studied. In vivo experiments of treatment with Nc tachyzoites administered locally (intra and peri tumoral) or remotely (subcutaneous) in a murine thymoma EG7 tumor and in human Merkel cell carcinoma (MCC).

**Results** We demonstrated that the treatment of thymoma EG7 by Nc strongly inhibited tumor development. Analysis of immune responses and interactions between Nc and tumor cells showed that Nc had the ability to lyze infected cancer cells, reactivated immune competence within the Tumor Microenvironment (TME), and activated the systemic immune system by promoting the recruitment of immune cells to the site of tumor. We also established in a NOD/SCID mouse model that Nc was able to induce a strong regression of human MCC. Recently, to further enhance oncotherapeutic effect, we engineered an Nc strain to secrete human IL-15 (cross reactive with mouse cells), associated with alpha subunit of IL-15 receptor, increasing its stability.3 This strain induced proliferation of human PBMCs and their secretion of IFN-\(\gamma\).

In the EG7 model, human IL-15 secreting Nc showed greater protection against tumor development, confirming enhancement of immunotherapy by engineering Nc to deliver/secrete IL-15.

**Conclusions** These results highlight Neospora caninum as a potentially extremely efficient, and non-toxic anti-cancer agent, capable of being engineered to express at its surface or to secrete bio-drugs, like human IL-15 cytokine. Our work has identified the broad clinical possibilities of using N. caninum as an oncolytic protozoan in human medicine capable of vectoring molecular therapy, overcoming TME defenses.

**REFERENCES**

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**Abstract 847**

**INFLAMMASOME ACTIVATION IN M2 MACROPHAGE RESTRAIN THE IMMUNE SUPPRESSIVE FUNCTION**

Ronghua Zhang, Tienan Wang*, Qing Lin. WXi ApTec, Shanghai, China

**Background** Macrophage is an important component in tumor microenvironment (TME) and plays multiple roles in tumor initiation, progression and metastases. In response to various stimuli within TME, macrophage exhibits high level of functional heterogeneity. There are two distinct groups of macrophages: M1 macrophage exhibits pro-inflammatory phenotype with high levels of TNF-\(\alpha\), IL-6, and IL-1\(\beta\), while M2 macrophage displays immune suppressive phenotype with high levels of anti-inflammatory cytokines such as IL-10 and TGF-\(\beta\). In response to the M2 cytokines, myeloid cells within the TME further acquire higher expression of PD-L1 and thus inactivate T cells. M2 cytokines can also directly inhibit T cell activation. As a result, re-polarizing M2 macrophages becomes a key concept for cancer immunotherapy. The NLRP3 inflammasome could be the potential target for cancer by modulating T cell activation through macrophage polarization regulation.

**METHODS** Here, we have established an in vitro human macrophage NLRP3 activation system (figure 1), coupled with M2 macrophage polarization assay, to dissect the role of NLRP3 in macrophage phenotype.

**RESULTS** Our results indicate that NLRP3 activation restrained M2 phenotype and further enhanced T cell activation in an M2/T cell co-culture system (figure 2).

**CONCLUSIONS** Inflammasome activation polarize M2 macrophage int Use LPS/ATP to stimulate NLRP3 in M2 macrophage and demonstrate NLRP3 activation could reduce CD163 and increase CD86

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