
  - Binds more effectively to HER2 positive cells, making the treatment less toxic to normal cells
  - Non-covalent binding of drugs - more efficient delivery to cancer cells
  - High capacity payload - can deliver tens to hundreds of molecules of drug
- Can be adapted to deliver various anti-tumor small molecule drugs such as doxorubicin, daunorubicin, etoposide, gemcitabine, etc.
- HER2+ cancer cells may become covalently crosslinked through affibody-HER2 binding making them less likely to metastasize
  - Induces cell apoptosis, making it a potential candidate for treatment of late stage metastatic cancers

For more information about this opportunity, please see

Zhang et al - Chem Commun (Camb) - 2017

Zhang et al - Int J Nanomedicine - 2020

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For more information about the inventor(s) and their research, please see

Dr. Hecht's departmental webpage

Dr. Chen's departmental webpage