CHARACTERIZATION OF WU-NK-101, A FEEDER CELL-FREE EXPANDED ALLOGENEIC MEMORY NK CELL PRODUCT WITH POTENT ANTI-TUMOR ACTIVITY

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Background Cytokine-induced memory NK cells, like WU-NK-101, offer several advantages over conventional NK cells. These advantages include enhanced functional persistence, efficacy, and metabolic fitness that improve their survival and activity in liquid and solid tumor microenvironments. Additionally, unlike conventional NK (cNK) cells derived from iPSC, cord blood, or adult peripheral blood, WU-NK-101 does not require engineering to enable anti-tumor activity.

The Moneta™ Platform is a feeder cell-free system of fusion protein complexes to generate, expand, phenotypically maintain, and cryopreserve memory NK cells for an ‘off-the-shelf’ allogeneic drug product. Here we define the molecular characteristics of WU-NK-101, through RNA and protein phenotyping, and elucidate pathways involved in memory NK cell expansion and activity.

Methods WU-NK-101 was generated from previously frozen NK cells derived from healthy donor whole blood using the Moneta™ platform. We evaluated pre- and post-expansion phenotype by flow cytometry, CyTOF, and RNA-Seq. We further assessed post-thaw functionality by cytokine secretion and cancer cell cytotoxicity in the absence or presence of monoclonal antibodies.

Results CyTOF analysis revealed that WU-NK-101 have an expression profile distinct from cNK. Compared to cNK, WU-NK-101 have elevated expression of Memory NK markers (CD25, CD69, NKG2A), cytotoxic molecules (GzmB, TRAIL), activating receptors (NKp30, NKp44, NKG2D), and nutrient transporters (CD71, CD98), providing mechanistic rationale for their enhanced anti-tumor activity and metabolic flexibility. Flow cytometry and RNAseq analysis confirm this phenotype. When stimulated by cancer cells, WU-NK-101 have enhanced secretion of IFN-γ, MIP-1α, and TNFα; and also demonstrate improved cytotoxicity compared to cNK. WU-NK-101 is able to utilize monoclonal antibodies to effectively drive antibody-dependent cellular cytotoxicity against solid tumor cancer cell lines.

Conclusions The Moneta™ platform expands memory NK cells while maintaining their cytokine-induced memory phenotype, as identified by RNA-Seq, flow cytometry, and CyTOF. As a result, WU-NK-101 demonstrates improved anti-tumor activity compared to cNK cells, even within the adverse tumor microenvironment. These data support the clinical development of WU-NK-101, an allogeneic Memory NK cell therapy in both liquid and in solid tumors, as a monotherapy and in combination with monoclonal antibodies, solid tumor engagers, or other anti-tumor modalities.

REFERENCES