

## Supplementary Material

**Supplementary Figure S1.** Sequence alignments of selected members of the family with well-defined models present in the PDB. The Asp residue marked in red is a metal ion-binding residue, while Lys in orange is a part of the dehydration mechanism necessary for phosphate condensation. The residues in the blue box constitute the base-binding loop and the following Arg in green is the part of the diphosphate release mechanism.

CLUSTAL W (1.83). multiple sequence alignment

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TM1418A      -----MREAI V L A S G A G K R L R S V T G D
2QQX        -----I K T A M I M A A G L G T R F G H Y T E L
2XME        M I N V -----D G E Y L K I F A G R I K L M K A V I L A A G L G T R L G ---G
1LVW        G-----A H M K G I V L A G G S G T R L Y P I T R A
1TZF        M-----A S K A V I L A G G L G T R L S E E T I V
1JYK        M G S S H H H H H S S G L V P R G S H M K -----E I R V K A I L A A G L G T R L R P L T E N
                . . . . * . * * . * . :

TM1418A      V P K V F Y R F D G C E L V K Y P M I S L M K N G V E R F V L V S E G Y R D - L G E K V L N D L G
2QQX        V P K G F V E V G G K P M I I R S I E T L L S C G I E R I I L G T - G - Y K K E A Y E A L Q A D F P
2XME        V P K P L V R V G G C E I I L R T M K L L S P H - V S E F I I V A - S R Y A D D I - D A F L K D K G
1LVW        V S K Q L L P I Y D K P M I Y Y P L S V L M L A G I R D I L I I S - T P R D L P L Y R D L L G D G S
1TZF        K P K P M V E I G G K P I L W H I M K M Y S V H G I K D F I I C C - - G Y K G Y V I K E Y F A N Y F
1JYK        T P K A L V Q V N Q K P L I E Y Q I E F L K E K G I N D I I I I V - - G Y L K E Q F D Y L K E K Y G
                . * : .      : :      :      : : :

TM1418A      V-----E G I V V E N K K - - V E L G N A Y-----S F F - L S E P
2QQX        Q-----I E T C F S P R Y - - A D T N S M Y-----T L Y - N T R D
2XME        F-----N Y K I V R H D R - - P E K G N G Y-----S L L - V A K N
1LVW        Q-----F G V R F S Y R V Q E E P R G I A D-----A F I - V G K D
1TZF        L H M S D V T F H M A E N R M E V H H K R - - V E P W N V T L V D T G D S S M T G G R L K R V A E Y
1JYK        V-----R L V F N D K Y - - A D Y N N F Y-----S L Y - L V K E
                .
                :

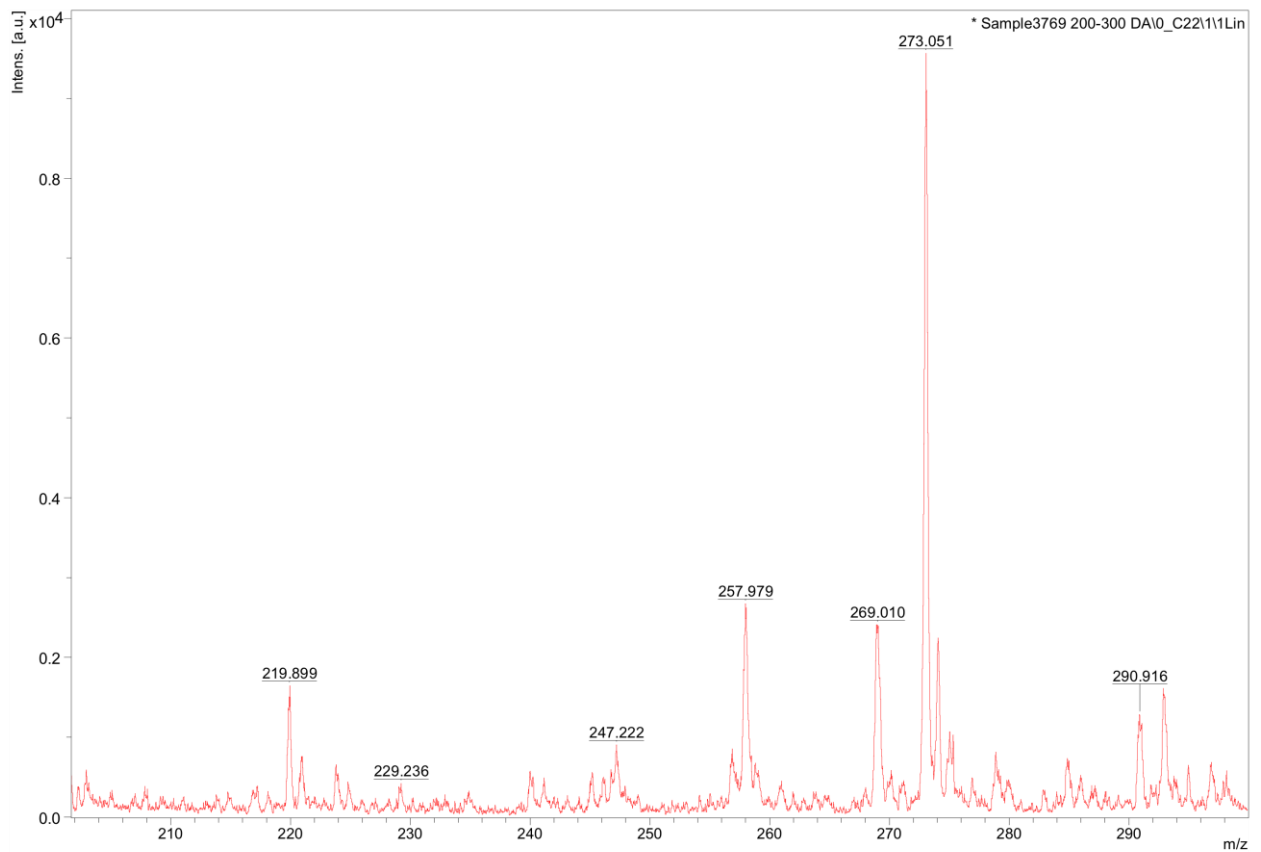
TM1418A      Y V E S E K F F L S C G D S L F P P E A L K S A F S E - - - - D E F H I K L G V S K R S D L I D P E
2QQX        V I G D D N F L L L E S D L V F E R K A I L S L L D - - - - D E F P D V - - - M L V S S L T K F Q
2XME        H V E D - R F I L T M G D H V Y S Q Q F I E K A V R - - - - G E G V I A - - - D R E P R F V D I G
1LVW        F I G D S K V A L V L G D N V F Y G H R F S E I L R R A A S L E D G A V I - - - F G Y Y V R D P R
1TZF        V K D D E A F L F T Y G D G V A D L D I - K A T I D - F H K - A H G K K A - - - T L T A T F - P P G
1JYK        E L A N - - S Y V I D A D N Y L F K N M F R N D L T R S - - - T Y F S V Y - - - R E D - - - C T N
                .
                : . * :

TM1418A      E - A S K V L V N - E D R I V K I G K R - - I D E Y N Y F D T G V F V M T K K V - - - Y S L K E S
2QQX        D - Q Y Y V E Y D - R N H I L S V D K N A L - - E A K G E L V G I H K L S N T F - - - Y R Y A T I
2XME        E - A T K I R V E - D G R V A K I G K D - - L R E F D C V D T G F F V L D D S I - - - F E H A E K
1LVW        P - F G V V E F D S E G R V I S I E E K P S R P K S N Y V P G L Y F Y D N Q V - - - V E I A R R
1TZF        R - F G A L D I Q - A G Q V R S F Q E K P - K G D G A M I N G G F F V L N P S V - - - I D L I D N
1JYK        E - W F L V Y G D - D Y K V Q D I I V - - - D S K A G R I L S G V S F W D A P T A E K I V S F I D K
                : :      : : . .      .      * .

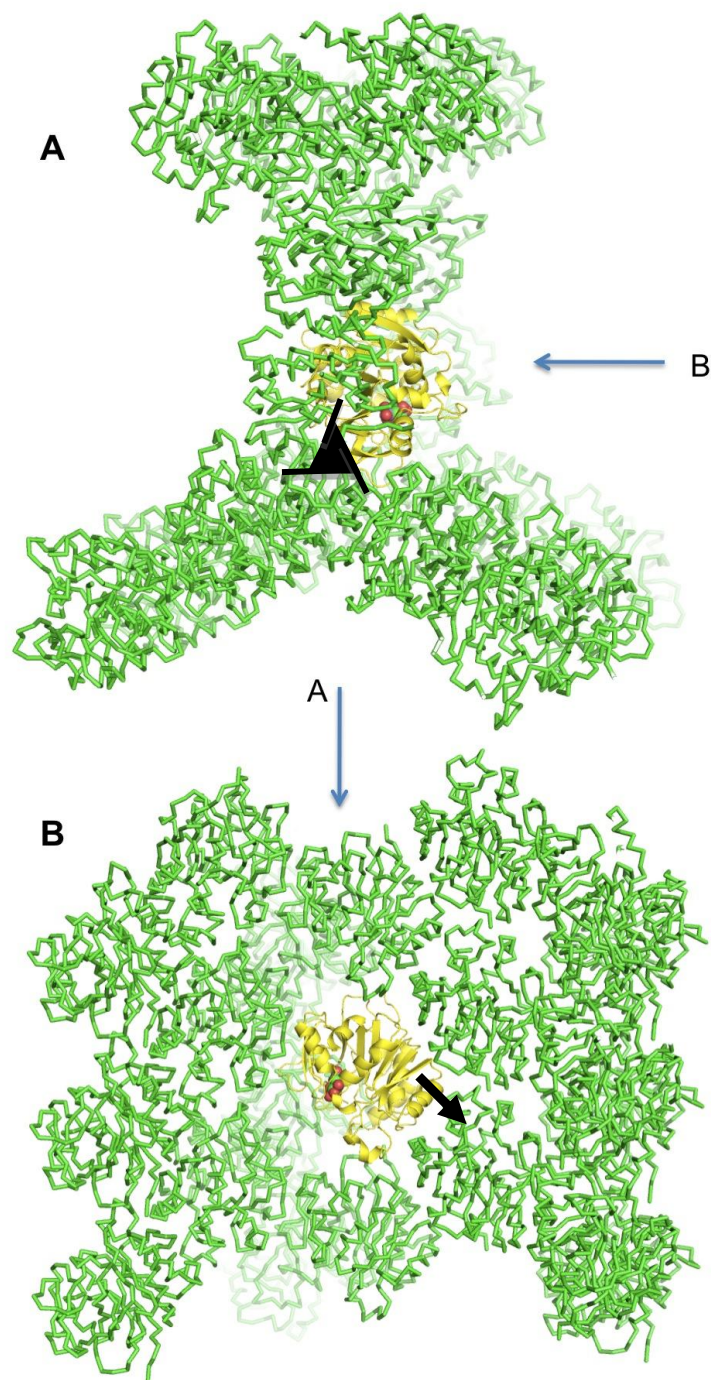
TM1418A      F S W T - - E E I S L Y - - - - H V L Q K A V D T G M I V K V F D F - G N A L W T E I D S P E D L N
2QQX        L E S - - Q P K L G Y E - - - - Y E L L R M S R S V S P V R V L R V - E G L K W Y E I D D E A D L S
2XME        L R D R - - E E I P L S E - - - - I V K L - - - - A - R L P V T Y V - D G E L W M D V D T K E D V R
1LVW        I E P S D R G E L E I T S V N E E Y L R M G - - - - K L R V E L M G R G M A W L D T G T H D G L L
1TZF        D A T T W - E Q E P L M T - - - - L A Q Q - - - - G - E L M A F E - - H P G F W Q P M D T L R D K V
1JYK        A Y V S G - E F V D L Y - W - D N M V K D N I K E L - D V Y V E E L - E G N S I Y E I D S V Q D Y R
                :      :      .      .
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TM1418A	EKVY-----ELMKK-----
2QQX	Y-AE-----EH-----
2XME	R-AN-----
1LVW	E-ASSFIETIQKRQGFYIACLEEIAYNNGWITREDVLEMAEKLEKTDYGK
1TZF	Y-LE-----GLWEK-----
1JYK	K-LE-----EIL-----

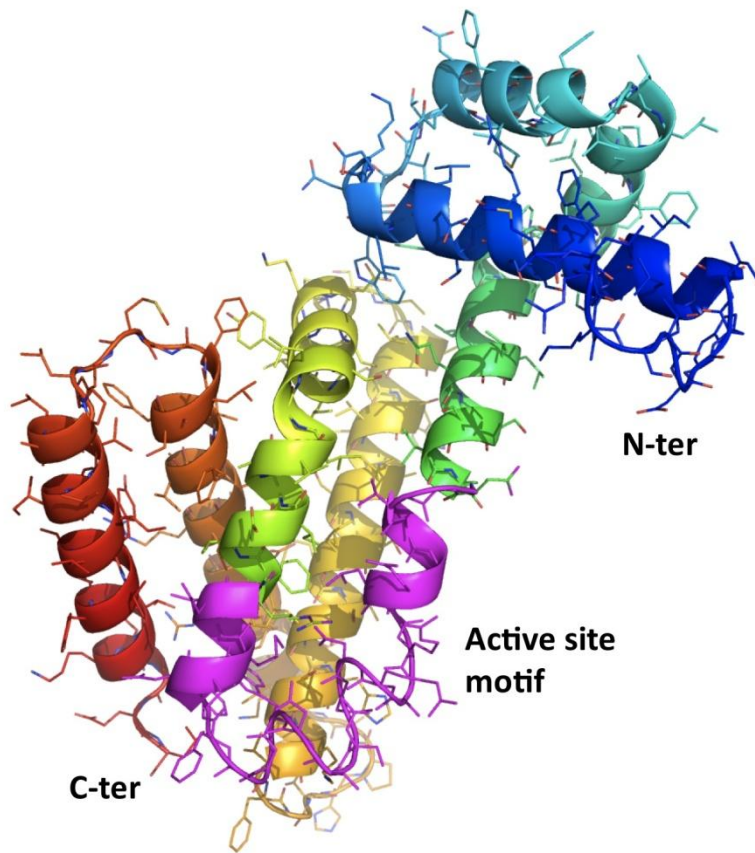
TM1418A	-----IKEGVAC
2QQX	-----IIRYC
2XME	-----RAL
1LVW	YLRDLAEGNFHG
1TZF	---GKAPWKTWE
1JYK	-----KNEN



**Supplementary Figure S2.** The MS profile of low molecular weight range of the dissolved crystals solution. The prominent peak at 273.05 Da corresponds to the arsenoribose compound found and described by crystallography.



**Supplementary Figure S3.**  $C\alpha$  representation of the multiple molecule representation as packed in the crystal structure of IMPCT organized by the space group  $P3_221$ . The original molecule is represented in yellow ribbon. Blue arrows indicate the direction of view depicted on the second panel. The black symbols represent symmetry axes (triangle – a threefold, arrow – twofold axis). (A) View along the three-fold axis, showing the wall-like arrangement of the side by side packed molecules. (B) View perpendicular to the three-fold axis and roughly parallel to the twofold axis.



**Supplementary Figure S4.** Ribbon diagram of the model created by I-Tasser of phospho-diinositol phosphate synthase (P-DIPS). The ribbon is coded from N (blue) to C-terminus (red). The purple portion indicates the location of the consensus sequence for this family of proteins and most likely represents the location of the active site. The vertical helical bundle represents the transmembrane portion of the protein while the horizontal bundle represents the interface for IMPCT binding.