CD47 AND PHOSPHATIDYLSELINE CONTRIBUTE TO THE INTERACTION BETWEEN ANTIGEN PRESENTING CELLS AND THE ALLOGENEIC CELL-BASED RELAPSE VACCINE DCP-001

¹Haoxiao Zuo, ¹Satwinder Kaur Singh*, ¹Marie-José Van Lierop, ¹Jorn Kaspers, ¹Remco Bos, ²Alwin Kamermans, ²Helga E de Vries, ²Tanja de Gruijl, ¹Ada Kruisbeek, ¹Erik Manting, ¹Satwinder Kaur Singh. ¹Immunicum AB, Leiden, Netherlands; ²Amsterdam University Medical Center, Amsterdam, Netherlands

Background DCP-001 is a cancer relapse vaccine derived from the DCOne[®] human leukemic cell line. During manufacturing, DCOne[®] cells are shifted towards a mature dendritic cell (mDC) phenotype, combining an endogenous tumor antigen repertoire (e.g. WT-1, RHAMM and PRAME) with a mDC costimulatory profile and providing the basis for the highly immunogenic vaccine DCP-001. In a phase I clinical study in acute myeloid leukemia (AML), DCP-001 demonstrated to be safe and to induce multifunctional antitumor immune responses.¹ It has also been reported that DCP-001 induces antitumor immunity against multiple myeloma cells in peripheral blood mononuclear cells (PBMC) from multiple myeloma patients and that DCP-001 antigenic material is transferred to host antigen presenting cells (APC), possibly via extracellular vesicles.² However, the possibility of direct interactions between DCP-001 and host APC has not yet been investigated.

Methods To further elucidate the mode of action of DCP-001, we studied the interactions of DCP-001 with human PBMC and isolated immature monocyte-derived DCs (iMoDC) in in vitro co-culture studies. A human skin explant model was used to determine uptake of DCP-001 by migrating skin DCs after intradermal injection.

Results We found that DCP-001 stimulates the secretion of various proinflammatory cytokines (IL-1 β , GM-CSF, IFN- γ , IL-2, TNF- α , and IL-6) and chemokines (IL-8 and RANTES) in PBMC. In addition, we demonstrate that DCP-001 is efficiently taken up by iMoDC via direct cell-cell interactions and that this phagocytic process is influenced by "eat-me" and "don't eat me" signaling pathways. Blocking of the "eat-me" signals calreticulin and phosphatidylserine inhibited the uptake of DCP-001, whereas blockade of the "don't eat me" signal CD47 enhanced DCP-001 uptake. After intradermal injection of DCP-001 in an ex-vivo human skin model, its uptake by skin-emigrating DCs was demonstrated as well as simultaneous activation of these DCs.

Conclusions Our data suggest a key role for host antigen presenting cells in the triggering of immune responses upon DCP-001 vaccination. In addition, the data provide rationale for potential combination therapies based on DCP-001 and inhibitors of the CD47 pathway.

REFERENCES

1. van de Loosdrecht AA, et al. A novel allogeneic off-the-shelf dendritic cell vaccine for post-relapse treatment of elderly patients with acute myeloid leukemia. *Cancer Immunol Immunother* 2018;**67**(10):1505–1518.
2. Leaf RK, et al. DCOne as an allogeneic cell-based vaccine for multiple myeloma. *J Immunother* 2017;**40**(9):315–322.

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.219>