

**MIT Chemical Engineering Department &
Biological Engineering Department, & Ragon Institute
Spring 2021 Seminar Series**

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Unraveling Cytokine Pleiotropy through Structure-guided Engineering



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4:00-5:00PM**

Abstract: Cytokines play essential roles in coordinating inflammatory immune responses and maintaining organismal homeostasis. However, the clinical use of cytokine-based drugs is limited by the highly pleiotropic nature of cytokine signaling, resulting in off-target toxicities and limited efficacy. Interleukin-10 (IL-10) and the related cytokine IL-22 are prime examples of pleiotropic cytokines with significant unmet therapeutic potential. Here we determined the structures of both the IL-10 and IL-22 receptor complexes and used them to engineer IL-10 and IL-22 analogs with tuned functional responses and narrowed cell-type specificity, decoupling their beneficial homeostatic functions from their pro-inflammatory side-effects. These results demonstrate how structure-based protein engineering can be used to harness immune cell signaling pathways for therapeutic benefit.