

31st Nano Congress for Future Advancements

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13th Edition of International Conference on Nanomedicine and Advanced Drug Delivery

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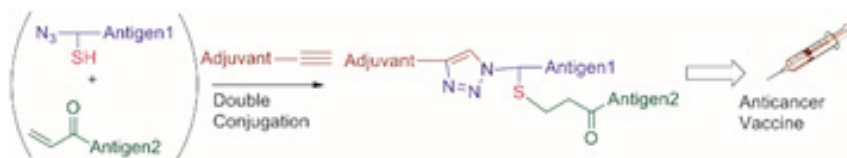
Multiantigenic peptide-based therapeutic vaccine against cervical cancer

Waleed M. Hussein¹, Tzu-Yu Liu¹, Pirashanthini Maruthayanar², Saori Mukaida¹, Peter M. Moyle³, James W Wells², Istvan Toth^{1,2,3} and Mariusz Skwarczynski¹

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Conjugation of multiple peptides by their N-termini is a promising technique to produce branched multiantigenic vaccines. We established a double conjugation strategy that combines a mercapto-acryloyl Michael addition and a copper-catalysed alkyne-azide 1,3-dipolar cycloaddition (CuAAC) reaction to synthesise self-adjuvanting branched multiantigenic vaccine candidates. These vaccine candidates aim to treat cervical cancer and include two HPV-16 derived epitopes and a novel self-adjuvanting moiety. This is the first report of mercapto-acryloyl conjugation applied to the hetero conjugation of two unprotected peptides by their N-termini followed by a CuAAC reaction to conjugate a novel synthetic lipoalkyne self-adjuvanting moiety. *In vivo* experiments showed that the most promising vaccine candidate completely eradicated tumours in 46% of the mice (6 out of 13 mice).



Recent Publications

1. W.M. Hussein, S. Mukaida, F. Azmi, S. Bartlett, C. Olivier, M.R. Batzloff, M.F. Good, M. Slovarczyński, I. Toth, Comparison of Fluorinated and Nonfluorinated Lipids in Self-Adjuvanting Delivery Systems for Peptide-Based Vaccines, *Acs Medicinal Chemistry Letters* 8 (2017) 227-232.
2. W.M. Hussein, T.Y. Liu, P. Maruthayanar, S. Mukaida, P.M. Moyle, J.W. Wells, I. Toth, M. Skwarczynski, Double conjugation strategy to incorporate lipid adjuvants into multiantigenic vaccines, *Chemical Science* 7 (2016) 2308-2321.
3. T.Y. Liu, W.M. Hussein, A.K. Giddam, Z. Jia, J.M. Reiman, M. Zaman, N.A. McMillan, M.F. Good, M.J. Monteiro, I. Toth, M. Skwarczynski, Polyacrylate-Based Delivery System for Self-adjuvanting Anticancer Peptide Vaccine, *J Med Chem* 58 (2015) 888-96.
4. T.Y. Liu, A.K. Giddam, W.M. Hussein, Z.F. Jia, N.A.J. McMillan, M.J. Monteiro, I. Toth, M. Skwarczynski, Self-Adjuvanting Therapeutic Peptide-Based Vaccine Induce CD8(+) Cytotoxic T Lymphocyte Responses in a Murine Human Papillomavirus Tumor Model, *Current Drug Delivery* 12 (2015) 3-8.
5. T.-Y. Liu, W.M. Hussein, Z. Jia, Z.M. Ziora, N.A.J. McMillan, M.J. Monteiro, I. Toth, M. Skwarczynski, Self-Adjuvanting Polymer-Peptide Conjugates As Therapeutic Vaccine Candidates against Cervical Cancer, *Biomacromolecules* 14 (2013) 2798-2806.

JOINT EVENT

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Biography

Hussein focus on the development of peptide-based vaccines against infectious diseases and cancer. This includes (1) synthesis of adjuvanting moieties for stimulation of immune system; (2) applying different methods for conjugation of peptides and lipids; (3) determination of the size, shape and charge of the self-assembled vaccine particles; (4) investigate the biological efficiency of vaccines in both *in vitro* and *in vivo*.

Gene delivery: Currently, Dr. Hussein is working on the development of targeted nanoparticle delivery system to deliver the siRNA to cytoplasm. This delivery system includes peptide-based, micelles and/or liposome formulations.

Notes: