Déruaz M, Bonvin P, Severin IC, Johnson Z, Krohn S, Power CA, Proudfoot AE. (2013). Evasin-4, a tick-derived chemokine-binding protein with broad selectivity can be modified for use in preclinical disease models. *FEBS J*. Oct;280(19):4876-87.

Rhipicephalus sanguineus, the common brown dog tick, produces several chemokine-binding proteins which are secreted into the host in its saliva to modulate the host response during feeding. Two of these demonstrate very restricted selectivity profiles. Here, we describe the characterization of the third, which we named Evasin-4. Evasin-4 was difficult to produce recombinantly using its native signal peptide in HEK cells, but expressed very well using the urokinase-type plasminogen activator signal peptide. Using SPR, Evasin-4 was shown to bind most CC chemokines. Investigation of the neutralization properties by inhibition of chemokine-induced chemotaxis showed that binding and neutralization did not correlate in all cases. Two major anomalies were observed: no binding was observed to CCL2 and CCL13, yet Evasin-4 was able to inhibit chemotaxis induced by these chemokines. Conversely, binding to CCL25 was observed, but Evasin-4 did not inhibit CCL25-induced chemotaxis. Size-exclusion chromatography confirmed that Evasin-4 forms a complex with CCL2 and CCL18. In accordance with the standard properties of unmodified small proteins, Evasin-4 was rapidly cleared following in vivo administration. To enhance the in vivo half-life and optimize its potential as a therapeutic agent, Fc fusions of Evasin-4 were created. Both the N- and C-terminal fusions were shown to retain binding activity, with the C-terminal fusion showing a modest reduction in potency.