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MACROMOLECULAR NANO IMMUNOCONJUGATES TARGETING CHECKPOINT INHIBITORS CTLA-4 AND PD-1 FOR TREATMENT OF BREAST CANCER

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Breast cancer (BC) is the most diagnosed malignancy and the second cause of cancer death in women in the United States. It is estimated that 252,710 new cases of BC will be diagnosed in 2017 and 40,610 women are projected to die from breast cancer in the US. Human epidermal growth factor receptor *HER2/neu* overexpression is found in 25-30% of human BCs and correlates with high aggression, high risk of relapse, high rate of metastasis, and poor survival. We have developed novel nano immune conjugate (NIC) versions with single conjugated anti-mouse CTLA-4 mAb (a-msCTLA-4) and anti-PD-1mAb (a-PD-1). The NIC activities were tested in BALB/c mice bearing subcutaneous (sc) syngeneic murine mammary carcinoma cells D2F2. This cell line is the parental line of the D2F2/E2 that expresses human HER2. Tumor growth was significantly inhibited when treated with NIC's containing a-CTLA-4 and tumour targeting anti-mouse TfR mAb (a-msTfR) compared to free a-CTLA-4. Inhibition was accompanied by reduced levels of CD4+FOXP3+ Tregs that are also targets of a-CTLA-4. Anti-PD-1 treatment was performed with animals carrying primary HER2+ D2F2/E2 sc tumours using the NIC P/a-msTfR/a-PD-1. Serum cytokine IL10, and especially IL-12, were significantly enhanced in comparison with treatment of a-pD-1 alone, and increased further during treatment with NIC P/a-msTfR/a-PD-1/AON c-Myc. In all cases, size of sc D2F2/E2 breast cancer was significantly reduced. The expression of IL-12 and IL-10 was also induced in mouse sera treated with free a-pD-1. Interestingly, NIC with AON to c-Myc induced higher cytokine expression. It is expected that a much stronger anti-tumour activity is observed for co-administration and/or codelivery of the antibodies and antisense drugs.

Conclusion: Treatment of HER2 breast cancer with nano immune conjugates increased significantly client survival.

Biography

Eggehard Holler, PhD, is Professor of Neurosurgery and Biomedical Sciences, and Director of Syntheses at Nanomedicine Research Centre, Department of Neurosurgery, Cedars-Sinai Medical Centre, Los Angeles, USA. He has completed his PhD from University of Regensburg, DE and has Postdoctoral appointments at Cornell and Berkeley. He was Professor of Biochemistry at University of Regensburg until 2005, and since 2008, he is Research Scientist and Professor at Cedars-Sinai Medical Centre, USA. He has served at several international universities as Visiting Professor, published more than 150 papers and was Interims Director of Institute of Biophysical Chemistry at Regensburg.

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