BIOCHEMISTRY SEMINAR

Development towards a Folate-Targeted Dexamethasone and its Application in Murine Rheumatoid Arthritis

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Abstract: Immunosuppressive steroids are commonly used as a last resort for treating refractory autoimmune disorders because of their potent abilities to suppress inflammatory pathways. However, due to their toxicity in most healthy tissues, steroids cannot be administered chronically, forcing patients to experience prolonged periods of pain and/or progressive tissue damage before immunosuppressive steroids can be administered again. Because immunosuppressive steroids distribute indiscriminately into all cell types, toxicity can only be prevented if the steroid is specifically targeted to immune cells. Incorporating steroids into a small molecule targeted therapy platform may help reduce toxicities while enhancing anti-inflammatory potency. Based on previous studies demonstrating that a functional folate receptor beta (FRβ) is almost exclusively expressed on activated macrophages, we have hypothesized that a FRβ-targeted immunosuppressive steroid might successfully treat severe autoimmune/inflamed lesions without causing toxicity to healthy tissues. This research shows progress toward a folate-linked dexamethasone that specifically reverses inflammatory markers in arthritic joints, without toxicity to healthy organs.

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