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(54) **Title:** ORTHOGONAL IL-21 RECEPTOR/CYTOKINE SYSTEMS

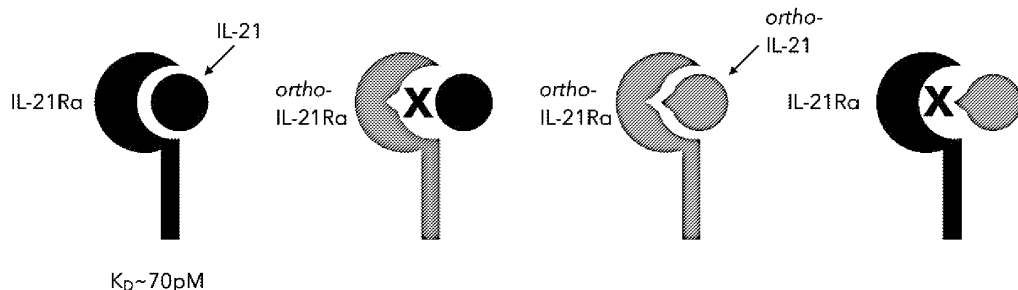


FIG. 1

(57) **Abstract:** Orthogonal IL-21 receptors and orthogonal IL-21 cytokines are described. The IL-21 receptor-cytokine pairs may include an orthogonal interleukin-21 receptor a chain ("ortho-IL-21Ra") that has impaired binding to native interleukin-21 cytokine ("IL-21") and an orthogonal IL-21 cytokine ("ortho-IL-21") that has impaired binding to native IL-21Ra, wherein the ortho-IL-21Ra binds to the ortho-IL-21. The IL-21 receptor-cytokine pair may activate IL-21 signaling. Cells engineered to express the orthogonal IL-21 receptors are also described, as well as methods for using such cells for treatment of various diseases and disorders.



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