A “Kick and Expand” strategy to generate large numbers of CIML NK cells for adoptive cell therapy for the treatment of cancer using novel fusion proteins HCW9201 and HCW9206.

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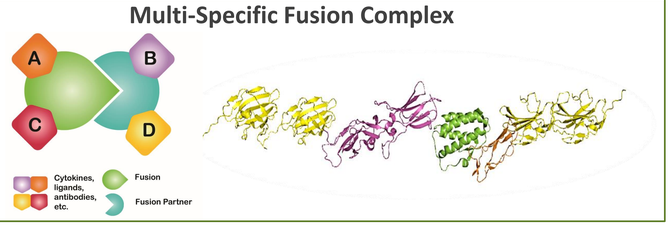
Abstract

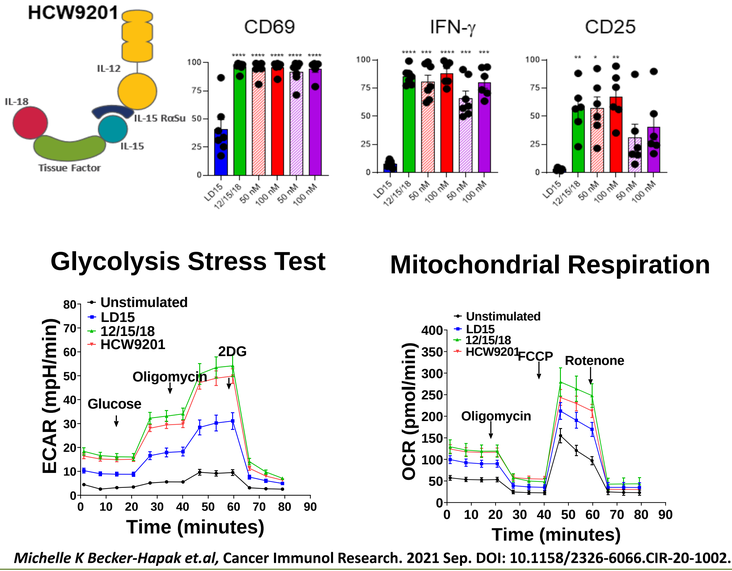
Adoptive cell therapy (ACT) using NK cells is a promising armament in the fight against cancer. Cytokine-induced memory-like (CIML) NK cells have been shown in clinical studies to have potent antitumor activity with superior *in vivo* persistence. Unfortunately, the current cell expansion protocols typically utilize tumor feeder cell-based strategies requiring additional processing. Using HCW Biologics' TOBI™ platform, we have developed fusion proteins, HCW9201 and HCW9206 comprising of IL-15/IL-18/IL-12 and IL-15/IL-7/IL-21, respectively, capable of activating and expanding CIML NK cell products, ideal for transfer to the clinic. Our "Kick and Expand" strategy allows clinically relevant expansion of CIML NK cells from donor PBMCs in as little as 14 days without the use of exogenous feeder cells. Continued expansion can yield sufficient CIML NK cells for cryopreservation and multiple ACT infusions. The CIML NK cells generated have enhanced antitumor activity across multiple cancer cell lines, higher metabolic capacity, stable epigenetic demethylation of the IFN-γ promoter, and increased persistence in NSG mice when compared to controlled NK cells. In conclusion, HCW Biologics' "Kick and Expand" process supports the generation of abundant CIML NK cells for multiple ACT infusions and provides a simpler, more regulatory friendly, off-the-shelf platform for generating NK cell products, including those with chimeric antigen receptor (CAR) constructs.

TOBI™ Platform Technology

Multi-Specific Fusion Complex

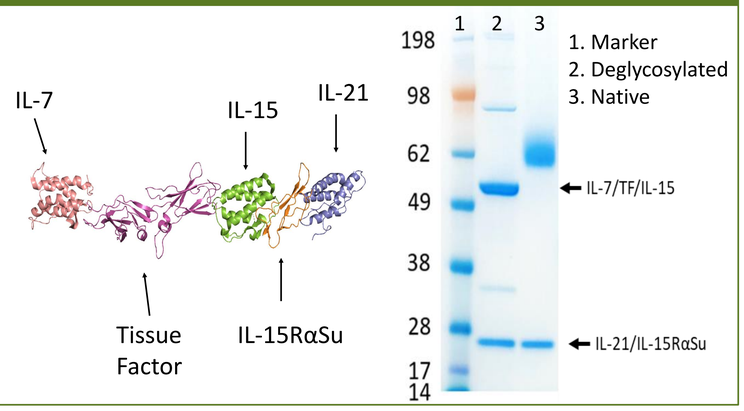


HCW9201 multimeric fusion protein containing IL-12, IL-15, and IL-18 generates CIML NK

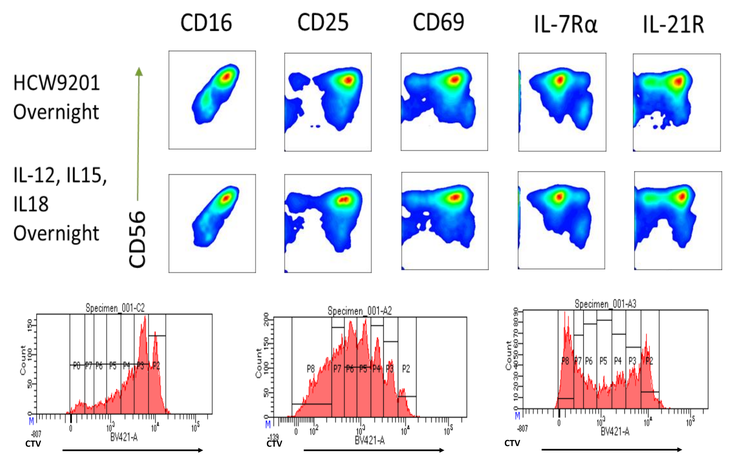


Michelle K Becker-Hapak et.al, Cancer Immunol Research. 2021 Sep. DOI: 10.1158/2326-6066.CIR-20-1002.

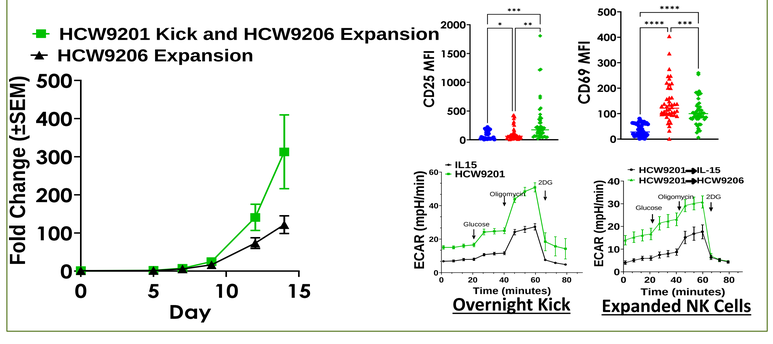
Construction of multimeric fusion protein HCW9206 containing IL-7, IL-15 and IL-21



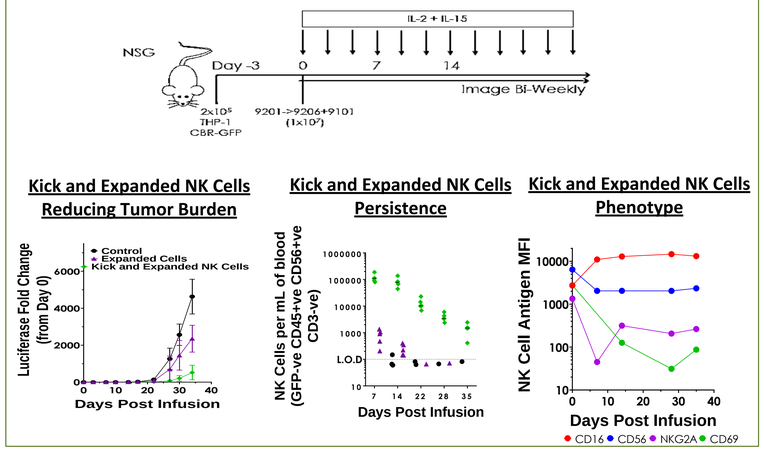
HCW9201 “Kick” improves HCW9206 based NK cell expansion



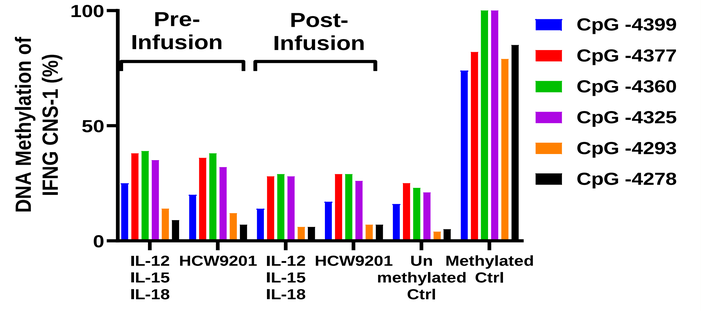
HCW's “Kick and Expand” strategy drives robust NK cell expansion and activation



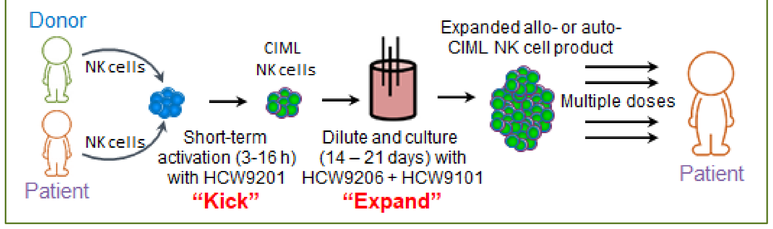
“Kick and Expand” infused NK cells reduce tumor burden and persist *in vivo*



“Kick and Expanded” Cells in NSG mouse transfer system retain IFN-γ CNS-1 DNA Demethylation



Clinical strategy for “Kick and Expanded” CIML NK cells for multiple infusions



Conclusions

HCW's TOBI™ platform technology is a novel and robust backbone to build active GMP biologics.

HCW9201 is GMP grade biologics that can be used to “Kick” NK Cells into CIML NK cells both phenotypically and functionally.

HCW9206 can effectively expand CIML NK cells that are phenotypical and functionally favorable for adoptive cell therapy.

Kick and Expand is a novel method combing two of HCW's GMP grade biologics to facilitate a superior adoptive cell therapy.

Kick and Expanded cells can be supported in vivo with exogenous cytokines to further improve their anti-tumor activities.

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