

Development of hY1R Specific Peptide-Drug Conjugates for the Treatment of Metastatic Breast Cancer

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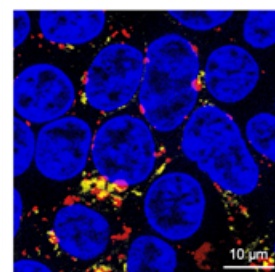
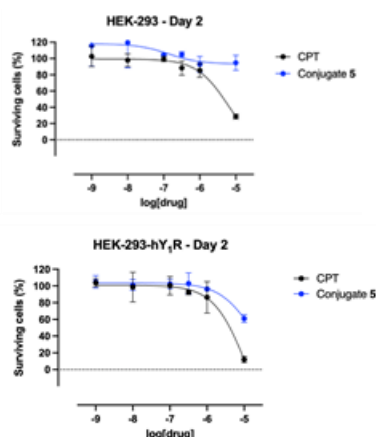
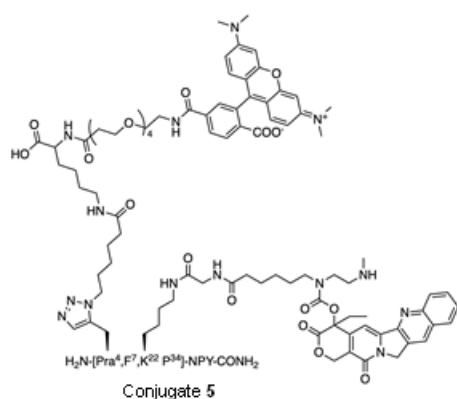
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Abstract

Breast cancer accounts for over 15% of cancer mortalities in women, and late-stage metastatic breast cancer is currently considered incurable. Peptide-drug conjugates (PDCs) have emerged as a promising way of targeting specific disease sites in the body, and the neuropeptide Y analogue [F^7 , P^{34}] NPY has been found to selectively target the human Y1 receptor which is overexpressed in 100% of breast cancer metastases. Camptothecin is a small molecule drug that can be used as a payload for inducing cancer-cell apoptosis but is hampered by unfavourable drug properties and damaging off-target effects. It was hypothesised that binding the active site of camptothecin to a PDC via a self-immolative linker would increase drug solubility and decrease off target effects. This presentation will describe the design, synthesis and in-vitro testing of a lead candidate PDC, which displayed selective binding, rapid internalisation and pronounced cell death in hY1R-expressing breast cancer cells. Variants of this lead will also be discussed that were bound to diagnostic and therapeutic radionuclides, showing versatility of the PDC beyond pure chemotherapeutic applications.



Biography

Dr. Luke Darveniza was the first doctoral candidate to complete a joint PhD between Monash University and Leipzig University (Germany), focused on developing peptide-drug conjugates for the treatment of metastatic breast cancer. He currently works as a post-doctoral fellow in the Molecular Imaging and Therapy Research Unit of SAHMRI, specialising in the development of novel radiopharmaceuticals for the detection and treatment of disease.

