Background Mucosal melanoma is a rare subtype of melanoma originating from mucosal tissues, metastases are very aggressive and respond poorly to therapy, including immune checkpoint inhibitors (ICI) such as anti-CTLA4 and anti-PD1 antibodies. CD8+ T cells constitute the most abundant immune infiltrate in metastatic melanoma, of which the Tissue Resident Memory Subset (TRM) is of particular interest. CD8+ TRM cells express the highest levels of immune checkpoint receptors, proliferate in response to ICI and correlate with longer disease-free and overall survival.

Methods We investigated the CD8+ T and TRM cells infiltrating two temporally- and spatially-distant subcutaneous metastases, these originated from a primary vaginal mucosal melanoma. One metastasis was excised prior to anti-PD1 treatment and one was anti-PD1 refractory, having progressed on therapy-naïve melanoma patients and expanded significantly during anti-PD1 treatment.

Results CD8+ TRM frequency increased with time and anti-PD1 treatment, forming clusters at the tumour margin. T cells could not be stimulated by anti-PD1 checkpoint inhibitors (ICI) such as anti-CTLA4 and anti-PD1 antibodies. In the anti-PD1 refractory lesion were more activated than T cells in the first tumour and were bound by anti-PD1 antibodies.

CD68+ macrophages were found to be closely associated with tumor cells, PD-L1+ macrophages were found to have the closest interaction with tumor cells. The potential of these cell phenotypes to generate a strongly immunosuppressive microenvironment need to be explored in additional cases.

Conclusions In this patient with vaginal mucosal melanoma, subsequent melanoma metastases of clonal origin attracted CD8+ T cells of similar specificity, among which TRM cells responded more vigorously to tumour cells than other T cells.

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Ethics Approval Patients diagnosed with stage 3 or 4 metastatic melanoma and undergoing clinically indicated surgery were enrolled in prospective studies approved by the Peter MacCallum Cancer Centre human ethics research committee (13/141). All experimental protocols have been approved and clinical data has been collected prospectively.

REFERENCES
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Pizzolla, A; Keam, S; Vergara, I; Caramia, F; Wang, M; Kocovski, N; ThuNgoc, N; Macdonald, S; Tantalo, D; Petrone, P; Yeang, HXA; Gyorki, D; Weppler, A; Au-Yeung, G; Sandhu, S; Perdicchio, M; McArthur, G; Papenfuss, T; Neeson, P

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