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Commentary – Programmed death (PD) 1 expressing regulatory T cells in vitiligo

Vitiligo is a common depigmenting skin disease with a prevalence of 1-2%.¹ The exact aetiology and detailed pathogenesis of vitiligo is not fully understood, but destructive CD8⁺ T cell responses against melanocytes are strongly implicated in the development of the disease.²⁻³ Regulatory T cells (Tregs) are a subset of CD4⁺ lymphocytes that play a key role in maintaining peripheral tolerance *in vivo* through the active suppression of self-reactive T cell activation and expansion.⁴ Several studies have reported dysregulation of Tregs in vitiligo patients,⁵⁻⁶ and repigmentation in a mouse model of spontaneous epidermal depigmentation was found to be accompanied by an increased Treg cell infiltration, suggesting their importance in preventing an ongoing immune response against melanocytes.⁷

In this issue of *BJD*, the findings of Tembhre *et al*⁸ support a role for Tregs in vitiligo pathogenesis. They report a decrease in the frequency of Treg cells and a reduction in the expression of Treg cell-associated molecules such as TGF- β , FOXP3 and chemokine receptor CCL21 in the peripheral blood and the lesional skin of vitiligo patients. Tregs mediate their suppressive function through the programmed death 1 (PD1)/PD1-ligand pathway.⁹ PD1 is an inhibitory cell surface molecule that inhibits activation of autoreactive T and B cells, suppresses their proliferation, and induces apoptosis on interaction with PD1-ligand on Treg cells.⁹ Blocking PD1-ligand *in vitro* causes the expansion of Tregs suggesting the mechanism by which Treg function is contra-regulated on PD1/PD1-ligand engagement.¹⁰ In the current report⁸, the authors observed an increase in the frequency of peripheral PD1⁺Tregs and CD3⁺CD4⁺PD1⁺ T cells in vitiligo patients compared to healthy controls. They hypothesise

that increased expression of PD1 on Treg cells may be acted upon by autoreactive T cells expressing PD1-ligand leading eventually to the apoptosis of Tregs and their consequent deficiency in vitiligo patients. However, their hypothesis requires much further investigation to provide evidence to support it as a mechanism for Treg cell dysfunction in vitiligo.

Conflicts of interest

None declared

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