

Dopamine-2 receptor-specific responses in adult patients with dystonia

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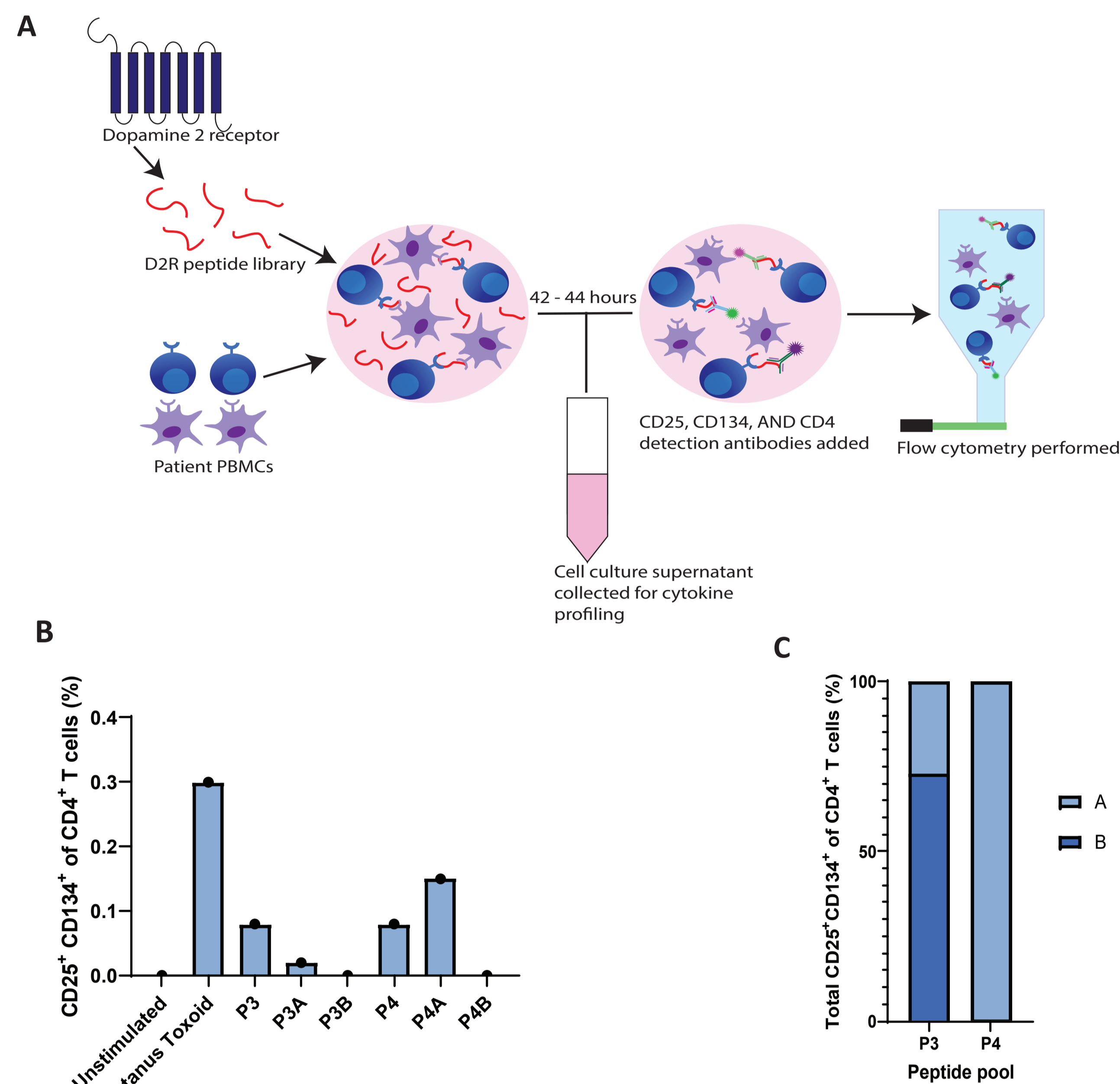
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Introduction

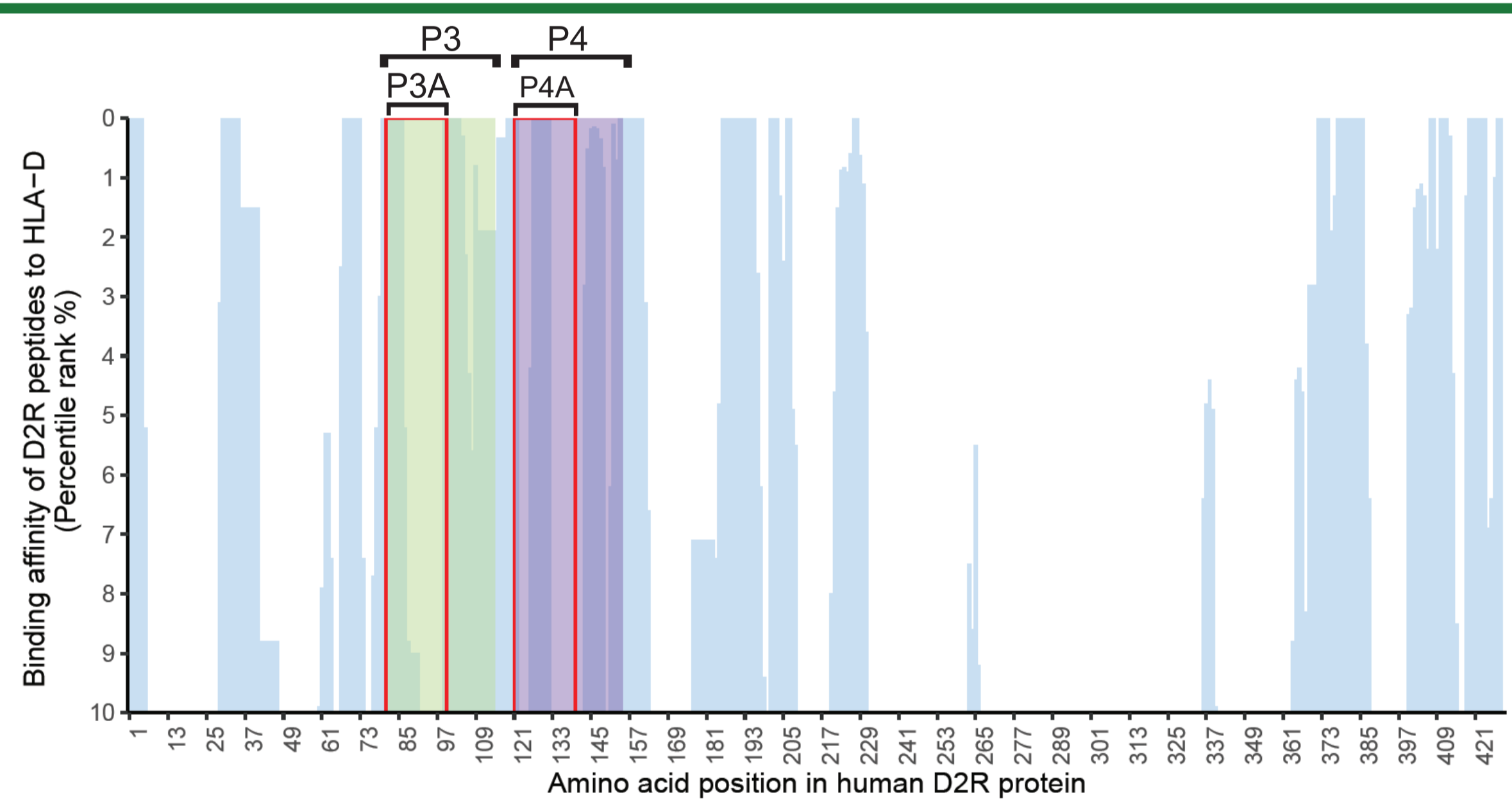
Dystonia is a hyperkinetic movement disorder caused by sustained or intermittent muscle contractions. While it has low morbidity, it can greatly impact quality of life through debilitating pain. Currently no pathogenesis-targeted treatments for dystonia exist. Dopaminergic system dysregulation through the dopamine-2 receptor (D2R) is implicated in the pathophysiology of several movement disorders, including dystonia. This is due to the high density of D2R in movement centres of the brain. D2R-specific T cells and antibodies have been observed in certain paediatric movement disorders. This study will use flow cytometry-based techniques and HLA genotyping to **investigate the activation of the immune response against D2R in adult patients with dystonia**.

Hypothesis: D2R-specific T cells and antibodies will be detected in some adult patients with dystonia, as they have previously been implicated in patients with movement disorders. D2R immunological responses will result in a proinflammatory cytokine secretion profile and these patients will have regions of high binding on their HLA to epitopes of D2R
The immune responses of one adult dystonia patient are presented in this poster

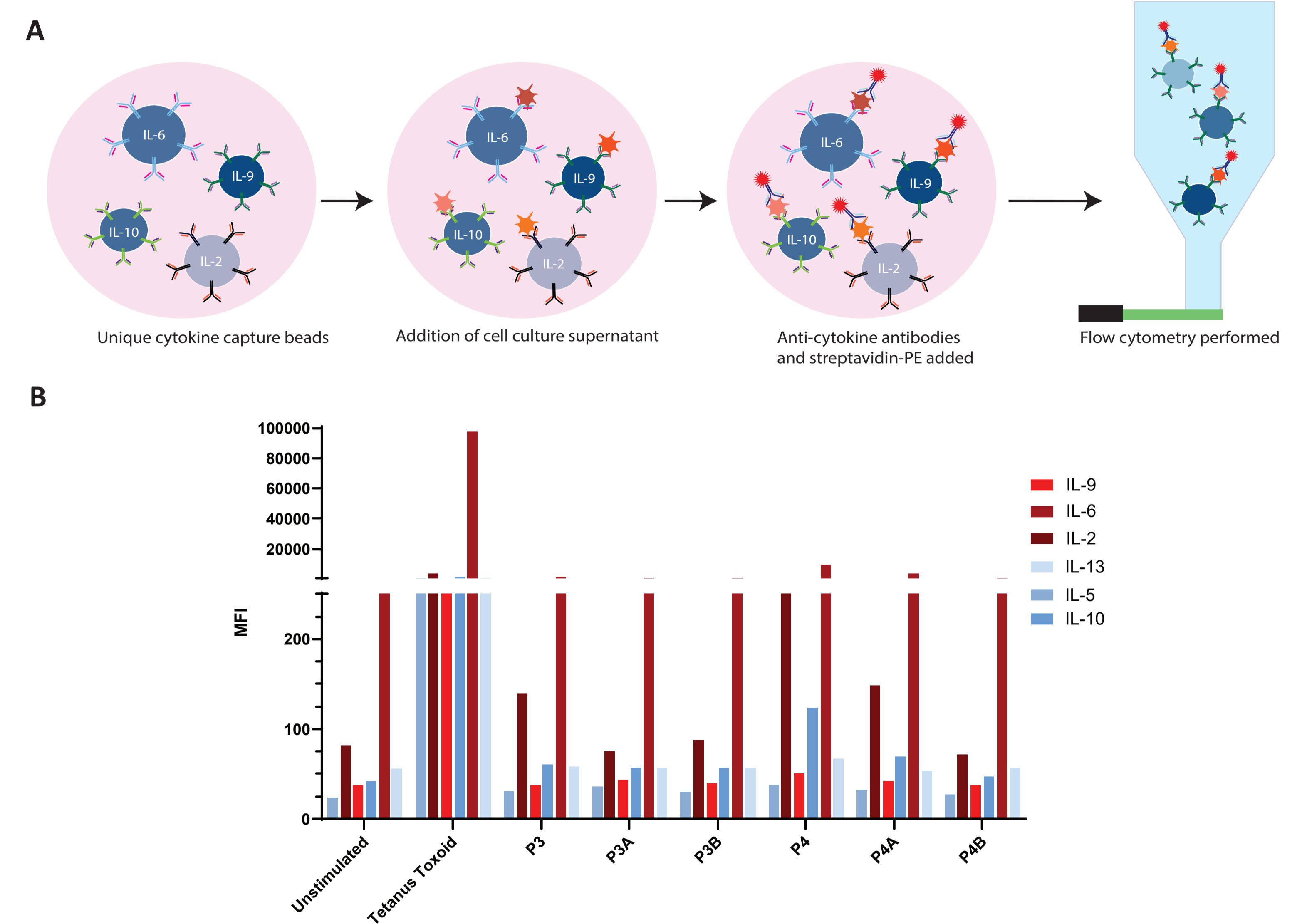
Aim 1: Identification of activated CD4+ D2R specific T cells



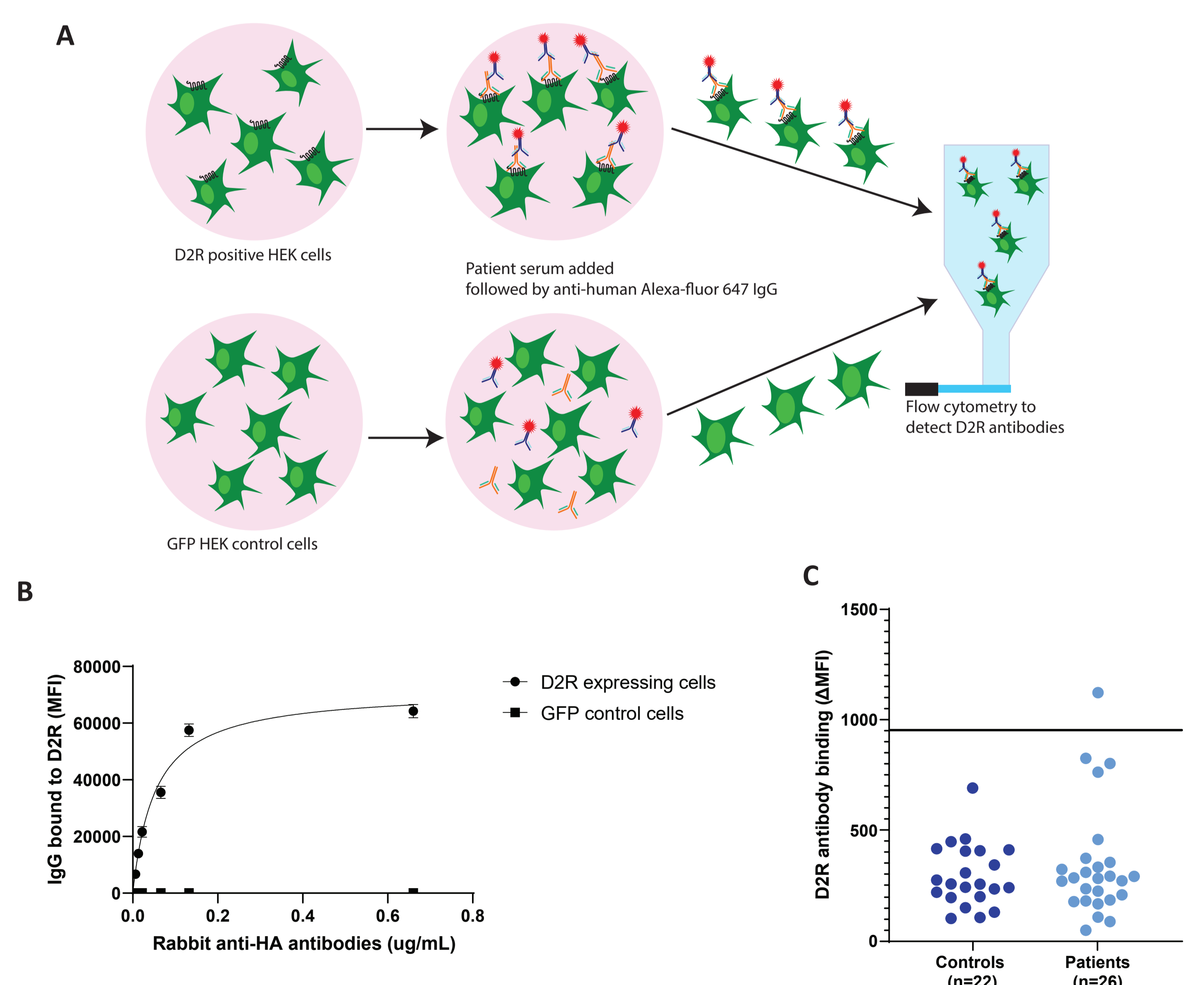
Aim 3: Identification of HLA genotypes that bind strongly to regions of D2R in patients with D2R-specific T cells



Aim 2: Investigate the cytokine secretion profile associated with D2R specific immunological responses



Aim 4: Identification of D2R antibodies in adult patients with dystonia



Conclusion

1. Activated CD4+ T cells were observed in Pools 3, 3A, 4 and 4A of a human D2R peptide library
2. The cytokine secretion profile of the D2R-specific immunological response was shown to be proinflammatory
3. Peptide pools 3 and 4 corresponded to regions of high affinity binding by HLA
4. D2R-specific antibodies were observed in an adult with dystonia

Significance: D2R-specific T cells and antibodies may be used as important biomarkers for diagnosis of dystonia and may help to design and implement better treatment strategies

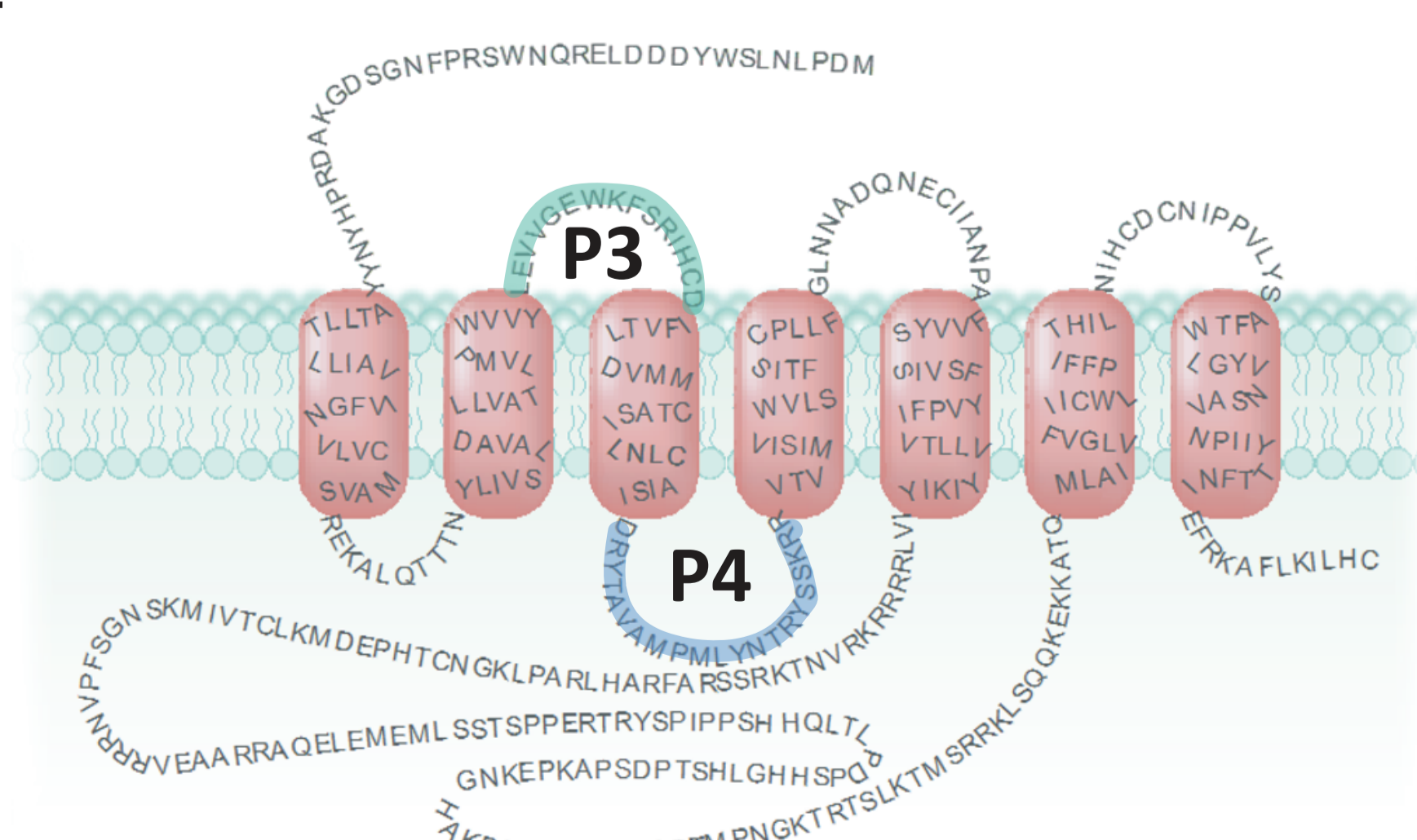
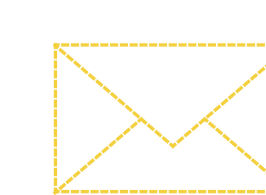


Figure 5. Peptide epitopes from extracellular loop one (Pool 3 and 3A) and intracellular loop 2 (Pool 4 and 4A) were shown to be immunogenic and corresponded to areas of high affinity binding by HLA

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