Inhibitor complexes of Arginase-1, a target for cancer immunotherapy

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Arginase-1 is a manganese-dependent metalloenzyme that catalyzes the hydrolysis of L-arginine into L-ornithine and urea. Recently, Arginase-1 has gained much attention as a target for cancer immunotherapy, as it is abundantly expressed by tumor-infiltrating myeloid cells that promote tumor immunosuppression. Interestingly the enzyme has a very high pH optimum of 9.0.

Here we will discuss the crystal structure of the human Arginase-1 in complex with various inhibitors at various pH values, and discuss the implications for drug discovery.