

Identifying structural determinants of product specificity in *Leishmania major* farnesyl diphosphate synthase

Sweta Maheshwari¹, Yu Seon Kim¹, Srinivas Aripirala¹, Michael Murphy², L. Mario Amzel^{1,*}, Sandra B. Gabelli^{1,3,4,*}

¹Department of Biophysics and Biophysical Chemistry, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA

²Cytiva, Marlborough, Massachusetts 01752

³Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205, USA.

⁴Department of Oncology, Johns Hopkins University School of Medicine, Baltimore, Maryland 21287, USA.

*To whom correspondence should be addressed. L.M.A., E-mail: mamzel@jhmi.edu; S.B.G., E-mail: gabelli@jhmi.edu.

Table S1. List of primers used for generating *Lm*FPPS mutants

Primer	Sequence (5'-3')
T164F_F	GACGTCGATCTCACTACCTTTATTGGTCAGCTGTACGAC
T164F_R	GTCGTACAGCTGACCAATAAAGGTAGTGAGATCGACGTC
T164Y_F	GACGTCGATCTCACTACCTATATTGGTCAGCTGTACGAC
T164Y_R	GTCGTACAGCTGACCAATATAGGTAGTGAGATCGACGTC
T164W_F	CGTCGATCTCACTACCTGGATTGGTCAGCTGTAC
T164W_R	GTACAGCTGACCAATCCAGGTAGTGAGATCGACG
E97F_F	GGCCCACTTCCTTGTGTTTGACGACATCATGGACC
E97F_R	GGTCCATGATGTCGTCAAACACAAGGAAGTGGGCC
E97Y_F	GGCCCACTTCCTTGTGTATGACGACATCATGGACC
E97Y_R	GGTCCATGATGTCGTCATACACAAGGAAGTGGGCC
E97W_F	CCCACTTCCTTGTGTGGGACGACATCATGG
E97W_R	CCATGATGTCGTCCACACAAGGAAGTGGG

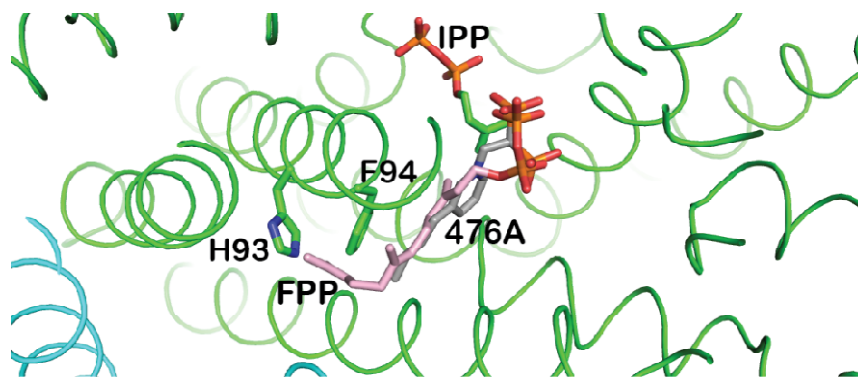


Figure S1. Active site of WT-*LmFPPS* (PDB ID: 4JZX) in complex with bisphosphonate inhibitor 476A (grey chain; colored by atoms), substrate IPP (colored by atoms). FPP is modeled from avian FPPS structure (PDB ID: 1UBX). The amino acid residues, H93 and F94, are shown as sticks.

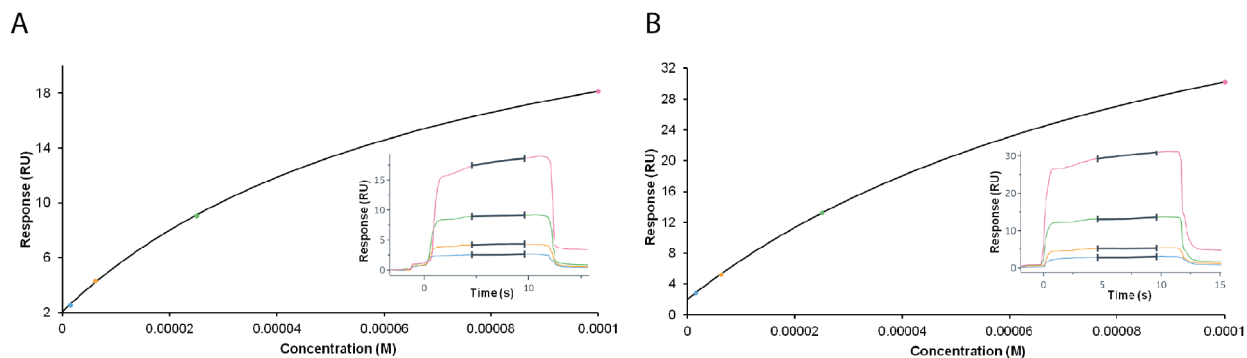


Figure S2. Binding of FPP to T164Y-*LmFPPS* (A) and T164W-*LmFPPS* (B) determined by SPR. Steady-state dose response curves are shown against concentration of FPP-1.5, 6.2, 25 and 100 μ M. Sensorgrams for multi-cycle kinetics are depicted as inserts.